



EPILEPSY REVISITED! CHALLENGE FOR PEDIATRIC DENTIST

Dental Science

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ABSTRACT

Introduction: Epilepsy is a disease that involves seizures which are characterized by an alteration of perception, behavior and mental activities, as well as by involuntary muscle contractions, temporary loss of consciousness and chronic changes in neurological functions that result from abnormal electrical activity in the brain. Epilepsy is a common heterogeneous constituent of neurological problem in children. A considerable treatment gap exists due to lack of trained manpower. Evidence-based clinical practice guidelines can improve the quality of care. Epilepsy has various negative effects on sufferers' overall oral health, which consequently leads to tooth loss, caries and periodontal disease and they need more dental treatment. Appropriate diagnosis and management of childhood epilepsy is very essential to improve quality of life in these children.

Epidemiology and Prevalence: It has prevalence of 0.5% - 0.9% in general population. Epileptic seizures are the second most common medical incident in dental surgeries. Reported figure of prevalence rates of epilepsy in children ranges from 1.5 to 121/1,000. The great variability in percentages is a reflection of true differences in prevalence rates of activity caused by differing socioeconomic and geographical situations, e.g., it is higher in rural populations and developing countries as compared with developed countries. **Management in dental operatory:** Proper case history and diagnosis, prior physician's consent, in case of an aura discontinue the treatment, place all instruments and sharp objects away from the patient. If the seizure lasts more than 3 minutes and recurs, drug administration is required.

KEYWORDS

epilepsy, seizures, medical emergencies, dental management, epileptic drugs

INTRODUCTION

The word "epilepsy" is derived from the Greek word "epilambanein" meaning to take or to seize. Hippocrates recognized that seizures originated in the brain. Modern medicine defines epilepsy as a chronic neurological disorder characterized by frequently recurrent seizures. A seizure is a sign of a disease, which manifests as an episodic disturbance of movement, feeling, or consciousness caused by sudden synchronous, inappropriate, and excessive electrical discharges that interfere with the normal functioning of the brain.¹

It exerts a significant physical, psychological, economic and social toll on children and their caregivers. The seizures and epilepsies in children are extremely diverse, differing markedly in age of onset, seizure characteristics, associated comorbidities, treatment and prognosis. Given that there is a shortage of pediatric epileptologists practicing around the world, it is impossible for all children with recurrent seizures to receive their care from subspecialists.²

Without a firm understanding of the complexities of childhood epilepsy, it may be not possible for such physicians to always make an accurate diagnosis and plan an effective treatment strategy. So it is important for the general pediatrician to be aware of the evaluation and management of patients.²

DEFINITIONS

A seizure is defined as an excessive burst of abnormal synchronized neuronal activity affecting small or large neuronal networks that results in clinical manifestations that are sudden, transient and usually brief.²

Epilepsy is defined as a disorder of the brain characterized by any of the following conditions: (1) At least two unprovoked (or reflex) seizures occurring >24 h apart, (2) One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years and (3) Diagnosis of an epilepsy syndrome (Hauser and Banerjee, 2008; Tamber and Mountz, 2012; Fisher et al., 2014). Provoked seizure is a seizure that occurs in reaction to an acute, transient condition affecting the brain. Provoking factors include, but are not limited to, head trauma, stroke, intracranial infections, acute metabolic disruptions (e.g., hypoglycemia, anoxia) and acute drug or toxin poisoning (Hauser and Banerjee, 2008; Tamber and Mountz, 2012).²

INCIDENCE

Epileptic seizures affect 1-2 % of the population and 4% of children. Developing countries have higher prevalence due to the poorer perinatal care and standards of nutrition and public hygiene and the greater risk of brain injury, cerebral infection or other symptomatic cerebral conditions. Childhood epilepsy has a prevalence of

approximately 0.5-0.8% and comprises a heterogeneous group of disorders, including a variety of epilepsy syndromes that range in severity from benign to progressive and catastrophic. Focal epilepsies predominate (59-63%) than generalized epilepsy (12-29%). In about 20% classification may change on follow up (Hauser and Banerjee, 2008; Sharma, 2013; Cross et al., 2013).²

