Evaluation of the child with seizures[1]

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The proper approach to evaluation of a child or adolescent with seizures is reviewed, with emphasis on the importance of the history, thorough physical examination, differential diagnosis, and laboratory testing prior to initiation of therapy. Follow-up is part of this evaluation process.

Index terms: Epilepsy · Seizures

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Epilepsy is the tendency to recurrent seizure activity. A seizure, as defined by Hughlings Jackson, is "an occasional sudden, excessive, rapid, and local discharge of gray matter." Actually, it is a group of disorders with multiple etiologies. Although there are many types of seizures, all are due to paroxysmal excessive neuronal discharge and result in a sudden disturbance of function. The episodes may be simple attacks of altered consciousness, convulsive movements, or simple staring spells. The basic physiology of the seizure episode is traceable to an unstable cell membrane or its surrounding supportive cells. The stability of these cells can be affected by numerous factors, including pH, oxygenation, and levels of glucose, sodium, potassium, and calcium. Changes in any of these factors may lower the seizure threshold. The location of the abnormal neurons determines the character of the seizure; for example, an occipital lobe focus on the right side would cause visual disturbances in the left visual field. Seizure disorders, including febrile seizures, are more frequent in children

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than in adults; it has been estimated that as many as 4% to 6% of children will have a single seizure, while 1% to 2% will have epilepsy. This disorder tends to affect all aspects of the child's existence, including development, socialization, learning, vocational choice, and quality of life.[1]

Etiology

Approximately 50% of all epileptic children have idiopathic seizures or seizure disorders in which a specific etiology cannot be found. In the other 50% a specific etiology can be found (symptomatic), the two most likely being (1) trauma related to birth and (2) congenital abnormalities of the central nervous system (CNS). It is not known how many children will have only a single afebrile seizure without recurrence. In any event, evaluation of the child or adolescent with a single seizure or recurrent seizures is similar, including a complete history, physical examination, laboratory testing, with the scope being determined by the clinical situation and the acuteness or chronicity of the seizures, treatment, and clinical follow-up. Since many patients are too young to give an accurate history, one must rely on the parents. Others may be unable to cooperate for a formal examination so that a playful approach and pleasant demeanor are most successful. Simple observation and play may be more useful than a direct approach.[2]

History[3]

The first part of the history should include data concerning the seizure and its precipitating factors. Important questions include (1) the frequency and duration of the spells, (2) precipitating factors, (3) times of occurrence, (4) the presence of an aura, (5) ictal activity (focal or generalized, tonic, clonic, or simple staring), and (6) the postictal state (confusion, fatigue, etc.). In addition, it should be determined whether more than one type of seizure has taken place.

The second part of the history includes factors which determine whether or not the patient is prone to seizures, including duration and complications of pregnancy, duration and complications of labor, mode of delivery, and problems associated with birth. The neonatal course is critical, including birth weight, Apgar scores, whether the child was placed in an observation nursery or intensive care unit, and whether any specialized care was needed, such as intubation and respiratory care, intravenous therapy, or exchange transfusions. Developmental factors include when the child first begins to walk, uses single words, speaks in sentences, and is toilet-trained.[4] Any history of encephalopathy, such as head injury, prolonged high fever, febrile seizures, and CNS infections such as meningitis and encephalitis would also be important. The physician should determine whether or not any other close family member has epilepsy. He must also discern whether or not the patient is taking any medication that could promote seizure activity or has any other disorder that may directly or indirectly affect the occurrence of seizures, such as diabetes, chronic lung disease, cyanotic congenital heart disease, allergy, or asthma. Intellectual function; motor ability; behavioral problems; and difficulties of speech, hearing, language, or vision should also be considered in evaluating CNS function.

The third part of the history is an effort to determine whether or not the disorder is progressive or due to an intracranial lesion. The physician should specifically inquire about the loss of motor or mental milestones (i.e., regression) as well as headaches, vomiting (with or without nausea), lethargy, personality changes, visual difficulties, or focal weakness, any of which should suggest the need for immediate evaluation. The examiner should monitor the affect of both the child and the parents during the interview, as such observations often provide unspoken insight into problems such as anxiety, depression, family conflict, and hostility. At the conclusion of the history, the examiner should have formed at least a tentative opinion as to whether the patient has epilepsy or some other paroxysmal disorder.

