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Leg length discrepancy: a brief review

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Abstract

Leg length discrepancy (LLD) is a common orthopedic condition, characterized by a length difference between the two lower limbs, usually associated with alignment disorders. Minor LLD is recognized as a normal variation and has no significant clinical manifestations. However, a discrepancy greater than 1 cm can potentially cause altered biomechanics. These changes can lead to functional limitations and musculoskeletal disorders.

This review aims to, not only do a brief consolidation of the current information about the classification, etiology and complications of LLD and angular deformity, but also summarize the various clinical and imaging methods for assessing discrepancy and present the available treatment options, which have been suffering some changes in the last years. Therefore, this essay gathers papers published up to March 2018 obtained through PubMed database using the following search terms: “leg length discrepancy” and “leg lengthening”.

Effectively, more accurate methods of assessment were developed, as EOS, which is expected to improve the medical management and therapeutic approach. On the other hand, the introduction of computer assisted devices allowed a reformulation on the treatment techniques with a decreased complexity and iatrogenic complications. PRECISE came up as the most promising technique, however, further investigation is needed in order to adopt it over the convensional devices.

Keywords

Leg length discrepancy, Children, Epiphysiodesis, Leg lengthening, External fixation, PRECISE
Introduction

Leg length discrepancy (LLD) is characterized by a length difference between the two lower limbs, usually associated with alignment disorders.

LLD is a very common medical condition, with a reported prevalence of 70% in the general population\textsuperscript{1,2,3}. In a retrospective study, it was determined that at least 1/1000 people have a LLD greater than 2 cm\textsuperscript{4}.

LLD can be classified etiologically as: structural LLD, as a consequence of a shortening or a lengthening of bony structures, and functional LLD resulting from soft-tissue or joint abnormalities, as muscle tightness or joint contractures, in the lower extremity\textsuperscript{5}.

In children, LLDs are usually mixed\textsuperscript{6} however, in this review, only structural etiologies of LLD, also known as true LLD, will be discussed.

The structural LLD may be a consequence of a congenital condition or due to an acquired injury. Proximal focal femoral deficiency and Fibular hemimelia, are two of the most common congenital causes\textsuperscript{7}, whereas infections and trauma are between the most prevalent acquired causes.

Minor LLD is recognized as a normal variation and has no significant clinical manifestations, however, a discrepancy greater than 1 cm can, potentially, cause altered biomechanics\textsuperscript{6}. These changes can lead to functional limitations, as abnormal gait and balance problems, and/or musculoskeletal disorders, as scolioses, lower back pain and premature degenerative arthritis of the lower extremity\textsuperscript{8,9}.

Therefore, in children, the assessment of LLD with a full length standing radiograph is fundamental as well as prediction of the expected discrepancy in the mature skeleton through Multiplier method, in order to determine the adequate treatment plan\textsuperscript{10,11}.

The treatment options vary from, shoe inserts to distinct surgical techniques, as epiphysiodesis, leg shortening or lengthening, depending on the severity of the inequality and presence of associated deformities\textsuperscript{12}.

This review aims to consolidate the current information about the classification, etiology and complications of LLD and angular deformity, summarize the various clinical and imaging methods for assessing discrepancy and presenting the treatment options.

The etiology of structural LLD

Congenital causes

Congenital LLD is a group of rare and heterogeneous diseases, in which the proportion of LLD tends to remain constant during growth, allowing a prediction of the LLD in maturity\textsuperscript{7}. The most common congenital causes include Proximal focal femoral deficiency (PFFD) and Fibular hemimelia (FH)\textsuperscript{7}.

PFFD is defined by a decreased length or absence of the femoral head, associated to varying varus deformity degrees, proportional to the shortening severity\textsuperscript{6,7}. PFFD is clinically characterized by a short and bulky thigh, with a lower extremity flexed, abducted, and externally rotated\textsuperscript{13}. The limb length repercussions are very severe and usually require lengthening procedures\textsuperscript{14}. 
FH, the most prevalent long bone agenesis of the body, comprehends a longitudinal deficiency of the fibula, ranging from mild hypoplasia to a complete bone absence, associated with a shortening of the tibia. The clinical manifestations of this condition commonly include LLD, equinovalgus foot, tibial anterior bowing and knee valgus. The proportion of LLD in patients with complete absence of the fibula averages 19% of the total extremity length.

