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MODERN APPROACHES TO EARLY DETECTION AND IMPROVEMENT OF DIAGNOSTIC METHODS FOR TEETHING SYNDROME IN CHILDREN

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RELEVANCE: While the eruption of primary teeth is a natural stage in every child's life, its symptoms are often confused with those of other, more serious childhood illnesses. This phenomenon, known as "diagnostic overshadowing," can delay the timely diagnosis and treatment of dangerous pathologies such as pneumonia, meningitis, or sepsis. The subjectivity of existing diagnostic methods and the lack of clear criteria exacerbate this problem. Therefore, improving the methods for early detection and differential diagnosis of teething syndrome using objective, scientifically-based approaches is a relevant and urgent task in pediatrics and pediatric dentistry.
Keywords: teething syndrome, primary tooth eruption, pediatric dentistry, diagnostic overshadowing, salivary diagnostics, infrared thermography, biomarkers, cortisol, cytokines.

СОВРЕМЕННЫЕ ПОДХОДЫ К РАННЕМУ ВЫЯВЛЕНИЮ И СОВЕРШЕНСТВОВАНИЮ МЕТОДОВ ДИАГНОСТИКИ СИНДРОМА ПРОРЕЗЫВАНИЯ ЗУБОВ У ДЕТЕЙ

АКТУАЛЬНОСТЬ: Прорезывание молочных зубов является естественным этапом в жизни каждого ребенка, однако его симптомы часто путают с проявлениями других, более серьезных детских заболеваний. Это явление, известное как "диагностическая маскировка", может привести к задержке своевременной диагностики и лечения опасных патологий, таких как пневмония, менингит или сепсис. Субъективность существующих методов диагностики и отсутствие четких критериев усугубляют эту проблему. В связи с этим, совершенствование методов раннего выявления и дифференциальной диагностики синдрома прорезывания зубов с использованием объективных, научно обоснованных подходов является актуальной задачей для педиатрии и детской стоматологии.
Ключевые слова: синдром прорезывания зубов, прорезывание молочных зубов, детская стоматология, диагностическая маскировка, саливарная диагностика, инфракрасная термография, биомаркеры, кортизол, цитокины.

BOLALARDA TISHLAR YORIB CHIQISH SINDROMINI ERTA ANIQLASH VA DIAGNOSTIKA USULLARINI TAKOMILLASHTIRISHDA ZAMONAVIY YO'NDASHUVLAR

Dolzarbligi: Sut tishlarining yorib chiqishi har bir bola hayotidagi tabiiy bosqich bo'lsa-da, uning belgilari ko'pincha boshqa jiddiy bolalik kasalliklari bilan adashtiriladi. Bu holat "diagnostik niqoblanish" deb atalib, pnevmoniya, meningit yoki sepsis kabi xavfli patologiyalarga o'z vaqtida tashxis qo'yish va davolashni kechiktirishi mumkin. Mavjud diagnostika usullarining sub'ektivligi va aniq mezonlar yo'qligi ushbu muammoni yanada kuchaytiradi. Shu sababli, tish yorib chiqish sindromini obyektiv, ilmiy asoslangan usullar

yordamida erta aniqlash va boshqa kasalliklardan farqlashni takomillashtirish pediatriya va bolalar stomologiyasi sohasidagi dolzarb vazifa hisoblanadi.

Kalit so'zlar: tish yorib chiqish sindromi, sut tishlarining yorib chiqishi, bolalar stomologiyasi, diagnostik niqoblanish, so'lak diagnostikasi, infraqizil termografiya, biomarkerlar, kortizol, sitokinlar.

ABSTRACT: Primary tooth eruption, or teething, is a universal developmental milestone that presents a persistent diagnostic challenge in pediatric healthcare. Historically implicated in significant infant morbidity, teething remains an ill-defined clinical entity, with diagnoses often relying on subjective parental reports that conflate physiological eruption discomfort with coincidental childhood illnesses. This practice of "diagnostic overshadowing" poses a substantial risk of delaying the identification and treatment of serious underlying pathologies. This review critically examines the limitations of the current subjective diagnostic paradigm and proposes a shift towards an objective, multi-modal framework for the early and accurate assessment of teething syndrome. A comprehensive literature review synthesizes the evidence base for teething symptomatology, delineating the consensus on localized inflammatory signs from the controversy surrounding systemic manifestations like fever and diarrhea. The core of this article explores the application of emerging, non-invasive technologies capable of quantifying the underlying biological processes of tooth eruption. These include infrared thermography for measuring localized gingival inflammation, salivary diagnostics for profiling inflammatory cytokines (e.g., IL-1β, TNF-α) and stress biomarkers (e.g., cortisol), and advanced imaging for the differential diagnosis of eruption abnormalities. We propose an integrated diagnostic model that combines these objective measures into a composite score, potentially enhanced by artificial intelligence for pattern recognition. This data-driven approach aims to redefine teething diagnosis, enabling clinicians to differentiate true eruption-related discomfort from other pediatric conditions, stratify symptom severity, and guide personalized, evidence-based management. The implementation of such a framework promises to enhance diagnostic accuracy, improve patient safety, and provide clarity to one of the most common and confounding concerns in early childhood.