Epilepsy affect millions of people worldwide having prevalence of 0.5% - 0.9% in the general population. It is the second most common medical incidence in dental surgeries. It is stated that statistically every dentist notice in his/her professional life 1.5 times generalized tonic-clonic seizures by the patients. It has been reported that the disease occurs independent of race, age and gender. However, epilepsy has been occur more frequently in men than in women. Epilepsy has been observed most frequently in children under 1 year of age. It has also been reported that those cases of epilepsy that develop in childhood are genetic in origin, while those that appear in adulthood are related to cerebrovascular diseases. Up to 50% of children displaying mental retardation have been diagnosed as suffering from epilepsy.⁷

CLASSIFICATION

Classifications for seizures and epilepsy were previously constructed in 1981 (ILAE, 1981), 1985 (ILAE, 1985) and 1989 (ILAE, 1989). Based on decades of accumulated clinical experience, the International League Against Epilepsy (ILAE) commissioned a new operational classification of seizure types and epilepsies. The new 2017 classifications, when compared to the 1981/1985/1989 classifications, utilize alternative terms and contain several important additions.⁸

I. According to the International League against Epilepsy (1997)³

Partial seizures

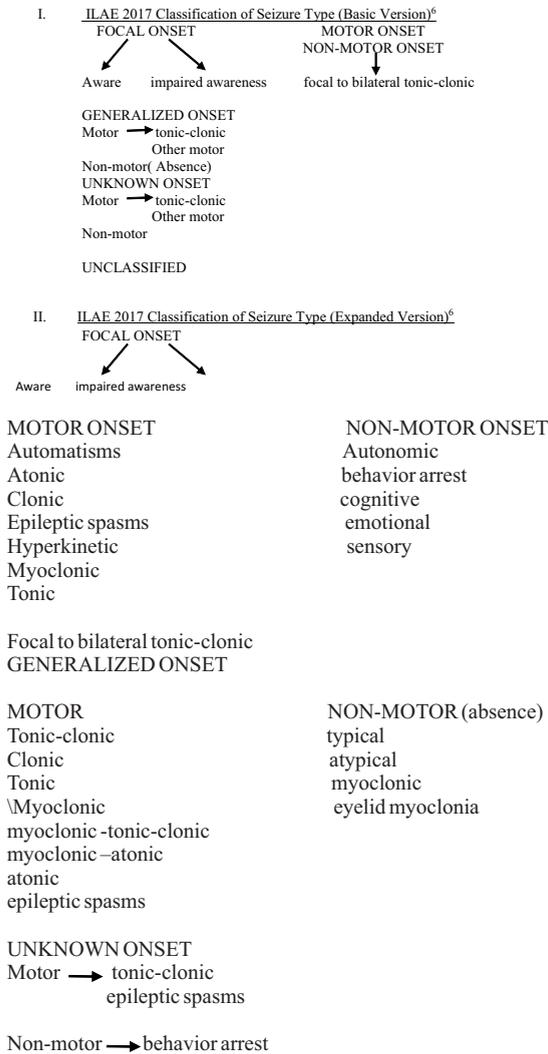
Simple partial seizures (awareness not impaired)

- with minor signs (focal motor, versive, phonatory)
- with somatosensory or special-sensory symptoms (somatosensory, visual, auditory, olfactory, gustatory)
- with autonomic symptoms
- with psychic symptoms (illusions, hallucinations) Complex partial seizures
- with simple partial onset followed by impairment of awareness
- with impairment of awareness at onset Partial seizures evolving to secondarily generalized seizures
- simple partial seizures evolving to generalized seizures
- complex partial seizures evolving to generalized seizures
- simple partial seizures evolving to complex partial and then to generalized seizures

Generalized seizures

- Absence seizures

- Myoclonic seizures
- Clonic seizures
- Tonic seizures
- Tonic-clonic seizures
- Atonic seizures
- Unclassified seizures



UNCLASSIFIED

(Source: Robert S. Fisher et al., Instruction manual for the ILAE 2017 operational classification of seizure types. *Epilepsia*,58(4):531-542,2017)