**Acquired causes**

Acquired causes include physical growth disturbance frequently from trauma or infection and other idiopathic causes, as Blount’s disease or Legg-Perthes disease.

- **Infection**

  The growth stimulus inherent to a metaphyseal osteomyelitis may lead to an overgrowth during the inflammatory process however, when the osteomyelitis expands to the physis, it can result in permanent cartilages’ damage. Approximately 10% of all cases of growth arrest are a consequence of osteomyelitis.

  Juvenile idiopathic arthritis (JIA) may affect the global growth of the physis through different forms. In the young children, with oligoarticular JIA, the unilateral neovascularization of the physis may complicate to an LLD, where the involved limb is longer. However, in early puberty, unilateral arthritis can cause a premature fusion of the physis, which leads to a shorter limb on the affected side.

  Meningococcemia, in children, may also affect the length and the alignment of the lower extremities, as a result of bone infarcts that damage the physis.

- **Trauma**

  Fractures involving the physis (Salter-Harris fractures), caused by disruptions in the cartilaginous physis of long bones, may alter the growth rate and result in progressive leg length discrepancies.

  An increase of the growth rate is a possible complication of an injury that crosses physis, due to a transphyseal vascular communication, this usually occurs just in the first 6-18 months after the fracture. Usually, the growth is insignificant but does necessitate future assessment until growth ceases.

  Despite being uncommon, a complete growth arrest can also occur due to formation of bony bridges and the outcome may differ depending on size, location and growth potential. Central physeal bridges can cause leg shortening while peripheral bridges may produce angular deformities. This physeal injuries rarely exceeds a discrepancy higher than 1.5 cm, however when is associated with avascular necrosis, the consequences on LLD could more severe.
- **Idiopathic causes**

  Blount disease, also known as tibia vara, is an asymmetrical development disorder that affects the posteromedial portion of the proximal tibial physis leading to a progressive LLD and a multiplanar deformity\(^{24}\).

  Blount disease has two clinical variants: early-onset or infantile, and late-onset or adolescent, based on whether the deformity development manifests before or after 10 years of age\(^{25}\). The pathogenesis of Blount disease is still unclear, however it is believed to be associated with the increased compressive forces on the physis of overweight children, causing a growth restriction\(^{24,26}\). Without treatment, the prognosis of the infantile form can be severe since there’s an earlier development of medial tibial epiphysiodisis\(^{25}\).

  Legg-Calvé-Perthes disease (LCPD) is an idiopathic osteonecrosis of femoral head, resulting in compromised bone formation and increased bone resorption\(^{27}\). The exact etiology for this insult is still unknown, however an early change in blood flow to femoral epiphysis appears to be a key factor in pathogenesis\(^{6}\). The physis is commonly affected due to the initial ischemic event or by its consequences, as epiphyseal osteonecrosis leads to collapse and deformity of the femoral head which, subsequently, compromises his cushioning and protective effects on the physis. As a result, the severity of LLD presented in LCPC depends on the age of onset, the extent of involvement and the presence of a growth arrest\(^{29}\).

**Complications**

Leg length discrepancy’s complications have been widely discussed in the medical community. Several studies about functional limitations in LLD have been carried out, however the lack of standard methodology causes divergent results in the literature, making it difficult to draw conclusions\(^{8}\).

The magnitude of discrepancy that contributes to musculoskeletal disorders is also a question of debate in the literature. However, it is generally recognized that a discrepancy greater than 1 cm is already enough to alter the normal biomechanics and cause functional limitations, as abnormal gait and posture disorders\(^{30}\). On the other hand, there are some musculoskeletal disorders that could be a consequence of LLD, as scoliosis, lower back pain (LBP), stress fractures and premature degeneration joint disease\(^{8}\).