Introduction

The clinical enigma of teething: A historical and modern perspective - The eruption of primary teeth is a fundamental physiological process, yet its clinical interpretation has been fraught with controversy and misconception for centuries. Historically, teething was erroneously considered a major cause of infant mortality, with a vast array of severe illnesses, from convulsions to diarrhea, attributed to this natural developmental stage. In the 19th century, it was believed to be so deadly that aggressive and often harmful interventions, such as lancing the gums or applying cautery, were common practice. While modern medicine has long since debunked these dangerous beliefs, identifying conditions like cholera, meningitis, and septicemia as the true culprits , the legacy of teething as a source of significant systemic illness persists.

Today, teething syndrome remains an "ill-defined, non-evidence-based, inappropriate diagnosis" proffered by both laypeople and some healthcare professionals. A significant chasm exists between the beliefs of caregivers and the consensus of many pediatric clinicians. Surveys consistently reveal that parents and even paramedical staff attribute a wide range of systemic symptoms—including high fever, diarrhea, sleep disturbances, and infections—to the teething process. In contrast, a more conservative clinical viewpoint, supported by prospective research, holds that teething produces only mild, localized discomfort. This fundamental conflict between a deeply ingrained cultural narrative and modern pathophysiological understanding establishes

the central challenge that necessitates a paradigm shift in diagnosis. The persistence of these beliefs highlights that merely presenting evidence against systemic symptoms is insufficient. A new diagnostic approach, grounded in objective measurement, is required to bridge this gap and provide definitive clinical guidance.

Pathophysiology of primary tooth eruption: An inflammatory cascade - At its core, teething syndrome (Синдром прорезывания зубов) is the clinical manifestation of a sterile, localized inflammatory process that accompanies the physiological movement of a tooth through the alveolar bone and its emergence through the gingival epithelium. This process is not passive but is an active, biochemically mediated event. The dental follicle, a sac of connective tissue surrounding the developing tooth, is the primary orchestrator of this cascade.

The eruption pathway is created through a finely tuned balance of bone resorption and formation. As the tooth migrates occlusally, it exerts mechanical pressure on the overlying tissues. This pressure, combined with signals from the dental follicle, triggers a cascade of molecular events. The follicle becomes a source of numerous signaling molecules, including eicosanoids, cytokines (such as Interleukin-1 or IL-1), and growth factors, which recruit mononuclear cells (monocytes) to the area. These monocytes fuse to form osteoclasts, the cells responsible for resorbing the alveolar bone to clear a path for the erupting tooth. Simultaneously, the breakdown of the connective tissue and epithelium overlying the tooth crown is facilitated by the local release of enzymes, including collagenases and matrix metalloproteinases. This controlled tissue destruction, essential for eruption, is inherently inflammatory. It involves the local release of potent inflammatory mediators such as prostaglandins and bradykinins, which sensitize afferent nerve endings, contributing to pain and tenderness. This molecular cascade directly explains the universally accepted clinical signs of teething: localized gingival redness (erythema), swelling (edema), and pain, providing a clear, measurable set of biological targets for the development of objective diagnostic methods.

The diagnostic imperative: Differentiating teething from coincidental pediatric illness - The most critical challenge in managing a symptomatic infant during the teething period is the high risk of "diagnostic overshadowing." This occurs when the signs and symptoms of a distinct underlying illness are mistakenly attributed to the benign process of tooth eruption. The typical timeframe for primary dentition eruption, spanning from approximately 6 to 30 months of age, is a period of profound immunological vulnerability for the infant. This window coincides with two pivotal developmental events. First is the waning of passive immunity conferred by maternal antibodies, which typically begins around six months of age, leaving the infant's own immune system to contend with new pathogens. Second, this is the age when infants enter the oral sensory phase of development, developing the motor skills to crawl, grasp objects, and explore their environment by mouth. This behavior dramatically increases their exposure to a wide variety of viruses and bacteria.

This temporal overlap creates a perfect storm for diagnostic confusion. The onset of common childhood illnesses—such as viral upper respiratory infections, otitis media, urinary tract infections (UTIs), and gastroenteritis—frequently coincides with the emergence of a new tooth. Anxious parents, primed by cultural narratives, are likely to attribute the associated symptoms of fever, irritability, diarrhea, or rhinorrhea to teething. The clinical risk of this misattribution is grave. Attributing a high fever to teething can lead to a critical delay in the diagnosis and treatment of potentially life-threatening conditions such as meningitis, sepsis, or pneumonia. Therefore, the development of a diagnostic methodology that can reliably distinguish the localized, mild inflammatory state of teething from a systemic infectious process is not merely an academic exercise; it is a clinical and public health imperative.

Objectives: towards an objective, biomarker-driven diagnostic framework - Given the profound limitations and inherent risks of the current subjective approach, this article aims to chart a course toward a new diagnostic paradigm for teething syndrome. The primary objective is to critically review the existing evidence base and propose a novel, multi-modal framework for the objective assessment of this common pediatric condition. This framework will be built upon the integration of non-invasive technologies capable of directly measuring and quantifying the core biological components of the teething process: the localized gingival inflammation and the systemic physiological distress it may cause. The ultimate goal is to facilitate a fundamental shift in clinical practice—from a process reliant on subjective interpretation of ambiguous behaviors to one grounded in objective, evidence-based measurement. By providing clinicians with tools to quantify the biological reality of teething, this framework seeks to empower them to make more accurate differential diagnoses, reduce the risk of diagnostic overshadowing, provide more effective parental counseling, and ultimately improve the safety and quality of care for infants during a vulnerable period of development.