Etiology and Pathogenesis

In approximately 70% of all cases the specific cause of seizures cannot be determined. These cases are classified as idiopathic or primary epilepsy. When the cause of the seizure is known, the terms used are either acquired or secondary epilepsy. The reason for secondary epilepsy can be metabolic, structural, and functional abnormalities including seizures secondary to head trauma, especially if consciousness was lost for more than 30 minutes. The most common cause of adult epilepsy is cerebrovascular disease (stroke, brain attack) followed by primary and metastatic brain tumors. Systemic disorders that can cause epilepsy include infections, hypertension, and diabetes as well as electrolyte imbalances, dehydration, and lack of oxygen. High doses and withdrawal from chronic use of drugs such as heroin, cocaine, barbiturates, amphetamines, and alcohol can also lead to seizures. There appears to be a genetic predisposition to epilepsy associated with chromosome 12 anomalies. These anomalies increase the risk of epilepsy in children of epileptic women.¹

Epilepsy pathogenesis, at the cellular level, relates to systems that maintain the balance between excitation and inhibition of brain electrical activity. There is a loss of inhibitory activity or an

overproduction of excitatory activity. The imbalance appears to occur in abnormal cells or injured cells, which become the foci of the seizure. Those cells create a burst of abnormal electrical signals that spread to adjacent cells creating a “storm” of electrical activity. As the storm progresses, the seizure becomes apparent.¹

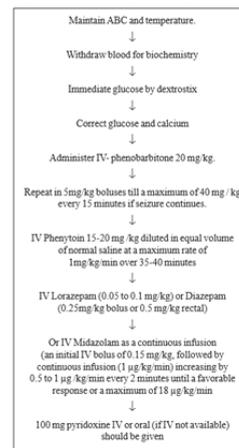
Seizures of Pediatric significance and management

1. Neonatal seizures

Neonatal seizures are often acute symptomatic due to underlying brain insults.¹⁵ It is the most frequent and distinctive clinical manifestation of neurological dysfunction in the newborn infant. Infants with NS are at a high risk of neonatal death or neurological impairment/epilepsy disorders in later life.²⁶

Table 1: Investigations of neonatal seizures²⁶

Essential investigations	Additional investigations
<ul style="list-style-type: none"> • Blood sugar • Serum sodium and calcium • Cerebrospinal fluid (CSF) examination • Cranial ultrasound (US) and 	<ul style="list-style-type: none"> • Hematocrit (if plethoric and/or at risk for polycythemia) • Serum bilirubin (if icteric) • Serum magnesium • Arterial blood gas and anion gap (lethargy, vomiting, family history, etc.) • Imaging: CT and/or MRI (if no etiology found after essential investigations) • TORCH screen for congenital infections • Work-up for inborn errors of metabolism



Management of neonatal seizure¹⁵

1. Acute Symptomatic Seizures

A seizure occurring within a week of an acute brain insult (trauma, infection, toxic, metabolic or vascular insult) is called an acute symptomatic seizure⁽⁸⁾. Future risk of unprovoked seizures is only 3-10%. CT scan is indicated in traumatic brain injury and a contrast enhanced CT scan is indicated in children above 2 years of age. In a hypocalcemic breastfed infant, an underlying vitamin D deficiency state in the child and the feeding mothers should be corrected first. Antiepileptic drugs (AED) are required in the acute phase and can be withdrawn in a week in acute traumatic brain injury.¹⁵

2. Febrile seizures

These are the most common type of seizure in young children with 2-5% incidence rate children experiencing atleast one seizure before the age of 5 years. The peak age of febrile convulsions is between 18 to 24 months. Its pathophysiology is unknown but it is seen that fever lowers the seizure threshold in susceptible children. There is strong genetic predisposition and family history exists between 25-40% children with febrile seizures.¹¹ Lumbar puncture should be done in children with suspected meningitis, especially in infants. Management includes definitive diagnosis, restraint in investigations, treatment of an acute episode, prophylaxis for future episodes and family counseling. Parents can be taught to use rectal liquid diazepam (0.5 mg/kg) or buccal or nasal Midazolam (0.3 mg/kg) for acute termination of seizures that last for two minutes or more. . Intermittent prophylaxis

with oral Clobazam in a dose of 0.75 mg/kg for 2-3 days in 2 divided doses during fever is useful to prevent recurrence.¹⁵

