Temporomandibular joint arthritis in juvenile idiopathic arthritis: the forgotten joint
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Purpose of review
This review explores the prevalence, clinical and radiographic signs, and treatment of temporomandibular joint arthritis in children with juvenile idiopathic arthritis.

Recent findings
Temporomandibular joint arthritis seems to be a more frequent manifestation in patients with juvenile idiopathic arthritis than previously believed, in part due to the paucity of clinical symptoms and poor sensitivity of conventional radiographs used for diagnosis. Antinuclear antibody positivity, early onset of disease, and presence of systemic or polyarticular disease are all risk factors for temporomandibular joint arthritis but may underpredict temporomandibular joint involvement in juvenile idiopathic arthritis. Magnetic resonance imaging enhanced with gadolinium is currently the gold standard in detection of temporomandibular joint arthritis, and treatment with intra-articular corticosteroids has been shown to be effective and safe, with minimal side effects.

Summary
Given the paucity of clinical symptoms in temporomandibular joint arthritis, detection of temporomandibular joint inflammation using contrast-enhanced magnetic resonance imaging is essential for instituting appropriate therapy in a timely fashion. The use of intra-articular corticosteroids holds promise for control of temporomandibular joint inflammation and prevention of associated morbidities.

Keywords
diagnosis, juvenile idiopathic arthritis, prevalence, temporomandibular joint arthritis, treatment

Abbreviations
CT computed tomography
JIA juvenile idiopathic arthritis
JRA juvenile rheumatoid arthritis
MRI magnetic resonance imaging
OPG orthopantomogram
TMJ temporomandibular joint
TNF tumor necrosis factor-\(\alpha\)

Introduction
Temporomandibular joint (TMJ) arthritis affects all subtypes of juvenile idiopathic arthritis (JIA). Resultant abnormalities include micrognathia in as many as 30% and malocclusion in as many as 69% of children with JIA [1,2]. Other complications include decreased mouth opening, chewing difficulties, and pain with jaw movement. Despite these morbidities, TMJ arthritis remains one of the most underdiagnosed and undertreated conditions in JIA. Lack of clinical symptoms and difficulty examining the TMJ often delay this diagnosis, leading to progression of inflammatory damage to the growing mandibular condyle. This review focuses on current concepts in early diagnosis of TMJ arthritis and the importance of treatment with intra-articular corticosteroids.

Incidence and prevalence
The reported prevalence of TMJ arthritis has varied widely, between 17 and 87%, based on subtype of JIA, methods used for diagnosis, and population studied [1]. In one of the largest studies evaluating TMJ involvement in children with JIA [1], 62% of 169 patients exhibited condylar resorption on orthopantomogram (OPG). The worst outcomes are reported in patients with systemic or polyarticular disease, young age at disease onset, or an extended disease course. Among this subgroup of patients, those with a positive antinuclear antibody titer have a higher prevalence of condylar resorption, and those with a positive HLA-B27 have a lower risk of TMJ involvement [2–4]. The incidence of TMJ arthritis is not as well studied, although two initial studies [5,6] report a range of 65–76% based on detection of joint effusion by magnetic resonance imaging (MRI), ultrasound, or both. Arabshahi et al. [6] reported one of the only studies evaluating the incidence of TMJ arthritis in JIA at disease onset using MRI and ultrasound.

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Diagnosis

Clinical symptoms are not reliable in detection of TMJ involvement in children with JIA, because neither pain nor swelling is present in the majority of cases. In a study of 97 children with JIA [4], only 12% complained of pain and 5% had swelling. Among those with pain, only half had evidence of TMJ arthritis on OPG. Other studies [7,8**,9**] have shown similar results, suggesting that clinical symptoms are neither sensitive nor specific in detection of TMJ arthritis. Ronchezel *et al.* [7] published one of the first reports to use computed tomography (CT) to study the prevalence of TMJ arthritis in juvenile rheumatoid arthritis (JRA), correlating lesion type to cephalometric alterations to demonstrate altered mandibular growth.

Findings on TMJ examination in children with JIA include decreased mouth opening, clicking or crepitation, tenderness to palpation, asymmetric opening, and absence of translation (forward movement of the jaw upon maximal opening). Studies evaluating maximal mouth opening in normal subjects versus those with periodontal or TMJ disease [10,11] have shown that failure to open 3.5–4.0 cm (interincisor distance) or more is indicative of a restraining effect on mandibular function warranting further investigation. Ingervall [11] established normal maximal incisal opening ranges at 7, 10, and 20 years of age. In a recent report on 23 children with JIA and TMJ arthritis confirmed on MRI [8**], all had maximal mouth opening below mean age-matched norms. Larger studies of patients with JIA [4,7] have confirmed this finding albeit in a lower percentage of children, mainly those with severe or prolonged TMJ arthritis. Similarly, clicking, crepitation, asymmetric opening, and absence of translation have been shown to be important predictors of TMJ arthritis with good specificity but low sensitivity [4]. Not all children with JIA and TMJ involvement have findings on clinical examination.