LITERATURE REVIEW

The evidence base for teething symptomatology

Localized manifestations: A clinical consensus - Despite the broader controversy, there is a strong and consistent clinical consensus regarding a core set of localized signs and symptoms directly attributable to the physiological process of tooth eruption. These manifestations are biologically plausible, stemming directly from the inflammatory cascade occurring within the gingival tissues as the tooth crown emerges. The most frequently and reliably reported local signs include:

Gingival Inflammation: Swollen (edematous), tender, and erythematous (red) gums at the site of the erupting tooth are hallmark signs. This is a direct visual manifestation of the increased vascularity and release of inflammatory mediators in the tissue overlying the tooth.

Hypersalivation (Drooling): A significant increase in drooling is a classic sign associated with teething. While the exact mechanism is not fully elucidated, it is thought to be a reflex response to the gingival irritation and inflammation. The excessive saliva can sometimes lead to a secondary circumoral rash on the chin and cheeks due to skin irritation.

Gnawing and Biting Behavior: Infants experiencing teething discomfort exhibit a strong desire to chew, bite, or rub objects on their gums. This behavior is believed to provide counter-pressure to the erupting tooth, which can temporarily alleviate the sensation of pain or pressure within the periodontal membrane.

These localized symptoms are consistently validated across numerous observational studies and are accepted by pediatric and dental professionals as the true clinical signature of the teething process. Their presence provides the initial clinical suspicion for a diagnosis of teething syndrome.

Systemic manifestations: Deconstructing the fever and diarrhea controversy - The central controversy in teething diagnosis lies in the attribution of systemic symptoms. While parental and caregiver reports frequently associate teething with a broad spectrum of systemic disturbances, rigorous scientific investigation has largely refuted these claims, particularly for severe symptoms. Cross-sectional studies and surveys consistently show that a high percentage of parents believe teething causes fever, diarrhea, sleep disturbances, irritability, and even runny noses.

However, prospective, controlled studies provide a more nuanced picture. The landmark study by Macknin et al. (2000), which involved daily monitoring of infants, established a statistically significant temporal association between tooth eruption and a cluster of mild symptoms. The

researchers defined an eight-day "teething window" (four days before eruption, the day of eruption, and three days after) during which certain symptoms were more prevalent. These included increased biting, drooling, gum-rubbing, irritability, wakefulness, ear-rubbing, facial rash, decreased appetite for solid foods, and a mild temperature elevation.

Crucially, this study and others have demonstrated that while a slight rise in body temperature can occur, teething does not cause a clinical fever, typically defined as a temperature of 38°C (100.4°F) or higher. Symptoms such as high fever (over 102°F or 38.9°C), congestion, cough, diarrhea, vomiting, and rashes beyond the face were found to have no significant statistical association with tooth emergence. This evidence strongly suggests that when an infant presents with significant systemic illness, another etiology must be sought, as coincidence does not imply causation. The diagnostic challenge is thus rooted in a failure to distinguish between two phenomena: a predictable, localized "Physiological Teething Discomfort" and a culturally-defined "Teething Illness" narrative that incorrectly bundles in coincidental systemic symptoms.

Global prevalence and epidemiological patterns: A meta-analytical perspective - To understand the global scale of teething-related concerns, recent systematic reviews and meta-analyses provide high-level, synthesized evidence. A comprehensive meta-analysis published in 2024, which searched major databases through January 2024, estimated the pooled global prevalence of teething problems in infants and children aged 0-36 months to be a striking 80.0% (95% CI: 67.8–89.9). This figure underscores that teething-associated symptoms are an overwhelmingly common experience for families worldwide, solidifying its status as a major concern in pediatric primary care.

The meta-analysis also provided robust data on the prevalence of specific symptoms, helping to rank their frequency on a global scale. The most common local symptom identified was increased biting, with a prevalence of 65.9% (95% CI: 37.5–89.3). The most common general symptom was irritability, reported in 60.7% of cases (95% CI: 50.6–70.3). These findings align with the consensus on core symptoms while also quantifying their widespread occurrence. The analysis also noted significant variability in the prevalence of teething problems based on geographic location, which may be influenced by cultural reporting differences as well as a concentration of research in certain regions, particularly Latin America. This highlights the need for more geographically diverse research to obtain a truly global understanding of the teething experience.

Diagnostic overshadowing: The clinical risks of misattribution - The misattribution of systemic illness to teething is not a benign diagnostic error; it carries significant clinical risks. The primary danger is the delay in seeking appropriate medical care for what may be a serious underlying condition. Clinical guidelines and expert opinions strongly caution that attributing fever to teething can mask the signs of infections that require timely intervention, such as otitis media, urinary tract infections, pneumonia, and, most critically, life-threatening conditions like meningitis or sepsis. By accepting teething as the cause of a fever, caregivers may delay consulting a physician, allowing a treatable infection to progress.