**Standing posture**

Taillard et al.\(^{31}\), in an electromyographic study, reported a substantial increase of muscle activity in LLD between 1-2 cm, which would make it impossible to stand in a complete resting position.

The most usual compensation mechanisms of the longer leg are pronation of the foot\(^{32}\) and/or flexion of the knee and hip\(^{33}\). In addition, the shorter leg commonly compensates with a supination and/or plantar flexion of the foot\(^{34}\) and extension of the knee and hip\(^{33}\).
**Gait patterns**

However, if there is no compensation by the leg, pelvic obliquity may appear\(^3\), which can evolve to functional scolioses with convexity directed towards the shorter leg\(^4\).

Children combine multiple complex compensatory mechanisms in order to maintain a grossly symmetric gait pattern\(^5\). Some of the compensatory mechanisms include increasing pelvic obliquity, knee extension and/or toe walking on the short limb, vaulting, circumduction and hip and/or knee flexion (steppage gait) and/or ankle dorsiflexion on the longer limb\(^6\).

These different combinations of compensation strategies for LLD appear to be influenced by the location, the magnitude of the discrepancy and underlying pathology\(^7\). A LLD caused by femoral shortening results in increased work at the ankle while a tibial shortening may increase hip work on the short side and total work on the long side. Several studies\(^8\), reported that most children perform more mechanical work with the longer limb.

**Premature degenerative joint disease**

The association between early-onset osteoarthritis and LLD is still not clear.

Some authors have reported a higher prevalence and severity of osteoarthritis in the longer leg, both in knee and hip, which may be due to the asymmetrical weight bearing in this joints during gait and postural changes\(^9\)–\(^11\).

In addition, it has been described that varus alignment is associated with a higher risk of medial osteoarthritis, and valgus deformity increases the risk of lateral osteoarthritis\(^12\).

**Low back pain**

Leg-length discrepancy (LLD) may be associated with an increased risk of LBP although it remains controversial.

A commonly surmised mechanism that may cause low back syndromes is the pelvic obliquity present in most LLD\(^13\). Friberg\(^14\) reported that scoliosis, as a compensation mechanism of LLD, may predispose to LBP due to the wedging of intervertebral discs and axial rotation, inherent to scoliosis. The presence of LBP after LLD’s treatment has also been previously analyzed by different studies\(^15\)–\(^17\), and most of them revealed a pain relief after equalizing of the leg length.

While several studies show a positive association between LLD and LBP\(^13\)–\(^17\), others have not found such a relation\(^18\)–\(^20\).

**Stress fractures**

There have been reports of a correlation between LLD and stress fractures in the lower extremities\(^21\). It was reported a higher incidence of fractures on more severe LLD and on the longer leg, which is consistent with the higher mechanical work commonly done by the longer leg\(^22\).


Methods for assessing LLD

The use of appropriate physical examination and imaging techniques for measuring and assessment of three-dimensional deformities is fundamental both to the classification and treatment of children with LLD and related symptoms\textsuperscript{6,12,50}.

According to literature findings, the most widely used clinical method to determine LLD is tape measurements from anterior-superior iliac spine (ASIS) to medial malleolus, allowing a precision of 1 cm\textsuperscript{51}. However, there are potential sources of error that can contribute to a wrong length assessment associated with the presence of concomitant deformity, differences in girth and difficulty in identifying bony prominences\textsuperscript{50,52}.

The use of increasingly thick blocks under the short leg, in standing position, to level the pelvis has been shown to be a more precise clinical test than tape measurements\textsuperscript{53}. This “indirect” clinical method takes into account the height and posture of the foot and it also helps to determine the functional LLD, which tape measure methods ignore\textsuperscript{50}.

While the clinical evaluation is an easy, cheap and non-invasive method of assessing LLD, imaging techniques demonstrated to be a more precise method, playing an important role in the LLD and concomitant deformity diagnosis and treatment management\textsuperscript{54}.