Imaging the TMJ is perhaps the most objective and sensitive means of detecting TMJ arthritis in children with JIA. OPG, CT scanning, MRI, and ultrasound have all been used with varying degrees of success to detect condylar resorption secondary to TMJ arthritis. MRI and ultrasound have the added advantage of detecting pannus and joint effusions and are therefore more sensitive in identifying early inflammatory changes preceding condylar resorption or signs of acute inflammation that may be overlying chronic bony erosions. Historically, OPG has been the most common method of TMJ evaluation due to its low cost and ease of administration. OPG detects alterations in condylar integrity, which are graded using Rohlin and Petersson’s [12] scoring system of 0–6, from least to most severe condylar damage. This technique requires the cooperation of the patient to hold still during the long radiation exposure time, however, and the condylar lesions identified do not differentiate between chronic joint damage versus active inflammatory arthritis, making treatment decisions difficult. Similarly, CT scanning has been used with success for better visualization of the mandibular condyles, with less radiation exposure (Fig. 1) [13], using the classification scheme of mild, moderate, or severe lesions based on degree of erosion [7,14,15]. CT is unreliable in detecting soft tissue changes indicative of acute TMJ arthritis, however.

Recently, MRI and ultrasound have gained increasing popularity in detection of TMJ arthritis. The use of MRI enhanced with gadolinium (gadopentetate dimeglumine) in other joints has shown that the degree of enhancement is strongly correlated with the degree of pathologic findings in the synovial membrane [16]. Animal models of TMJ arthritis have confirmed this finding [17] (a useful animal model description of histologic findings in TMJ arthritis), and several studies comparing enhanced MRI of the TMJ with radiographs [9**,18–20] have shown that synovial proliferation (pannus) and effusions precede the development of cartilage destruction and bony erosions detected on radiographs. Therefore, radiographic findings demonstrate an important delay in time compared with contrast-enhanced MRI, resulting in delayed treatment and further progression of TMJ arthritis. Currently, gadopentetate dimeglumine-enhanced MRI is the gold standard in evaluation of TMJ arthritis, and the severity of TMJ lesions using this technique can be graded using the scoring system by Cahill *et al.* [21].

Ultrasound is an attractive alternative to MRI given that it is safe, noninvasive, and can be easily performed at bedside, particularly for follow-up of disease activity or assessment of treatment response. Evaluation of
ultrasound in other joints has shown that it is quite sensitive in making the distinction between effusion and synovial hypertrophy, allowing identification of acute joint inflammation [22]. Several recent studies have evaluated the diagnostic quality of TMJ ultrasound, using MRI as a reference [23]. In 100 patients with TMJ disorders (200 TMJs), high-resolution ultrasound yielded a sensitivity of 81%, a specificity of 100%, and accuracy of 95% in detection of effusion [24]. Another group of investigators [5] evaluated the role of ultrasound in assessment of TMJ involvement in children with JIA and found that 65% had TMJ effusions at disease onset. Attempts to reproduce these results at our institution, however, were not successful, yielding an 11% incidence of TMJ effusion by ultrasound, which reflected only a 10% agreement between MRI and ultrasound [6]. Several factors could explain this discrepancy. The majority of studies evaluating the role of ultrasound in TMJ arthritis have come from the same two centers in Europe [23,24,25–27], which presumably have a great deal of experience in performing this highly operator-dependent procedure. Furthermore, there is currently no published standard technique for performance of TMJ ultrasound, and no classification system for TMJ sonography. Therefore, although ultrasound shows promise in detection of TMJ arthritis, further studies to improve its reproducibility are needed.

Pathogenesis
The condylar chondrogenic zone, located on the articular surface of the mandibular condyle, is an important growth center that is active from the prenatal period until 2 years after the peak of puberty [7]. Unlike other diarthrodial joints, the mandibular growth plate is located just beneath the fibrocartilage of the condylar head, making it particularly vulnerable to inflammatory damage. Arthritis-induced destruction of this fibrocartilage can lead to significant limitations in mandibular growth and development [28]. Analysis of inflammatory mediators in the arthritic TMJ have confirmed high levels of IgA, IgG, and β-glucuronidase contributing to the destruction of the articular cartilage via complement activation, immune complex deposition, and recruitment of neutrophilic leukocytes and the associated release of lysosomal enzymes [29].