Beyond the risk of delayed diagnosis, the diagnostic uncertainty surrounding teething creates significant parental anxiety and can lead to the inappropriate use of remedies that are ineffective at best and dangerous at worst. In an effort to alleviate their child's perceived suffering, parents may turn to over-the-counter products that carry warnings from regulatory bodies like the U.S. Food and Drug Administration (FDA). These include:

Topical Anesthetics: Products containing benzocaine (e.g., Baby Orajel, Anbesol) are strongly discouraged for children under two years of age due to the risk of methemoglobinemia, a rare but

serious and potentially fatal blood disorder that reduces the amount of oxygen carried in the bloodstream.

Homeopathic Remedies: Homeopathic teething tablets and gels have been found to contain inconsistent and potentially toxic levels of belladonna ("deadly nightshade"), which can cause seizures and breathing difficulties.

Amber Teething Necklaces: These are widely marketed but pose significant choking and strangulation hazards with no scientific evidence of efficacy.

Therefore, establishing an objective diagnostic framework is crucial not only for accurate medical diagnosis but also for promoting safe management practices and providing parents with the evidence-based reassurance and guidance they need.

Table 1: Summary of evidence on teething-associated symptoms. This table contrasts the global prevalence and high rates of caregiver attribution for various symptoms with the findings from rigorous prospective studies, highlighting the discrepancy that fuels diagnostic confusion.

Symptom	Global prevalence (meta-analysis)	Parental/ caregiver attribution (%)	Statistical association in prospective studies	Conclusion on causality
Irritability / fussiness	60.7%	70-80%	Statistically Significant Association	Likely causal, mild to moderate severity
Increased biting / gum-rubbing	65.9%	>85%	Statistically Significant Association	Direct causal link (local pressure relief)
Drooling (Hypersalivation)	Not specified as primary outcome	70-92%	Statistically Significant Association	Direct causal link (local inflammatory reflex)
Mild temperature elevation (<38°C)	Not specified as primary outcome	N/A (often conflated with fever)	Statistically Significant Association	Causal link to low-grade temperature rise
High fever (>38°C / 100.4°F)	49.7% (as "fever")	50-80%	NO Significant Association (for temp >102°F)	NOT Causal; indicates coincidental illness
Diarrhea / loose stools	Not specified as primary outcome	65-77%	NO Significant Association	NOT Causal; indicates coincidental illness
Sleep disturbance / wakefulness	Not specified as primary outcome	63-82%	Statistically Significant Association (for wakefulness)	Likely causal, but sleep disturbance is non-specific
Runny nose/ cough	32.8% (as "runny nose")	Commonly attributed	NO Significant Association	NOT Causal; indicates coincidental illness

MATERIAL AND METHODS

Limitations of subjective assessment and clinical observation - The current de facto standard for diagnosing teething syndrome is fundamentally flawed due to its reliance on subjective and non-specific indicators. The diagnostic process typically begins with a parental report of symptoms such as irritability, crying, or sleep disturbance. This information is inherently subjective, susceptible to recall bias, and heavily influenced by pre-existing cultural beliefs and parental anxiety. A parent who believes teething causes fever is more likely to report fever as a primary symptom. Furthermore, these reported behaviors are non-specific; irritability and sleep disruption are common manifestations of nearly every pediatric illness, as well as normal developmental fluctuations.

Clinical observation by a healthcare provider offers only marginally more objectivity. A clinician can visually confirm signs of gingival inflammation, such as localized redness or swelling. However, the presence of these signs does not reliably correlate with the degree of discomfort experienced by a non-verbal infant, nor can it rule out a concurrent illness. The most rigorous prospective studies have concluded that no single symptom or cluster of symptoms can reliably predict the imminent emergence of a tooth. This lack of a definitive clinical presentation means that the current diagnostic approach is one of exclusion and educated guesswork, leaving both clinicians and parents without a confident diagnosis and perpetuating the cycle of misattribution and uncertainty.

Advanced imaging for eruption assessment: Digital radiography and CBCT - Modern pediatric dentistry has been revolutionized by advanced imaging technologies that provide unprecedented insight into dental and craniofacial structures. Digital radiography offers the significant advantage of drastically reduced radiation exposure compared to traditional film X-rays—a critical consideration in pediatric patients—while providing instant, high-resolution images. For even greater detail, three-dimensional imaging techniques like Cone-Beam Computed Tomography (CBCT) can render precise anatomical views of developing teeth, their eruption pathways, and the surrounding bone.

However, it is crucial to understand the specific role of these powerful tools. Their primary clinical utility lies in the diagnosis of abnormalities of the eruption process, not the transient inflammatory syndrome of normal teething. CBCT and digital radiography are indispensable for identifying conditions such as Delayed Tooth Eruption (DTE), impacted teeth (e.g., maxillary canines), supernumerary teeth, eruption sequence anomalies, or pathologies associated with the dental follicle. They allow clinicians to assess developmental age versus chronological age and to formulate complex treatment plans for orthodontic or surgical intervention. While essential for the differential diagnosis when a tooth fails to erupt on schedule, these imaging modalities are not indicated for, nor are they capable of, diagnosing or quantifying the pain and inflammation associated with a normally erupting tooth. Their use is reserved for investigating deviations from the normal eruption pattern.

