REVIEW ARTICLE

Movement Disorders in Children

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Context: Movement disorders represent a common presentation in pediatrics and are often a source of clinical and diagnostic dilemmas. In this review, we provide an overview of common causes along with simplified clinical approach and management options for major movement disorders. **Sources:** This narrative review is based on contemporary evidence and personal experience. Medline was searched for recent advances, current understanding and consensus on classification, clinical features, diagnosis and treatment. **Results:** Movement disorders are classified as hyperkinetic and hypokinetic disorders, the latter being rare in childhood. The hyperkinetic disorders include dystonia, chorea, athetosis, tics and tremor, stereotypies, myoclonus, startle syndromes and functional disorders. Some movement disorders can be benign and developmental. A large proportion of conditions are genetic in origin with a guarded prognosis. Some of the conditions may be post-infectious, immune-mediated or drug induced. Multiple types of movement disorders are present in many conditions. The age at onset, type and distribution of abnormal movements and presence of associated neurological and systemic features help in narrowing the differential diagnosis. The pharmacotherapy of movement disorders is complex and evolving. **Conclusion**: A synopsis of movement disorders presenting in pediatric age has been provided, incorporating the latest evidence. A simplified approach for clinical diagnosis has been developed for dystonia and chorea.

Keywords: *Approach, Chorea, Dystonia, Myoclonus.*

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Movement disorders are conditions characterized by involuntary postures and/or movements. It represents a common presentation in pediatrics and is often a source of clinical and diagnostic dilemmas [1]. Classically, movement disorders are classified into hyperkinetic and hypokinetic disorders. Hyperkinetic disorders are characterized by abnormal involuntary movements and include dystonia, chorea, athetosis, stereotypies, myoclonus, tics and tremor. Hypokinetic disorders have in common a paucity of movements and include rare conditions like parkinsonism [2]. Dystonia and chorea are the most common forms of movement disorders. In many conditions, multiple types of movement disorders co-exist and it may be difficult to identify the type of movements.

There are no estimates on the prevalence of movement disorders in children or their proportion amongst pediatric presentations. The exact pathophysiology of movement disorders is not well understood; however, evidence suggests the involvement of either basal ganglia or cerebellar circuits in most of the conditions, which includes parts of thalamus and cortex [3]. We, herein, cover common movement disorders with emphasis on treatable conditions.

DYSTONIA

Dystonia is characterized by sustained or intermittent muscle contractions causing abnormal, often repetitive movements, postures, or both. Dystonic movements are typically patterned (repeatedly involve the same group of muscles), twisting, and may be tremulous [4]. The postures are exaggerated on voluntary actions and during stress and subside during sleep. It may be painful, if severe and continuous. In the affected body parts, muscle tone is typically variable, fluctuating from low to high. Children also demonstrate a splaying approach (spreading of fingers while approaching an object) and striatal toe sign (intermittent/persistent extension of the great toe). Sometimes, patients may show the oscillatory movement of limbs due to intermittent muscle contractions, known as dystonic tremors [5]. Often dystonia co-exists with spasticity in children with a severe brain injury like those with cerebral palsy.

According to a recent consensus [4], each patient with dystonia should be classified on a set of clinical (axis I) and etiological (axis II) descriptors (**Fig. 1**), as it aids in diagnosis and treatment. Historically, dystonia has been classified as primary and secondary. Primary refers to conditions that manifest with pure dystonia, without any associated other neurological features and without evidence of pathological abnormalities. All non-primary dystonia are labelled as secondary. In this review, disorders are grouped based on the presence of associated features, with an added category of acute-onset dystonia and paroxysmal dystonia.