Several distinct radiographic techniques have been used to assess LLD. Orthoroentgenogram and scanogram use three distinct exposures centered over the hip, knee and ankle joints, in an attempt to minimize measurement errors by magnification\textsuperscript{8,50,55}. However, they are susceptible to error from movement during the exam. Teleoroentgenogram is a conventional radiograph that, although also associated with magnification error risk, minimizes radiation exposure by capturing the entire lower limb at once\textsuperscript{8,50,55}. Between these three techniques, the scanogram is the most commonly used one due to its extreme accuracy and high reliability for measuring LLD\textsuperscript{56,57}.

However, LLD often presents with associated angular deformities which are not correctly assessed with these non-weight-bearing techniques, requiring a standing full-length radiograph, which has been shown as reliable as scanogram for measuring LLD\textsuperscript{56}. An anterior-posterior standing full-length radiograph, from hip to ankle, also known as the standing teleoroentgenogram, is considered the gold standard for deformity analysis, since it allows an accurate measurement of the overall limb alignment and a comprehensive evaluation of potential associated angular deformity\textsuperscript{10,56,57}. Besides its minimum probability of presenting magnification errors\textsuperscript{10,57}, these methods just assess two-dimensional lower extremity deformities, which are not the most frequent in children, the majority of them having a LLD associated with a three-dimensional deformity\textsuperscript{58,59}.

In these cases, accuracy may be improved by using a more recent assessing method, the EOS imaging system\textsuperscript{60}. EOS has the capacity to create three-dimensional models from biplanar radiographic images. This technology is also associated with a significantly lower radiation exposure when compared with standard radiographic techniques\textsuperscript{7,61-63}. However, further validation of diagnostic efficacy and cost-effectiveness is needed\textsuperscript{61}.

Ultrasonography (US) is a useful screening tool for children younger than 1 year when the epiphyses are entirely composed of cartilage\textsuperscript{50,64}. 

Measurements can also be made with digitalized computed tomography (CT) which displays the entire limb length and allows a rotational malalignment evaluation, while minimizing the measurement error and requiring a lower radiation exposure. MRI also gives information about the physis, however, it provides an even more accurate assessment of the location and extent of the Physal injury, predicting its effects on leg’s length and angular deformities as well as treatment options. Once the current LLD and the deformity have been evaluated, the determination of the expected discrepancy in the maturity is essential, in order to decide the appropriate management course.

There are several methods to predict the remaining growth in children, the most commonly used being the Moseley straight line graph method. The Moseley method is based on a growth percentile graphic, where through the child’s age and his limb length, the final discrepancy can be predicted. However, this method has shown to be less reliable in children under the age of ten years old and in the cases without linear pattern of growth.

Although as accurate as the Moseley method, the multiplier method appeared to be a simpler and quicker way to predict the remaining growth, as it only requires the child’s chronological age and sex. This method uses an arithmetic formula in which the current leg length is multiplied by a variable coefficient, that depends of chronological age and sex. Currently, there is a Multiplier application which improved the practicality of this method.

**Treatment**

Successful treatment depends on a rigorous clinical evaluation, with a precise discrepancy and associated deformities assessment and an accurate etiology identification.

The main treatment goal includes hip stability, equalization of the leg length and the accomplishment of a normal anatomic alignment. There are different approaches in order to achieve this, ranging from shoe inserts to distinct surgical techniques, as epiphysiodesis, leg shortening or lengthening.

In general, surgical treatment options are indicated for LLD greater than 2 cm and they depend on discrepancy’s magnitude and the children’s age: from 2 to 5 cm, a correction with a shoe lift, epiphysiodesis or leg shortening is suggested; from 5 to 20 cm, leg lengthening procedures are recommended and in discrepancies higher than 20 cm, a prosthetic fitting is advised. The children’s age is also an important factor to take into consideration since some treatment options can just be applied after the skeleton reaches maturity.

Shoe Lift is the most common treatment option recommended for symptomatic children, for which surgical treatment is rejected or not recommended. A lift smaller than 2 cm can be inserted into the shoe while larger corrections require building up the shoe’s sole. Shoe lift beyond 5 cm is not recommended due to the muscular difficulty resisting the inversion stress, on the subtler joint.