Physical examination[5–8]

During the physical examination, each organ system should be examined, keeping in mind its possible relationship to the patient's seizure disorder. The vital signs may give a clue to the underlying etiology; for example, fever may be the only indication of an infectious process. Blood pressure must be measured, even in an infant, as hypertension can predispose to CNS problems; in addition, if no femoral pulses are palpable, the blood pressure in the legs must be measured to rule out coarctation of the aorta. If height and weight are significantly below or above average, a pituitary or hypothalamic neoplasm could be present. Cardiac murmurs or chronic lung dis-

ease could predispose the patient to brain abscess, and dysmorphic features may suggest a congenital anomaly of the brain. Organomegaly may suggest a storage disease, while an unexplained mass may have caused a CNS metastasis. If the neck is stiff, meningitis or subarachnoid hemorrhage should be suspected.

Examination of the skin is critical and frequently yields useful information. Petechiae may indicate a blood dyscrasia with hemorrhage into the central nervous system; striae may indicate Cushing's disease; five or more café-au-lait spots suggest neurofibromatosis and a possible CNS disorder; hypopigmented macules and adenoma sebaceum could be a sign of tuberous sclerosis; and a hemangioma or vascular abnormality may suggest similar changes within the CNS. The spine should be examined for scoliosis, as well as cutaneous markers indicating maldevelopment of the CNS.

The neurological examination begins with measurement of the head circumference; significant enlargement could be a sign of megalencephaly or hydrocephalus, while a measurement below the third percentile should suggest microcephaly produced by impairment of normal brain growth. Auscultation of the cranium may reveal an asymmetric bruit indicating an arteriovenous malformation, though soft, bilaterally symmetrical bruits in a young child are probably normal. The presence of a bulging or prematurely closed fontanelle is significant. It may be wise to save the funduscopic examination for last in very young children, since they frequently refuse to cooperate; nevertheless, the evaluation is not complete unless the fundi can be adequately visualized. Any funduscopic abnormality, including hemorrhage, papilledema, optic atrophy, chorioretinal scarring, or vascular abnormality, is significant. For example, optic atrophy may indicate chronic increased intracranial pressure or a lesion in the area of the optic chiasm. Asymmetry of the cranial nerves should suggest a structural abnormality. Inability to move the eyes to the side may be due to palsy of the sixth nerve and a nonspecific increase in intracranial pressure. Gross visual acuity and perimetry can be tested even in the very young. Abnormalities of the lower cranial nerves, ataxia, or cerebellar dysfunction may indicate a lesion of the posterior fossa. The symmetry of the child's smile should be noted. Testing of corneal or gag reflexes should be avoided at this point, as cooperation will be lost. Strength and reflexes must be carefully noted, along with tone; if asymmetry is apparent, a hemispheric abnormality should be suspected. Gait must be assessed, looking for any difficulties with balance. Testing sensation with a pin should be avoided if possible. In infants, the presence or absence of primitive reflexes should be noted, whereas in a child, attention must be paid to speech, state of alertness, and activity level.[7-9]

Before ordering the laboratory tests, a differential diagnosis should be formulated, since the extent of testing will differ in a well child with a single uncomplicated generalized seizure, a child with degeneration and myoclonic seizures, and one who is brought to the hospital in status epilepticus without an available history.[10] Formulation of a differential diagnosis involves consideration of a number of questions, such as (1) whether the child does indeed have seizures, or whether they are being simulated by some other paroxysmal phenomenon such as breath-holding spells, hypoglycemia, syncope, or abnormal mannerisms; (2) whether the child has an emotional problem causing hysterical seizures; (3) what type of seizures are involved (for example, a child with simple petit mal may require no more than electroencephalography (EEG) and hyperventilation, whereas one with myoclonic seizures and neurological regression requires a more detailed evaluation); and (4) the age of the patient, since in a patient under 2 years one would not think of petit mal, and conversely in an adolescent one would not think of infantile spasms. If the patient is acutely ill on being brought to the emergency room, factors such as drugs, trauma, and infection need to be considered; however, if the patient has a chronic seizure disorder, these are not likely to be involved. The sequence C-I-T-T-E-N—D-V-M may serve as a useful mnemonic in reviewing the possible etiologies of seizure disorders:

C = congenital anomaly,
I = infection (intrauterine vs. acquired),
T = trauma,
T = toxin (lead),
E = endocrine (calcium/glucose),
N = neoplasm,

D = degenerative disorder,
V = vascular abnormality,
M = metabolic or miscellaneous (genetic).