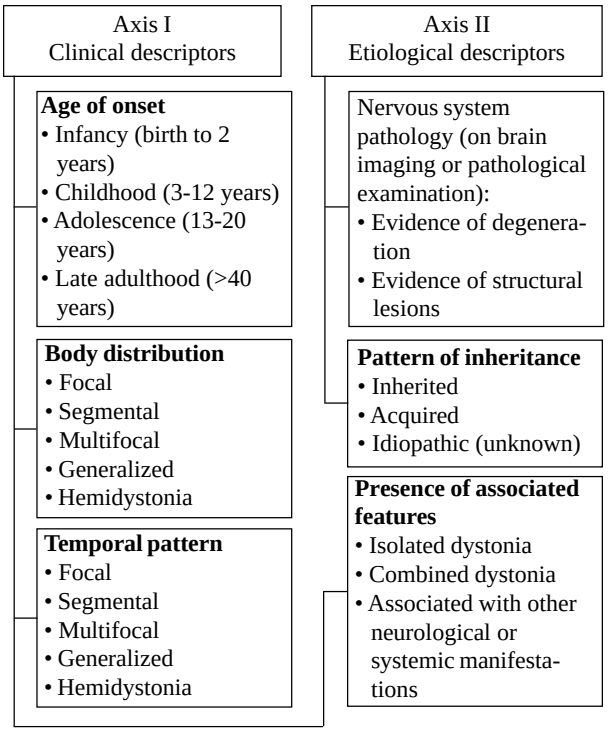

Fig. 1 Classification of dystonia [4].

Isolated Dystonia

Isolated dystonia refers to conditions in which dystonia is the only motor feature, with an exception of tremors [4]. Almost all these conditions are genetic in origin and most children have a period of normal motor development before the onset of dystonia. Most often there is a focal onset of dystonia with gradual progression. As most dystonia are associated with other movement disorders/ neurological comorbidities; with the increasing number of cases described in literature, entities with isolated dystonia are shrinking.

DYT-TOR1 dystonia is the most common entity within this group. It an autosomal dominant disorder with onset in late childhood or adolescence. It starts with focal limb dystonia, later progressing to generalized dystonia. DYT-HCPA dystonia starts within first decade with upper limb and cervical dystonia. Other forms of isolated dystonia can start with cranial or cervical dystonia (DYT-THAP and DYT-ANO3) [5,6].

Combined Dystonia

This group includes conditions in which dystonia is accompanied by features of parkinsonism or myoclonus, in absence of other neurological abnormalities. Dopa-responsive dystonia or Segawa disease (DYT-GCH1) is an important condition in this group. It is an autosomal dominant disorder that presents between 5-10 years of age with limb dystonia, with more severe involvement of lower limbs. The most characteristic feature is diurnal variation with children typically performing motor activities better in the morning or after a nap. Few children have some associated features of parkinsonism. Some cases may mimic spastic cerebral palsy. Dopa-responsive dystonia is a treatable condition and small to moderate doses of levodopa bring about a complete response. This also forms the basis of a trial of levodopa in any child with dystonia [5,7].

Other entities in this group include myoclonus-dystonia (DYT-SGCE, DYT-ANO3, DYT-TOR1A or DYT-CACNA1B) and rapid-onset dystonia-parkin-sonism (DYT-ATP1A3). Myoclonus-dystonia is genetically heterogeneous and can present any time after infancy with upper body myoclonus and limb dystonia. In patients with rapid onset dystonia-parkinsonism, symptoms are triggered with emotional or physical stress and there is often a stuttering course [5,8].

Associated With Other Manifestations

Children with cerebral palsy, and neurodegenerative and metabolic disorders form a major part of this group. Dystonia is often a feature in children with bilirubin induced neurological damage (BIND) and severe hypoxic-ischemic brain injury at birth.

Monoamine neurotransmitter disorders are a heterogeneous group of conditions that result from deficiency of cerebral dopamine, serotonin, or both. Most patients become symptomatic in infancy or early childhood with varying combination of developmental delay, encephalopathy, epilepsy, spasticity, dystonia, chorea and autonomic dysfunction. Some children may show diurnal variation. Analysis of CSF neurotransmitter levels aid in diagnosis. Dopa-responsive dystonia is also a monoamine neurotransmitter disorders but has fewer manifestations [9]

Progressive dystonia and spasticity in early childhood may be a manifestation of hypomyelinating leukoencephalopathies like Pelizaeus Merzbacher syndrome, which typically presents with pendular nystagmus, developmental delay and hypotonia in early infancy. Dystonia and ence-phalopathy can be seen in organic academia and mitochondrial encephalopathies [5]. Pantothenate kinase–associated neurodegeneration (PKAN) presents around 3 years of age with clumsiness and gait abnormality due to lower limb dystonia and spasticity, along with pigmentary retinopathy [10].