Permanent epiphysiodesis or temporary epiphysiodesis have long been the most accepted surgical procedure for uniplanar LLD between 2 and 6 cm in children with an adequate growth left and a predicted mature height above percentile. Temporary physical suppression presents more advantages due to his reversibility, low mobility and complication rate.
Percutaneous epiphysiodesis using transphyseal screws (PETS) is a minimally invasive procedure, and is therefore considered the treatment of choice.\textsuperscript{78,79} It consists of the insertion of two screws on the medial and lateral side of physics to promote temporary bone growth arrest.\textsuperscript{77} Implants are then removed when the leg length equalizes or the skeleton reaches maturity. A precise prediction of the remaining growth potential and the final LLD at skeletal maturity are crucial to determinate the optimal epiphysiodesis timing.\textsuperscript{72,77} However, due to its delayed effects, recent studies,\textsuperscript{77,80,81} recommend performing PET at least 6 months to 1 year earlier than the initial calculated time, in order to avoid under correction. This procedure could be associated with other complications including secondary angular deformities and failure of screw removal\textsuperscript{77,79}.

In children with skeletal maturity, shortening techniques can be considered.\textsuperscript{8} This procedure could be managed with an intramedular nail or through subtrochanteric and supracondylar osteotomies fixed with a blade-plate, this last technique being also indicated to LLD with associated deformities.\textsuperscript{64} Tibial shortening is associated to higher risk of complications, due to the compromised muscular function and neurovascular injuries, limiting the shortening to a maximum of 20-30 mm, unlike the femur that is able to reach about 50-60 mm.\textsuperscript{85}

PETS and shortening techniques could also be performed in LLD greater than 10 cm, as a supplementary procedure, in conjunction with leg lengthening, avoiding a probable second lengthening procedure.\textsuperscript{64}

Leg lengthening techniques are generally indicated for discrepancies greater than 5 cm. These techniques depend on a gradual osteogenesis distraction which requires an adequate cortical osteotomy technique (corticotomy) with the preservation of periostium and medullary blood flow as the main blood sources. After surgery, it is recommended a latency period between 5-10 days before starting the longitudinal distraction across the osteotomy sites, through external or internal fixation devices.\textsuperscript{83-85} The lengthening rate, according to the principle of callotasis, is classically 1mm/day, in order to optimize the osteoblastic activity and minimize the pain.\textsuperscript{84,86} The consolidation phase starts with the architectural remodeling of the regenerated bone and the unprotected weight-bearing is now possible.\textsuperscript{12} Radiographic consolidation of the regenerate bone is defined by the presence of at least 3 cortical columns on anterior-posterior and lateral radiographs.\textsuperscript{87} The osteotomy level depends on deformity’s location and type, the treatment strategy and soft-tissue status.\textsuperscript{88} However, some studies\textsuperscript{85,89} indicate that better consolidation occurs when osteotomy is performed on the distal third of the femur, near the metaphysis.

A recent study\textsuperscript{90} divided the leg lengthening complications in two categories according to whether they are related to the technical device or the process of distraction. The distraction related complications consist of premature or delayed consolidation, failed bone formation, nerve or vascular injury, muscle retraction and joint subluxation.

The gold standard of leg lengthening is the external fixation approaches\textsuperscript{90} which can be classified as circular or monolateral external fixators. For a long time, the lengthening procedures were based on the modular Ilizarov ring external fixator (EF). In order to minimize the complications and improve the complex deformities correction of the Ilizarov method, a computer-assisted hexapod external fixator was developed. Hexapod EF consists in 6 adjustable telescopic struts joined by 2 rings, which give the freedom to apply, either simultaneously or sequentially, lengthening, translation and rotation precise forces to correct multi-planar deformities and leg length discrepancy.\textsuperscript{12,58,85} Besides this, they have a risk of angular deformity development, which could be corrected by reprogramming during the correction, without modifying the basic EF construction.\textsuperscript{58,91}
Monolateral external fixator is a reliable and better tolerated external plate method suitable for all ages, for simple small-to-moderate leg lengthening, lesser than 25% or 6 cm\(^{85,89,92}\). Comparing to the ring external fixation techniques, this method is associated with lower infection rate and a faster recovery of knee motion; however it could be also associated with increased risk of angular deformities during the lengthening process\(^{85}\).