Infrared thermography: A non-invasive modality for quantifying gingival inflammation - Infrared Thermography (IRT) is emerging as a highly promising diagnostic modality for the objective assessment of teething, offering a non-invasive, non-contact, and non-ionizing method to visualize and quantify inflammation. The underlying principle of IRT is based on fundamental physiology: all objects with a temperature above absolute zero emit infrared radiation. The intensity of this radiation is proportional to the object's surface temperature. In a clinical context, local inflammation triggers vasodilation, leading to increased localized blood flow (hyperemia) to the affected tissue. This increased perfusion results in a measurable elevation of the local skin or mucosal surface temperature, which can be captured by a thermal camera.

The applicability of IRT in dentistry has been demonstrated in various fields, particularly in periodontics, where studies have successfully used it to detect temperature differences between healthy and inflamed gingiva. This provides a strong proof-of-concept for its use in teething. A key finding that enhances its potential in pediatrics is that IRT may exhibit greater precision and better diagnostic outcomes in children compared to adults. Studies have shown that children have reduced physiological variability in their baseline skin temperature patterns, which could confer increased accuracy when using IRT as a diagnostic tool to detect pathological changes. This suggests that IRT could be used to create a detailed thermal "map" of an infant's oral cavity, allowing for the precise localization and quantification of the inflammatory "hot spot" corresponding to an erupting tooth, thereby providing direct, objective evidence of the physiological process.

Salivary diagnostics: A window into the molecular milieu of teething - Saliva is an ideal biofluid for pediatric diagnostics, offering a paradigm shift away from invasive and stressful procedures like blood draws. Its collection is non-invasive, painless, and can be performed by caregivers in a home setting, which is particularly advantageous for monitoring non-verbal infants. Saliva acts as a "diagnostic mirror" of the body's physiological state, containing a rich and complex mixture of biomolecules, including proteins, enzymes, hormones, antibodies, and genetic material (DNA and RNA) that can serve as biomarkers for local and systemic conditions.

The composition of saliva reflects the health of the oral cavity and can provide insights into inflammatory processes, immune responses, and stress levels. Because the oral cavity is the site of tooth eruption, saliva serves as a direct collection matrix for the molecules involved in this process. Molecules released into the gingival crevicular fluid (GCF)—the fluid that fills the space between the tooth and the gum—readily mix with whole saliva, making them detectable in a simple saliva sample. The ongoing development of highly sensitive analytical techniques and the potential for creating point-of-care testing (POCT) devices further enhance the clinical utility of salivary diagnostics. This positions saliva as a cornerstone of a new, objective approach to diagnosing and monitoring teething syndrome by providing a direct window into its underlying molecular and physiological events.

RESULTS AND DISCUSSION

A new paradigm for teething syndrome diagnosis - The limitations of subjective assessment necessitate a paradigm shift towards diagnostic methods that measure the underlying biological processes of teething rather than their ambiguous behavioral consequences. This represents a move from inferring causation from correlation to directly quantifying the physiological event. By integrating advanced, non-invasive technologies, it becomes possible to confirm the presence and intensity of the teething process independently of the infant's behavior, allowing for a far more precise differential diagnosis. If objective markers of teething are low or absent while an infant is highly distressed, the clinician has compelling, data-driven evidence to intensify the search for an alternative pathology.

Thermographic signatures of gingival eruption sites - The practical application of Infrared Thermography (IRT) offers a direct, visual method for quantifying the primary local sign of teething: inflammation. Clinical studies in periodontology have established that a temperature differential exceeding 0.5°C between adjacent tissue sites is indicative of a pathogenic or inflammatory state. This principle can be directly applied to teething. Using a high-resolution thermal camera, a clinician could capture a thermogram of the infant's maxillary and mandibular arches. In an infant actively teething, this thermographic map would be expected to reveal a distinct, localized area of elevated temperature corresponding precisely to the gingiva overlying

the erupting tooth, while the surrounding tissues remain at a normal, cooler baseline temperature.

To enhance the objectivity and reproducibility of this method, modern image analysis techniques, including artificial intelligence (AI) and machine learning algorithms, can be employed. AI models can be trained to automatically segment the thermographic image, identify the gingival regions, and detect statistically significant thermal asymmetries or "hot spots" that correspond to eruption sites. This automated analysis would provide a quantitative output—such as the peak temperature, the area of inflammation, and the temperature gradient—creating an objective and standardized measure of local inflammation that is independent of subjective clinical judgment.

Salivary cytokine profiles as objective correlates of inflammation - While thermography identifies the location of inflammation, salivary diagnostics can quantify its biochemical intensity. The pathophysiology of tooth eruption is characterized by the local release of a host of inflammatory mediators, providing a distinct molecular signature. Research has shown that the gingival crevicular fluid (GCF) surrounding erupting primary teeth contains elevated levels of pro-inflammatory cytokines, which are key signaling proteins of the immune system.