Treatment
Due to the relatively delayed diagnosis of TMJ arthritis in most children with JIA, treatment has most often been directed toward correction of malocclusion, micrognathia, and dysfunction in severely affected patients. These treatments have included functional appliances such as distraction splints or bimaxillary activators or surgery such as vertical ramus elongation by distraction osteogenesis [30,31,32]. Although favorable cosmetic and functional outcomes have been obtained with surgery, it is associated with increased morbidity, including a 62% incidence of neurosensory dysfunction and 20% of patients requiring reoperation [33,34].
Until recently, little attention has been paid to early diagnosis and prevention of inflammatory damage to the growing jaw and TMJ. Nonsteroidal anti-inflammatory drugs and methotrexate have been tried with varying success in treating TMJ arthritis [35,36]. Ince et al. [36] published one of the only studies to evaluate the efficacy of methotrexate therapy in minimizing TMJ destruction and cranifacial dysmorphology in patients with JRA. Arthrocentesis, with or without injection of sodium hyaluronate, has been used in adults with TMJ osteoarthritis, but no data are available for its use in JIA [37,38].

In adults with rheumatoid arthritis, tumor necrosis factor (TNF)-α has been associated with increased chemokine gene expression by synovial fibroblasts in the TMJ, and several studies using TNF blockers alone or in combination with methotrexate [39–41] have shown favorable outcomes in TMJ pain and range of movement. Pain is infrequently a symptom in children with TMJ involvement, however, and attention should be focused on preventing mandibular growth disturbances that precede malocclusion and jaw dysfunction.

A recent promising therapeutic intervention for treatment of TMJ arthritis in JIA is intra-articular corticosteroid injection. Previously, intra-articular corticosteroids were proven beneficial in prevention of leg-length discrepancy in children with oligoarthritis of the knee [42]. By inference, their use in TMJ arthritis can potentially prevent mandibular growth alterations, which lead to micrognathia and jaw deviation. Until recently, there were very few studies of TMJ corticosteroid injection in JIA [43]. Horten [44] first reported this procedure in 1953, but many pediatric rheumatologists have been reluctant to recommend it based on reports of steroid-induced chondrolysis in adults with osteoarthritis of the TMJ [45,46]. By contrast, a recent study of 30 children with JIA who underwent CT-guided TMJ corticosteroid injection [8**] showed a very favorable response, with more than half the patients experiencing significant improvement in jaw opening and pain (Fig. 2). On follow-up MRI studies on 20 of these patients, 55% had resolution of effusion or synovial enhancement, and only two showed mild progression in condylar erosion (Fig. 3). Of note, 65% of these patients had already been maintained on methotrexate and 20% were also on TNF inhibitors, and the improvement in their TMJ arthritis was seen only after intra-articular corticosteroid injection [8**,47].

Long-term studies by two groups in Sweden [48,49] have shown a favorable prognosis, with condylar remineralization and remodeling, and symptomatic improvement in pain and jaw mobility 8–12 years following corticosteroid injection. Based on studies of intra-articular corticosteroids in other joints, triamcinolone hexacetonide appears superior to triamcinolone acetonide, with longer duration of action leading to an improved prolonged response rate [50,51]. Eberhard et al. [50] published a comparison of relapse time following intra-articular injection using triamcinolone hexacetonide versus triamcinolone acetonide. In our experience, 0.5 ml of triamcinolone hexacetonide (20 mg/ml) injected in the TMJ space under CT guidance was effective, with no side effects other than mild temporary facial swelling in two patients. Whether the efficacy of unguided corticosteroid injection is similar to that done under CT guidance remains to be studied. Ultrasound-guided injection of the TMJ is potentially the most cost-effective and precise means of steroid administration, but the technique remains to be standardized.
Conclusion
Despite the lack of clinical findings pertaining to the TMJ, prevalence of TMJ arthritis in children with JIA is quite high, making the TMJ the most, or one of the most, commonly involved joints. Children with JIA should ideally be screened for TMJ arthritis with contrast-enhanced MRI upon diagnosis, particularly if they have not yet completed their growth and have antinuclear antibody–positive polyarticular disease. Systemic therapy with disease-modifying antirheumatic drugs or TNF inhibitors is often insufficient in suppressing TMJ inflammation, and corticosteroid injection under CT or ultrasound guidance should be considered in all patients with evidence of effusion or pannus on TMJ MRI. An early detection scheme combined with an aggressive treatment approach using intra-articular corticosteroid injections may help prevent jaw growth abnormalities in children with JIA.

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References and recommended reading
Papers of particular interest, published within the annual period of review, have been highlighted as:
• of special interest
•• of outstanding interest
Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 569).
The only published study to use before-and-after MRI imaging as well as clinical examination to assess improvement in TMJ arthritis following CT-guided corticosteroid injection of the TMJ in children with JIA.
25 Of the largest studies to compare the sensitivity, specificity, accuracy, and positive and negative predictive values for high-resolution ultrasonography in diagnosing degenerative changes, effusion, and disk displacement using MRI as a reference.
An analysis of IgA, IgG, and β-glucuronidase levels in TMJ lavage samples of patients with TMJ pain and control subjects, looking for correlations between biochemical markers and joint pathology.
A long-term study of 72 children with JIA and TMJ involvement evaluating pain, function and facial profile, following nonsurgical orthopedic therapy with a bimaxillary activator.