In the last years, with the purpose of minimizing the high complication rates related to the external fixators, like pin infections, reduced range of motion in the adjacent joints and muscle contractures\(^{80,93,94}\), several techniques with early removal of the frame have been developed.

External fixation over an intramedullary nail, referred as lengthening over a nail (LON), is one of the most reliable LLD treatment options\(^{89,95}\). LON consists of a simultaneous placing of the intern and extern devices at the time of the osteotomy and then, after the distraction phase, another surgery is required to remove the EF and lock the nail. This association reduces EF time, stabilizes the assembly during distraction and consolidation phases, accelerates the consolidation process and improves the control over callotasis\(^{85,89,95}\). Nevertheless, in order to prevent major complications, an extensive experience and solid knowledge is required\(^{85,96}\).

Further progress has been made through the development of a magnetic intramedullary expanding nail system, The PRECISE, which is currently the most promising technique of leg lengthening\(^{89}\). This recent technique uses a telescopic rod with a magnetic expansion control which is activated by a external electromagnetic remote control allowing a very precise and controlled lengthening rate\(^{85,96}\). PRECISE could be applied through two different approaches, the anterograde and the retrograde\(^{85,90}\). The anterograde approach is the usually recommended technique for skeletally mature children with rotational or angular deformities centered on the proximal half of femoral diaphysis. When this approach is contraindicated, the retrograde technique is suggested. This procedure also enables lengthening with the correction of periarticular knee deformities\(^{65,85,96}\). PRECISE telescopic nail could also be applied on the skeletally matured tibia with uniplanar leg length discrepancies. However, tibial intramedullary nail corrections are quite difficult as the proximal third of the tibia intramedullary canal is well wider than the nail and nail implanting on the distal half of the tibia is not recommended since it would pull out the distal osteotomy site during the lengthening\(^{65}\). When the consolidation process is taking longer than expected, PRECISE nail can stimulate the callus formations by providing a longitudinal compression-distraction\(^{90,97}\).

Nevertheless, intramedullary nail techniques reduce the external fixation complications, they are not exempted from their devices risks, which include non-unions of the bone, nerve injuries and nail fractures\(^{73,98}\).

PRECISE intramedullary nail provides a greater lengthening control and functional results, better consolidation indices, lower pain during the treatment process, faster recovery of rage and mobility, a lower number of surgeries required and better psychological tolerance, which counterbalance the high cost of the implant\(^{65,87,98}\).

**Conclusion**

Nowadays, there are higher expectations related to the medical approach and treatment outcome of LLD\(^{99}\). For this reason, a deep understanding of LLD and three-dimensional deformity, including the identification of etiology and, functional and musculoskeletal, consequences is crucial. Additionally, more
accurate methods of assessment, as EOS, are expected to become more available in the future\textsuperscript{99}, improving the medical management and therapeutic approach.

The last years have been distinguished by the huge evolution in the field of leg lengthening techniques with introduction of computer assisted devices, which permits a better lengthening control with a decreased incidence and severity of device complications\textsuperscript{47}. There was an upgrade on the gold standard external fixation devices with the introduction of circular fixators controlled by computer and monolaters fixators having hinges and spanning joints\textsuperscript{90}.

However, the most promising technique introduced was PRECISE, the first leg lengthening nail capable of compress and distract. This device is characterized by an excellent rate control, forward and reverse capability and his resistance to weight-bearing forces\textsuperscript{90}. However, further investigation is needed in order to adopt PRECISE over the conventional devices for leg lengthening and deformity correction\textsuperscript{88}. On the other hand, with the introduction of remote control implant technology, wide variety of new devices will be developed, in order to reduce the complexity and the iatrogenic complications.