Laboratory tests[11]

Routine blood studies must be performed to rule out systemic illness; such studies include a complete blood count to check for infection, blood sugar to rule out hypoglycemia, blood calcium to test for hypocalcemia, and liver function tests to rule out Reye's syndrome, among others. Other tests that may be useful (depending on the clinical situation) include arterial blood gases, chromosome analysis, toxicology, and serum amino acids.

Urine tests may be useful to rule out kidney disease and urinary tract infection. The urine metabolic screen includes a test for reducing substances such as glucose, galactose, and fructose; amino acid chromatography; the ferric chloride test for phenylketonuria, maple syrup urine disease, tyrosinosis, histidinemia, propionic acidemia, and methylmalonic aciduria; dinitrophenylhydrozine to test for the same defects; and cyanide nitroprusside to test for homocystinuria, glutathionuria, and cystinuria. Tissue biopsy may be diagnostic of seizure-associated degenerative disorders such as ceroid lipofuscinosis.

The EEG is extremely important in the diagnosis and treatment of epilepsy. At the same time, it is important to recognize what it can and cannot do. The EEG does not "make" the diagnosis of epilepsy, which is a clinical judgment; rather, its value lies in assessing the type of seizure. At times, it may determine the location of the discharge; at others, it may be useful in differentiating between hysterical and true seizures. However, it should be kept in mind that there are no absolutes: a normal EEG does not rule out epilepsy, and conversely an "epileptiform" EEG does not necessarily indicate that the patient has a clinical seizure disorder. Nevertheless, it is still fair to say that most patients with epilepsy exhibit abnormal electrical discharges at some time or another, and the type of discharge may indicate the type of epilepsy. Infantile spasms often produce a pattern called hypsarrhythmia, while atonic, akinetic, or myoclonic seizures are frequently associated with a multifocal spike-wave discharge or slow spike-and-wave pattern, absence or petit mal seizures with a 3/second generalized spike-and-wave pattern, and complex or simple partial seizures with a spike or sharp wave pattern which is limited to a single area of the brain. When the routine EEG shows no abnormalities, activating techniques are frequently used, as they may not only elicit abnormal electrical activity but can even provoke seizures in some patients. One such procedure involves having the patient breathe in and out deeply for about 3 minutes (hyperventilation), which can often be used to elicit absence seizures. As some abnormalities may show up when the patient is in light sleep, an EEG should be taken when the patient is asleep or sedated as well as awake. Rarely, special sensory techniques may be used if certain stimuli precipitate seizures; these could include sound, touch, or even reading a book. Photic stimulation, which involves producing flashes of light near the face, may also induce abnormality. In some patients thought to have complex partial seizures, a pair of soft, coated wire electrodes is inserted into the nostrils until they rest against the back of the nasopharynx; while this is uncomfortable, they may record electrical activity in an area of the temporal lobe that cannot be reached by the usual scalp electrodes. Closed-circuit TV monitoring with continuous EEG may be useful in evaluating the patient for possible seizure surgery, or in evaluating the patient with spells of unknown etiology. Many normal children may have minor abnormalities. However, specific problems such as sharp waves, spikes, polyspikes and waves, and focal slowing require further evaluation.

Skull radiographs may be abnormal in many CNS conditions but are rarely useful in epilepsy, and I use them only infrequently as part of the routine evaluation. Unfortunately, even when neurological disease is present, most skull radiographs show either no abnormalities or nonspecific changes such as bone erosion, calcification, shift in the pineal gland, fractures, or separation of the sutures.

Computed tomography (CT) is a safe, rapid, and accurate method of evaluating the intracranial contents and is useful in a wide variety of conditions, including congenital malformations, intracranial infections and their sequelae, trauma, neoplasms, degenerative diseases, and vascular disorders. Its accuracy equals or exceeds that of skull radiography, angiography, and pneumoencephalography combined. CT is the single most valuable test in evaluating focal seizures, focal neurological symptoms or signs, progressive disease, increased intracranial pressure, or a possible architectural abnormality of the brain. Intravenous contrast injection increases visualization of vascular abnormalities or neoplasms when the blood–brain barrier is breached.