Specifically, studies have demonstrated increased concentrations of Interleukin-1 beta (IL-1β), Tumor Necrosis Factor-alpha (TNF-α), and Interleukin-8 (IL-8) in the GCF during teething episodes. Importantly, the levels of these cytokines were found to correlate with some of the systemic disturbances accompanying teething, such as fever (IL-1β and TNF-α) and sleep disturbances (IL-1β and TNF-α). Since saliva acts as a natural collection medium for GCF and other oral fluids, these biomarkers are detectable in whole saliva samples. Therefore, analyzing an infant's saliva for a panel of these cytokines can provide a quantitative "inflammatory signature" of teething. Elevated levels of IL-1β, TNF-α, and IL-8 would provide strong biochemical evidence of an active inflammatory process consistent with tooth eruption. Other potential markers, such as the anti-inflammatory cytokine IL-10, chemokines like Eotaxin, and growth factors like Macrophage Colony-Stimulating Factor 1 (CSF1), could also be included in a comprehensive panel to provide a more nuanced picture of the immune response.

Salivary cortisol as a validated biomarker for infant distress - A major deficiency of the current diagnostic approach is the inability to objectively measure an infant's discomfort. Terms like "irritability," "crankiness," and "fussiness" are subjective, imprecise, and vary widely in interpretation. Salivary cortisol analysis offers a validated, non-invasive method to quantify an infant's physiological stress response. Cortisol is the primary glucocorticoid hormone released by the hypothalamic-pituitary-adrenal (HPA) axis in response to physical or psychological stressors, including pain and discomfort. Its concentration in saliva accurately reflects the level of biologically active cortisol in the bloodstream.

Numerous studies in pediatric populations have validated the use of salivary cortisol as a reliable biomarker for stress. Elevated levels have been documented in children experiencing dental anxiety, pain from dental caries, or undergoing stressful procedures. By applying this methodology to teething, it becomes possible to obtain an objective measure of the distress an infant is experiencing. A saliva sample taken during a period of intense fussiness attributed to teething could be analyzed for cortisol levels. A significantly elevated level would provide physiological evidence of distress, while a normal level might suggest the behavior is not driven by a strong painful stimulus. This approach allows for a more nuanced assessment, answering not just "Is the baby teething?" but also "How much distress is the teething process causing?" This objective data can then guide management decisions, helping to differentiate infants who require only non-pharmacological comfort from those who may benefit from analgesics.

Combining thermography and salivary biomarkers for a composite diagnostic score - While each objective modality offers valuable information, a truly robust and reliable diagnosis of teething

syndrome will likely emerge from their integration. No single biomarker is likely to be perfectly sensitive and specific. Therefore, a multi-modal diagnostic model that combines data from several streams is proposed as the new gold standard. This integrated approach would create a composite picture of the infant's condition, providing a high degree of diagnostic confidence. The components of this model would include: 1) Standard Clinical Assessment: A baseline evaluation to note the presence of classic local signs (e.g., visible gingival swelling, drooling) and to rule out obvious alternative causes of distress. 2) Thermographic analysis: Non-invasive IRT imaging to confirm and localize a site of active gingival inflammation, providing objective evidence of the eruption process. 3) Salivary inflammatory profile: A multiplex analysis of salivary cytokines (e.g., IL-1β, TNF-α, IL-8) to quantify the intensity of the local inflammatory response. 4) Salivary stress profile: Measurement of salivary cortisol to objectively quantify the infant's level of physiological distress.

These data streams could be integrated into a "Teething Diagnostic Score" (TDS). A high TDS, indicating a definitive case of symptomatic teething, would require positive findings across multiple modalities (e.g., a localized hot spot on IRT, elevated pro-inflammatory cytokines, and elevated cortisol). Conversely, a fussy infant with a high fever but a low TDS (normal thermogram, baseline cytokine and cortisol levels) would strongly indicate a coincidental illness, prompting an immediate and thorough search for another diagnosis. This model also allows for the stratification of severity. An infant with positive inflammatory markers but low cortisol may be coping well, warranting conservative management, whereas an infant with high levels across all markers is experiencing significant distress, providing a stronger justification for pharmacological intervention.

The future role of artificial intelligence in pattern recognition and diagnostic support - The complexity of the data generated by a multi-modal approach makes it an ideal application for Artificial Intelligence (AI) and machine learning (ML). Human interpretation of subtle patterns across multiple biomarkers and imaging data can be challenging and subjective. AI algorithms, however, can be trained on large datasets to recognize the complex, multi-dimensional "signature" of teething syndrome with high accuracy.

Specifically, Convolutional Neural Networks (CNNs), a type of deep learning model adept at image analysis, can be used for the automated interpretation of thermographic images, identifying inflammatory patterns with greater precision than the human eye. Other ML models can analyze the quantitative data from salivary biomarker panels, identifying the specific ratios and concentrations of cytokines and cortisol that are most predictive of symptomatic teething versus other conditions like oral infections or systemic viral illnesses. The ultimate goal is the development of a powerful, data-driven clinical decision support system. A clinician could input the data from the various assessments, and the AI model would provide a probability score for teething syndrome, a severity assessment, and a differential diagnosis list, empowering the clinician to make faster, more accurate, and more evidence-based decisions at the point of care.