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INSTRUCTIONS FOR AUTHORS

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General guidelines

The article (including tables, illustrations and bibliographic references) should comply with the general requirements of articles submitted to biomedical journals (“Uniform Requirements for Manuscripts Submitted to Biomedical Journals”) published by the International Committee of Medical Journal Editors (see latest update from April 2010, available at http://www.icmje.org).

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e) all the authors have read and approved the final version;

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d) all the authors participated in the design of the study, analysis and interpretation of data, writing up and critical revision;

e) all the authors have read and approved the final version;

f) no information has been omitted as regards financing or any conflicts of interest that may arise between the authors and companies or individuals with possible interests in the material covered in the article;

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3. The original should be sent as a printout on white paper, size A4 (210x297mm); margins of 25mm; double spaced; font Times New Roman, size 10 or 12; pages numbered in right hand corner, beginning with the cover page. Formatting resources such as headers or footnotes should not be used. If possible, the articles should be in Word format, though PDF, Text, or RTF are also acceptable.

4. A copy of the original text should also be sent on a diskette or CD, which should contain only files pertaining to the article.

Guidelines for each section of the material submitted

Each section should begin a new page, in the following order: cover page, abstract in Portuguese including keywords, abstract in English including keywords, text, acknowledgments, bibliography, tables (each complete table, with title and footnotes, on a separate sheet), graphs (each complete graph, with titles and footnotes on a separate sheet) and captions for the figures.

Cover page

The cover page should contain the following information:

a) Title of article, which should be concise and informative and avoid abbreviations;

b) Title in English;

c) Abbreviated title (to appear at the header of the page) of up to 100 characters, including spaces;

d) Name of each author (first name and last name should be given in full; all other names may appear as initials);

e) Authors’ (most important) titles;

f) Name, postal address, telephone, fax and e-mail of the author responsible for correspondence;

g) Name, postal address, telephone, fax and e-mail of the author responsible for previous contacts with the publication;

h) Affiliation;

i) Declaration of any conflicts of interest (write “nothing to declare” or clearly declare any economic or other interests that could lead to conflicts of interest);

j) Identification of finance source or equipment/materials supplier, where appropriate.

Abstract

The abstract should be submitted in two languages: Portuguese and English, and should be up to 250 words in length. All information appearing in the abstract must also appear in the article.

Below the abstract, three to ten keywords should be given that will aid the inclusion of the abstract in bibliographic databases. Keywords in English should preferably be included in the list of “Medical Subject Headings”, published by the U. S. National Library of Medicine, of the National Institute of Health, and available on http://www.nlm.nih.gov/mesh/meshhome.html.

The abstract should be structured as follows:

Abstract of original article:

Aim: why the study was launched and the initial hypotheses, if these existed; precise statement of main aim and most relevant secondary aims.

Material and Methods: design of the study; context or place; patients, or materials and methods of working and of obtaining results.

Results: main data, reliability intervals and statistical significance.
Conclusions: this should only include conclusions supported by data from the study and which are relevant to its aims; practical applications.

**Abstract of review:**

Aim: why the review was done; factors specially focused upon, such as etiopathogeny, prevention, diagnosis, treatment or prognosis.

Sources of data: research sources, giving details of databases and years researched; criteria for the selection of articles and methods of extracting and assessing information quality.

Summary of data: main results of research, whether quantitative or qualitative.

Conclusions: conclusions and clinical applications, with generalizations restricted to the domain of the review.

**Summary of clinical case**

Aim: reasons why the case deserves to be published, emphasising its uniqueness or new forms of diagnosis and treatment.

Description: basic information of case presented succinctly, emphasising the same uniqueness.

Comments: conclusions about the importance of the clinical case and prospects for practical application of innovative approaches.