3. Generalized Seizures

These seizures are rapidly engaging, bilaterally distributed networks, which can be subcortical or cortical structures and in which consciousness is impaired from the onset.² Each hemisphere of the brain is affected synchronously. There is usually no indication (aura) before the seizure and the patient is un-conscious during the seizure. The generalized type is classified into three groups: generalized tonic-clonic seizures (grand mal), atonic seizures, and absence seizures (petit mal).⁷

a) Tonic clonic seizures are the classic form of epileptic seizure, with altered consciousness followed by tonic extension and then clonic convulsive movements of all four extremities. Generalized Tonic-Clonic seizures (GTCs) are the commonest seizures of childhood. The onset may occur at any time after the neonatal period. They may be associated with aura, suggesting a focal origin of the epileptic discharge. EEG during the seizure shows generalized repetitive spikes in the tonic phase and then periodic spikes in the clonic phase.²

b) Atonic Seizures may manifest as the classic drop attack, in which all postural tone is suddenly lost, or more subtle changes, such as a slight head drop or bowing at the knees. There is sudden loss of muscle tone, which may be confined to a group of muscles, such as the neck, resulting in a head drop, or it may involve all trunk muscles, leading to a fall to the ground. It begins suddenly and without warning and cause the patient, if standing, to fall quickly to the floor. Because total lack of tone may occur, the patient has no means of self-protection and injuries often occur. Consciousness is impaired during the fall, although the patient may regain alertness immediately on hitting the floor. The correlate of tonic seizures in the EEG includes an electrodecremental response. An electrodecremental response is a sudden generalized drop in amplitude of the EEG. This pattern may evolve into slow spike-and-wave complexes or diffuse polyspikes.²

c) Absence seizures can be suspected in a normal school age child with frequent absence seizures often upto a hundred a day. These occur in the awake state with sudden staring, unresponsiveness and minor brief automatisms, leading to interruption of ongoing activity and unassociated with any post ictal abnormality. Precipitation of seizure by hyperventilation is a simple clinical diagnostic test. Atypical absence seizures are prolonged, seen usually in catastrophic pediatric syndromes with neurocognitive deterioration. An EEG showing a typical pattern characterized by frontally predominant generalized bursts of 3 Hz spike wave complexes with abrupt onset is diagnostic.¹⁵

4. Myoclonic Epilepsy in Infancy (MEI)

Myoclonic seizures may begin in the first year of life. Myoclonic jerks may be focal, multifocal, or generalized and are more likely to be flexor than extensor. Myoclonus is termed epileptic when it occurs with a cortical epileptic form discharge, usually a generalized spike and wave discharge or spikes/sharp waves over the motor cortex.²

Idiopathic Partial Epilepsies in Childhood

5. Benign epilepsy with centro-temporal spikes

It can be considered when a normal school aged child presents with brief and infrequent, partial, nocturnal, hemi-facial, sensory or motor seizures. An awake-cum- sleep EEG is necessary, as it displays a characteristic pattern of sleep activated runs of centro-temporal spikes or sharp waves. It has an excellent prognosis with remission in most cases by the age of 15-16 years.¹⁵

6. Idiopathic generalized epilepsies of adolescent

When a child presents with absence, myoclonic or generalized tonic, clonic seizures for the first time after 10 years, a diagnosis of idiopathic generalized epilepsies of adolescent onset is considered. EEG shows generalized paroxysms of spike or polyspikes wave discharges. Photosensitivity is common. Juvenile myoclonic epilepsy (JME), juvenile absence epilepsy (JAE) and epilepsies with only GTC seizures should also be considered in diagnosis. JME presents in adolescents with history of early morning predominant upper limb myoclonic jerks leading to the patient dropping objects. This occurs often in sleep-deprived individuals, especially if suddenly awakened. JAE is similar to CAE, though the numbers of absences are much less and the onset is usually later. GTC seizures typically occur on awakening or in the evening. Sodium valproate is the most effective

drug in most cases of idiopathic generalized epilepsies, but it may cause weight gain, hair loss, and menstrual irregularities and has a higher incidence of fetal teratogenicity. Therefore, lamotrigine may be preferable in adolescent girls.¹⁵

Management of epilepsy by antiepileptic drugs

The goal of antiepileptic drug (AED) treatment is the elimination of seizures without the presence of treatment-emergent side effects that lower quality of life.¹⁰ There are certain conventional and new antiepileptic drugs are available:

1. Conventional Antiepileptic Drugs

Phenobarbitone : It could be used as a first line AED in neonatal seizures, in the first two years of life for partial/GTC seizures and in neonatal and early infantile status epilepticus(SE). The dosage varies between 3-6 mg/kg/day given as a single night-time dose for routine use and 20 mg/kg given as loading for SE. Since deleterious cognitive and behavioral side effects remain a concern, it should be avoided in school-going children.¹⁵

Phenytoin : Though effective, but should not be preferred as a primary AED in newly diagnosed epilepsy, especially in infancy, as levels fluctuate frequently in infants, making monitoring of drug levels imperative, and in adolescent girls as cosmetic side effects may be unacceptable. Maintenance dosages in older children are between 5-6 mg/kg given in one or two divided doses, but infants may need upto 15-18 mg/ kg in 3-4 divided doses.¹⁵

Valproate : As a result of its broad spectrum of efficacy, valproate could be the drug of choice for most children with newly diagnosed epilepsy, like idiopathic generalized epilepsy (CAE, JAE, BMEI, and JME), epilepsies with prominent myoclonic seizures or with multiple seizure types, and photosensitive epilepsies. However, in adolescent girls or obese patients, one may not use it as first line agent due to concerns of weight gain, hair loss and aggravation of polycystic ovarian disease (PCOD). It could be used in partial epilepsies in infants where carbamazepine might precipitate generalized seizures and in refractory status epilepticus. The dose averages between 10-40 mg/kg/day. Twice-a-day dosing is preferred with extended release preparations, except in syrup (3 times a day). Parents should be counseled regarding danger symptoms and signs of hepatitis, like nausea, vomiting, drowsiness etc, especially in children below the age of 2 years.¹⁵

Carbamazepine: It is the drug of first choice for all newly diagnosed partial epilepsies, after the age of 2 years. The dose varies between 10-30 mg/kg in the form of twice a day dosing and preferably given as slow release preparations if syrups are used they should be given three times a day. Carbamazepine may induce or exacerbate generalized seizures like infantile spasms, myoclonic, tonic and absence seizures in the younger child.¹⁵

2. Newer Antiepileptic Drugs

Table 2: Guidelines for new drugs in epilepsy¹⁵

	Clobazam	Lamotrigine	Levetiracetam	Topiramate	Oxcarbazepine	Tiagabine
New Onset	No	Yes (JME, CAE)	No	No	Yes (Partial)	No
Partial	Yes	Yes	Yes	Yes	Yes	No
Absence	Yes	Yes	Yes	Yes	No	No
Myoclonic	Yes	Yes	Yes	Yes	No	No
GTC	Yes	Yes	Yes	Yes	No	No
Refractory						
Partial	Yes	Yes	Yes	Yes	Yes	Yes
Absence	Yes	Yes	Yes	Yes	No	No
Myoclonic	Yes	Yes	Yes	Yes	No	No
Spasm	No	Yes	No	Yes	No	No
LGS	Yes	Yes	Possible	Yes	No	No

Table 3: Dosage and side effects of antiepileptic drugs¹⁵

Drugs	Daily dose	Common side effects
Phenobarbitone	3-8 mg/kg	Hypersensitivity, academic deterioration, reversal of sleep cycles
Phenytoin	5-15 mg/kg	Poor seizure control due to fluctuating drug levels, cosmetic side effects, hirsutism, ataxia
Valparin	10-60 mg/kg	Nausea, vomiting, loss of appetite, weight gain, irregular menstruation, alopecia, somnolence
Carbamazepine	10-30 mg/kg	Drug rash, worsening seizures, rarely worsening school performance
Oxcarbazepine	20-45 mg/kg	Somnolence, vomiting (hyponatremia), seizure exacerbation
Lamotrigine	0.2-15 mg/kg	Drug rash, Stevens-Johnson syndrome
Clobazam	0.4-1.2 mg/kg	Behaviour changes, aggression, sleep disturbances, constipation, weight gain
Topiramate	3-9 mg/kg	Cognitive/language deterioration, fever, acidosis in infancy
Levetiracetam	15-45 mg/kg	Behaviour changes
Tiagabine	0.5-2 mg/kg	Somnolence, Seizure exacerbation

Other Medical Conditions Resembling Epilepsy

Several disorders can often be mistaken for an epileptic seizure: hyperventilation, hypoglycemia, migraine, transient ischemic attacks, syncope, pseudoseizure, transient global amnesia, and sleep disorders. Of these, the most common conditions confused with epilepsy are syncope, pseudoseizure, and panic attacks.²