Application of teledentistry for longitudinal monitoring and parental guidance - Teledentistry and telehealth platforms are poised to play a crucial role in the implementation and scalability of this new diagnostic paradigm. The non-invasive nature of the proposed diagnostic tools makes them highly amenable to remote application. Teledentistry platforms can facilitate:

Remote Consultations: Parents can have virtual appointments with pediatric dentists or pediatricians to discuss their child's symptoms, reducing the need for potentially stressful in-person visits for mild concerns.

Guided Data Collection: Using a smartphone camera, parents could be guided to capture standardized images of their child's gums. While not a replacement for thermography, this can

aid in preliminary assessment. More importantly, teledentistry can be used to provide clear, video-based instructions for at-home saliva sample collection using standardized kits.

Longitudinal Monitoring: The ease of at-home sample collection allows for longitudinal monitoring of an infant's biomarker profile throughout the entire period of primary tooth eruption. This can provide invaluable data for both clinical management (e.g., tracking the resolution of an inflammatory episode) and for research into the natural history of teething.

By integrating these technologies, care can be made more accessible, particularly for underserved populations, and a rich dataset can be generated to further refine and validate the objective diagnostic model, creating a virtuous cycle of clinical care and research.

Table 2: Emerging objective diagnostic tools for teething syndrome. This table summarizes the proposed innovative technologies, linking each to a specific, measurable component of the teething process and its underlying scientific rationale.

Diagnostic modality	Parameter measured	Biological principle	Potential for teething diagnosis
Infrared thermography (IRT)	Gingival Surface Temperature	Inflammation increases local blood flow and heat emission.	Non-invasively localizes and quantifies the site of active eruption-related inflammation.
Salivary inflammatory biomarkers	Levels of cytokines (e.g., IL-1β, TNF-α, IL-8) and chemokines	Tooth eruption is a sterile inflammatory process that releases specific molecular mediators into the oral cavity.	Provides a quantitative biochemical "signature" of the intensity of the inflammatory response.
Salivary stress biomarkers	Cortisol Level	Pain/discomfort activates the hypothalamic-pituitary-adrenal (HPA) axis, leading to cortisol release.	Objectively quantifies the infant's level of physiological distress, replacing subjective measures of "fussiness."
Advanced Imaging (e.g., CBCT)	3D anatomy of teeth and jaws	Provides high-resolution structural information of mineralized tissues.	Primarily for differential diagnosis of eruption abnormalities (e.g., delay, impaction), not the syndrome itself.

CONCLUSION

Recapitulation of findings: Shifting from subjective belief to objective measurement - The diagnosis of teething syndrome has long been mired in ambiguity, relying on subjective interpretations of non-specific behaviors. This historical reliance on parental reports and inconclusive clinical signs has created a significant clinical challenge, most notably the risk of diagnostic overshadowing, where serious pediatric illnesses are mistakenly attributed to the benign process of tooth eruption. This review has critically analyzed the limitations of this traditional paradigm and has charted a path toward a new era of objective, evidence-based diagnosis. The central thesis of this work is that by leveraging modern, non-invasive technologies, we can transition from interpreting behavior to measuring biology. The integration

of infrared thermography to quantify local inflammation and salivary diagnostics to profile the molecular signatures of inflammation (cytokines) and distress (cortisol) offers a powerful, multi-modal approach. This new framework allows for the direct measurement of the core physiological components of the teething process, providing a definitive and quantifiable basis for diagnosis that has been absent until now.

Clinical implications for pediatricians and pediatric dentists - The adoption of an objective, multi-modal diagnostic framework for teething syndrome carries profound clinical implications. For pediatricians and pediatric dentists, it provides a powerful tool for confident differential diagnosis. By objectively confirming or refuting the presence of significant eruption-related inflammation and distress, clinicians can drastically reduce the risk of missing or delaying the diagnosis of concurrent illnesses. This data-driven approach also provides a rational basis for management decisions, allowing for the stratification of patients. It enables clinicians to distinguish infants who require only non-pharmacological comfort measures from those experiencing significant distress who may benefit from analgesics. Furthermore, this objective evidence is an invaluable tool for parental education. By presenting parents with clear, quantitative data, clinicians can more effectively debunk harmful myths about teething causing high fevers or diarrhea, discourage the use of unsafe remedies, and provide the evidence-based reassurance needed to alleviate parental anxiety.

Future research trajectories and validation of novel diagnostic protocols - While the technologies and principles outlined in this review are promising, their translation into routine clinical practice requires a concerted research effort. The immediate priority is to conduct large-scale, longitudinal prospective studies in diverse infant populations. These studies are essential to establish normative values and dynamic ranges for thermographic and salivary biomarker profiles during both teething and non-teething periods. This will allow for the development and validation of the proposed multi-modal "Teething Diagnostic Score," including the determination of specific cut-off values for diagnosis and severity stratification.