Radionuclide studies are infrequently used in

epilepsy, since CT is more accurate; however, they can be of value if a mass is suspected and CT is not available. Cerebral arteriography, which involves intra-arterial injection of dye, is useful in delineating certain vascular abnormalities but is not routinely used in the diagnosis of epilepsy. However, if the patient is thought to have a vascular abnormality, such as a malformation of the vein of Galen, this test is absolutely necessary. Although digital subtraction angiography (DSA) cannot completely replace intra-arterial angiography, it can demonstrate the vascular system of the neck and cranial region on an outpatient basis and without an intra-arterial injection and is already being used to examine brain tumors in conjunction with CT.

Pneumoencephalography (PEG) involves introducing air into the spinal canal via a lumbar puncture. The air ascends into the ventricles of the brain, where a routine radiograph will outline any abnormality that is distorting them. While PEG was once useful in evaluating the parasellar region and brainstem, the development of CT with water-soluble contrast material injected into the subarachnoid spaces offers a less invasive method of visualizing these areas. Positron computed tomography (PCT), also called positron emission tomography (PET), uses signals from positron-emitting particles to create three-dimensional computer images, measure cerebral blood flow, and monitor brain metabolism, as ictal and metabolic patterns may differ from those of the interictal state. This technique is not commonly in use, but may be helpful in the future for better understanding of the etiology and pathogenesis of seizure disorders.

In nuclear magnetic resonance imaging (NMR), radio waves are beamed at the patient, who is placed within a giant magnet. These waves are converted to electrical signals, which the computer then changes to numbers, assigning a different color to each one to form an image of the internal structures. This is safer than radiographic methods because it does not expose the patient to ionizing radiation. Only a few NMR systems are currently in operation, and clinical applications are still being investigated; however, this technique has been used experimentally to demonstrate the spinal cord and certain parts of the brain that cannot be seen as well on CT.

A lumbar puncture is useful in determining the presence of infection or increased intracranial pressure, though it should be preceded by an enhanced CT scan. With advanced studies of the globulin fraction, demyelinating disease as well as certain tumors can also be diagnosed. However, if an intracranial space-occupying lesion is suspected, a lumbar puncture is contraindicated, since it may cause herniation. It is not used routinely in evaluating a chronic seizure disorder.

Psychological tests are useful in individuals with possible functional disease, either alone or associated with epilepsy. Such tests can be helpful in determining whether or not certain stressful circumstances are factors in precipitating true or hysterical seizures. They may include tests of general intellectual function, such as the Wechsler Intelligence Scale for Children [Revised] (WISC-R), or personality tests such as the Minnesota Multiphasic Personality Inventory (MMPI). Projective testing is rarely helpful. Other tests, such as visual, somatosensory, or brainstem auditory evoked potentials, electromyography, nerve conduction velocity, chromosomal analysis, and lysosomal enzyme tests may be useful in specific neurological disorders associated with seizures.

Once the results of the history, physical examination, and laboratory tests have been collated, a tentative diagnosis should be made.[10] If a seizure disorder is suspected, the type of seizures should be specified. Effective treatment of any such disorder depends on selection of the appropriate drug and dosage as well as removal of seizure stimuli.[11,12] Compliance with the therapeutic regimen depends on patient education. The patient should be followed up with anticonvulsant blood level determinations as well as repeated examinations. If the clinical course changes, reevaluation may be necessary. A balance between therapeutic benefit and potential side effects must be maintained. Attempts should be made to use a single drug at the appropriate dosage, which can be arrived at over a period of time by small increments to decrease the likelihood of side effects. If seizures are not controlled, or if toxicity supervenes, alternative treatments must be considered. It should be kept in mind that if two drugs are used together, their side effects may be additive. If a given combination is unsuccessful, the patient should be reevaluated before additional medication is given.[12]

In children without neurological deficits, medication might be discontinued over a period of weeks to months once seizures have been fully controlled for three to five years, depending on the clinical condition and EEG. Patients who

continue to demonstrate significant EEG abnormalities, a permanent and fixed neurological deficit, and/or progressive disease are at greater risk for recurrence once medication is discontinued. While the prognosis of patients whose seizures have been controlled for three to five years is not well documented, a recurrence rate of 20% to 25% is not unusual in children. Patients with epilepsy may need ongoing counseling about psychological, educational, and vocational problems.

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