Considerations for the Dental Management of the Epileptic Patient

Epilepsy occurs in people who have a wide range of socio-economic, educational, environmental, and other factors impacting their

healthcare. Unlike non-epileptic patients, specific considerations for epileptic patients include the treatment of oral soft tissue side effects of their medication and correcting damage to their teeth that has occurred secondary to seizure trauma. Dental treatment planning must consider the fabrication of a dental prosthesis designed to minimize risk of future damage or displacement of teeth. The epileptic patient should also be properly educated and instructed in oral hygiene and provided an understanding of how their oral health impacts their general health.¹

When treating epileptic patients, the major difficulty a dentist faces is the high risk of seizures occurring. In order to prevent such seizures, three fundamental principles should guide the dentist during his or her interaction with the patient in a clinical environment: 1) knowledge of the patient's previous seizure episodes and medication, 2) knowledge of the conditions that provoke epileptic seizures, in order to avoid such conditions, and 3) dentist should be able to recognize the early signs of a seizure, take precautions before it occurs, and provide the patient with supportive care if it does occur.⁷

Factors to Be Taken into Consideration While Administering Treatment

Before initiating the treatment, a detailed history should be obtained from patient. This should cover the details like the frequency of seizures, date of the patient's last seizure, consciousness and respiratory state of the patient during seizures, physical condition of the patient after a seizure, Whether there is any aura before seizures, Whether experiencing an aura always leads to a seizure, factors provoking seizures, existence of status epilepticus. As stress is one of the most important factors that provoke seizures, stress-causing factors should be eliminated before starting the treatment. The patient's appointment should be in the early hours of the day, treatment sessions should be kept short, and sudden stimulants such as shimmering bright lights and extreme noise should be avoided.⁷

With regard to the safety of administering local anesthesia to epileptic patients, it has been reported that the issue is still inconclusive and not certain. Kennedy et al. stated that, in dental practices, local anesthetics administered in therapeutic dosages do not interact with standard antiepileptic drugs. Although it has been reported that local anesthetic administration during dental treatment is safe, it is also proposed that adrenalin in local anesthetics has a potential affect on epileptic seizures by intravenous injection. Therefore, general anesthesia has been said to be the right choice if epileptic seizures are difficult to bring under control. If a patient is mentally retarded, then general anesthesia should be considered necessary in view of the fact that a seizure may be triggered by stress due to difficulties in communication. During dental treatment, it has been suggested that seizure development can be controlled by sedation through nitrous oxide inhalation or intravenous benzodiazepine sedation. However, sometimes a seizure may develop during dental treatment despite intravenous sedation; in such a case treatment must be postponed.⁷

Actions to Be Taken If a Patient Has Epileptic Seizure during Dental Treatment

- Treatment should be stopped and dental tampons, prostheses and instruments should be removed
- The patient should be helped into the supine position.
- It is not necessary to restrain the patient or move him/her to the floor; neither is it necessary to place an object in the patient's mouth (e.g. to stop them swallowing their tongue). Preventing injury is the primary, most important goal of assistance
- Any tight clothing the patient is wearing should be loosened
- If the patient has an aura, thick gauze tampons should be placed in the patient's mouth in order to prevent any kind of injury or damage to the tooth
- Some patients fall into a deep sleep after seizure. In such cases the patient must be monitored closely
- If the seizure lasts more than 3 minutes and recurs, drug administration is required.
- The patient should be monitored to make sure his/her airway does not become obstructed. However, if the seizure lasts longer and continues in spite of medication, the patient should be sent to hospital
- After the patient regains consciousness, he/she should be sent home to rest. Treatment should be postponed until the patient feels well again.⁷

CONCLUSION

The impact is even larger when the impact on the families of epileptic patients is taken into consideration. The management of epilepsy and the medications available has improved vastly over the last ten years. Still, these patients have a variety of unique medical and dental needs. Patients with epilepsy can be safely managed in a general dental office by an informed practitioner. A good health history to fully understand the patient's disease and the medications they are taking is essential. A proper oral exam to uncover any dental problems and possible oral effects of anti-epileptic drugs is necessary. Some simple and straightforward treatment planning considerations will insure the patient's oral health is properly maintained.

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