**Text**

The text of original articles should contain the following sections, each with its respective subtitle:

a) **Introduction:** succinct, quoting only strictly pertinent references, to demonstrate the importance of the subject and justify the work; at the end of the introduction, the aims of the study should be clearly described.

b) **Material and Methods:** the population studied, sample and selection criteria; variables, clearly defined, and statistical analysis; standardized references to statistical methods and software used; procedures, products and equipment, described in enough detail to allow the study to be replicated. There should also be a declaration that all procedures have been approved by the ethics committee of the affiliated institution.

c) **Results:** these should be presented clearly and objectively and in logical order. The information contained in tables or figures should not be repeated in the text. The use of graphs is preferred over the use of tables when a large quantity of data is being used.

d) **Discussion:** results should be interpreted and compared with data already described in the literature, with emphasis given to new and important aspects of the study. The implications and limitations of findings should be discussed, and reference should be made to further research that needs to be carried out. Conclusions should be presented at the end of the discussion section, taking into consideration the initial aims of the study.

The text of reviews need not obey a rigid schema of sections.

The text of clinical cases should contain the following sections, each with its own respective subtitle:

a) **Introduction:** succinct presentation about what is known about the pathology in question and the present diagnostic and therapeutic approaches used.

b) **Description of case(s):** the case should be described in enough detail to enable the reader to understand the whole development and causes. When more than one case is described, the information should be presented in the form of a table.

c) **Discussion:** presenting correlations with other cases described and suggesting their importance for clinical practice.

**Acknowledgments**
These should be brief and objective, and involve only persons or institutions that have contributed significantly to the study, but which do not fulfill the criteria of authorship. Those included in the acknowledgments list should give written consent for their names to be divulged, since readers may presume that they endorse the conclusions of the study.

**Bibliographical references**

Bibliographical references should be numbered in the order in which they appear in the text, and identified by Arabic numerals given in brackets. If there are more than 6 authors, the first 6 names should be cited, followed by “et al”. Titles of journals should be abbreviated in accordance with the style used in the Index Medicus. An extensive list of periodicals, with their respective abbreviations, is available in the NLM publication “List of Serials Indexed for Online Users” at http://www.nlm.nih.gov/tsd/journals.

Bibliographic references should comply with the standard requirements for articles submitted to biomedical journals (“Uniform Requirements for Manuscripts Submitted to Biomedical Journals”), published by the International Committee of Medical Journal Editors (examples of bibliographic references are available on http://www.nlm.nih.gov/bsd/uniform_requirements.html). Some examples of bibliographic references are listed below:

1. **Standard article**

2. **Book**

3. **Chapter from book**

4. **Theses or dissertations**

5. **Work presented at a conference or similar (published)**

6. **Article in electronic journal**

7 **Internet site**

Articles accepted for publication but as yet unpublished may be cited provided that they are followed by the indication “in press”. Unpublished observations and personal communications may not be cited as references; if it is essential to include information of that nature in the article, this should be followed by the observation “unpublished observation” or “personal communication” in brackets within the body of the article.

**Tables**
Each table should be presented on a separate sheet, numbered according to order of appearance in the text and with a succinct explanatory title. All explanatory notes should be presented as footnotes and not in the title, identified with the following symbols in this order: *, †, ‡, §, ||, **, ††, ‡‡. Tables should not contain vertical or horizontal lines delimiting internal cells.

**Figures** (photographs, diagrams, graphs)

All figures should be numbered in the order in which they appear in the text. Explanatory notes should be presented as captions. Figures reproduced from other sources should indicate the source and be accompanied by a letter giving copyright permission. Photographs should not allow the patient to be identified or should be accompanied by a written letter of consent for publication.

Digitalised images should be attached in TIFF or JPEG formats, between 300 and 600 dpi, size between 15 cm and 20 cm and colours. The figures will be converted to black and white only for print edition. If the authors consider it essential that a particular image is presented in colours, they are asked to contact the editors.

Images in paper format should be endorsed on the back with their number, name of the first author and an arrow indicating the top.

**Captions of figures**

These should be presented on a separate page, and be duly numbered.

**Abbreviations, symbols and acronyms**

These should be avoided, particularly in the title and abstract. The complete term in its full form should precede the first use of an abbreviation, symbol or acronym.

**Units of measurement**

The International System of Units (SI) should be used, though other conventional units in common usage