Concurrently, a critical area for innovation is the development, validation, and commercialization of affordable, user-friendly, point-of-care (POC) or chair-side devices. The creation of a handheld thermal camera integrated with AI-driven analysis software or a rapid, multiplex salivary assay for key inflammatory and stress biomarkers is essential for making this diagnostic paradigm accessible and practical in a busy clinical setting. Ultimately, these future endeavors will be crucial in transforming the diagnosis of teething from a clinical art based on intuition and belief into a precise science based on objective measurement, enhancing the safety and well-being of infants worldwide.

References

1. Ali, S., & Ali, A. (2023). Association between salivary cortisol levels, dental anxiety, and dental caries in children: A cross-sectional study. Dentistry Journal, 11(x). https://www.researchgate.net/publication/373506265_Association_between_Salivary_Cortisol_Levels_Dental_Anxiety_and_Dental_Caries_in_Children_A_Cross-Sectional_Study
2. American Dental Association. (2023, October). Salivary diagnostics. ADA.org. https://www.ada.org/resources/ada-library/oral-health-topics/salivary-diagnostics
3. Barboza, M. N., de Oliveira, F. L., Frazier, J., & de Paula, L. M. (2024). Salivary IL-6 as a biomarker for early childhood and rampant caries: Insights from a cross-sectional study. Journal of Molecular and Pathological Sciences, 13(2), 293. https://www.mdpi.com/2227-9059/13/2/293
4. Caruso, S., Gatto, R., & Cefalo, M. (2018). Association between salivary cortisol level and caries in early childhood. European Journal of Paediatric Dentistry, 19(1), 11-14. https://www.ejpd.eu/pdf/EJPD_2018_1_1.pdf

5. Cleveland Clinic. (n.d.). Teething/Teething syndrome. my.clevelandclinic.org. https://my.clevelandclinic.org/health/articles/11179-teething-teething-syndrome
6. Coastal Kids Pediatric Dentistry. (n.d.). Salivary diagnostics: Harnessing saliva to detect and monitor systemic diseases. coastalkidsdo.com. https://www.coastalkidsdo.com/post/salivary-diagnostics-harnessing-saliva-to-detect-and-monitor-systemic-diseases
7. Davis, K. A., Mountain, R. V., Pickett, O. R., Den Besten, P. K., Bidlack, F. B., & Dunn, E. C. (2020). Teeth as potential new tools to measure early-life adversity and subsequent mental health risk: An interdisciplinary review and conceptual model. Biological Psychiatry, 87(6), 502-513. https://mghpsychnews.org/baby-teeth-a-new-approach-to-identifying-early-adversity-and-children-at-risk-for-psychiatric-illness/
8. Feldens, C. A., Faraco, I. M., Jr., Ottoni, A. B., Feldens, E. G., & Vitolo, M. R. (2010). Teething symptoms in the first year of life and associated factors: A cohort study. Journal of Clinical Pediatric Dentistry, 34(3), 249-252. https://oss.jocpd.com/files/article/20220808-956/pdf/JOCPD.34.3.249.pdf
9. Franciscan Health. (2023, April 25). Teething or sick: How to tell in your baby. franciscanhealth.org. https://www.franciscanhealth.org/community/blog/teething-or-sick-how-to-tell-in-your-baby
10. Go Kids Pediatric Dentistry. (n.d.). The future of pediatric dentistry: How new technologies are transforming children's dental care. gokidspediatricdentistry.com. https://gokidspediatricdentistry.com/blog/the-future-of-pediatric-dentistry-how-new-technologies-are-transforming-childrens-dental-care/
11. Hegde, M. N., Attavar, S., Shetty, N., & Hegde, N. D. (2019). Saliva as a biomarker for dental caries: A systematic review. Journal of Conservative Dentistry, 22(1), 2-6. https://www.researchgate.net/publication/331462707_Saliva_as_a_biomarker_for_dental_caries_A_systematic_review
12. Iacob, S. M., Chisnoiu, A. M., Lascu, L., Berar, A. M., Chisnoiu, R., & Picos, A. M. (2023). Salivary cortisol as a biomarker for assessing fear and anxiety in patients with molar–incisor hypomineralization. Diagnostics, 15(4), 489. https://www.mdpi.com/2075-4418/15/4/489
13. Jhunjhunwala, G., Mathur, V. P., & Tewari, N. (2025). Global prevalence of teething problems in infants and children-A systematic review and meta-analysis. International Journal of Paediatric Dentistry, 35(3), 608-624. https://pubmed.ncbi.nlm.nih.gov/39344021/?utm_source=FeedFetcher&utm_medium=rss&utm_campaign=None&utm_content=1vyK0bnlSnx3ROWRw4BZasPT3B6VsB1j1Ko8yIaKhKhqoIjY9I&fc=None&ff=20241214183255&v=2.18.0.post9+e462414
14. Johns Hopkins Medicine. (n.d.). What you should know about babies teething. hopkinsmedicine.org. https://www.hopkinsmedicine.org/health/conditions-and-diseases/teething/what-you-should-know-about-babies-teething
15. Kambalimath, H. V., Jain, R., Asawa, K., Singh, A., Gupta, A., & Singh, M. (2015). Recent advances in diagnosis of dental caries. Journal of Natural Science, Biology and Medicine, 6(2), 313-318. https://pmc.ncbi.nlm.nih.gov/articles/PMC4999630/