In children with onset of dystonia in late childhood or adolescence, Wilson disease is an important differential. Besides dystonia, tremors, dysphagia, dysarthria, drooling and walking difficulty may be present. Almost all patients have Kayser-Fleischer rings on eye examination [11].

Acute-Onset Dystonia and Paroxysmal Dystonia

Acute-onset dystonia can be a manifestation of adverse effects of drugs, stroke, encephalitis, and functional disorder. Anti-emetics (like metoclopramide) and antipsychotic drugs (like haloperidol and risperidone) are most commonly implicated in drug induced dystonia [12]. Dystonia is a common manifestation of neurotuberculosis and Japanese encephalitis.

Some genetic conditions manifest with episodic involuntary movements lasting from seconds to hours, most often with well-defined triggers. In between the episodes, the child is usually normal. This group includes conditions like Paroxysmal kinesigenic dystonia (triggered by sudden movement), Paroxysmal non-kinesigenic dystonia (triggered by stress, alcohol, etc.) and Paroxysmal exertional dystonia (triggered by exercise) [5,13].

Glut-1 deficiency is a rare condition that occurs due to a deficiency of glucose transporter type 1 in the brain. It manifests as absence epilepsy, ataxia, developmental delay and paroxysmal exertional dystonia in early childhood. Low CSF glucose is the biochemical hallmark and symptoms show a dramatic response to ketogenic diet [14].

Status Dystonicus

Status dystonicus, or dystonic storm is a life-threatening condition characterized by frequent or continuous severe episodes of generalized dystonic spasms. Although it can occur in any condition causing dystonia, it is most often seen in children with cerebral palsy and neurodegenerative disorders. Infections (febrile illnesses) and other stressors act as triggers. Severe spasm may result in pain, dehydration, respiratory compromise, rhabdomyolysis and acute renal failure [15,16].

Clinical Approach

While evaluating a child with dystonia, ascertain the age of onset, distribution (focal or generalized), temporal pattern (i.e. diurnal, static, or progressive) and associated neurological and systemic abnormalities. An important clue to etiology is that primary dystonia begins as action dystonia and can persist in kinetic form while secondary or symptomatic dystonia often begins as sustained postures or tonic form. **Fig. 2** provides an algorithm for clinical diagnosis.

Eye examination and brain MRI help in narrowing the differential diagnosis. Eye evaluation should be focused on KF ring, optic atrophy and retinitis pigmentosa. MRI is essentially normal in primary dystonia (DYT dystonia). MRI has diagnostic significance in Wilson disease (T2 hyperintensity in basal ganglia), PKAN ('Eye of the Tiger' sign in globus pallidus), hypomyelinating disorders (white matter changes) and Japanese encephalitis (bilateral thalamic involvement) [5].

Metabolic screening is warranted in a child with encephalopathy. In a child with fluctuating weakness, CSF analysis will help in ruling out neurotransmitter defect and Glut-1 deficiency. A therapeutic trial of levodopa is recommended for all children; although, very few dystonias are levodopa responsive, and there is a lot of variability in dose range for children who do respond [17]. In patients with suspected genetic etiology, dystonia gene panel testing may provide the definitive diagnosis. With the increasing availability of whole exome sequencing (WES), the diagnostic process can be significantly shortened [18].

Management

The drugs used in management of dystonia are detailed in **Table I**. In most patients with severe dystonia, outcomes are unsatisfactory. Neurosurgical procedures like deep brain stimulation (DBS) and intra-thecal baclofen pump (ITB) can be used in refractory dystonia. DBS has shown substantial benefits in children with primary dystonia, whereas in children with dyskinetic cerebral palsy, mild to moderate improvement occurs [22].

The management of status dystonicus is multi-pronged. Patients should be monitored for renal functions, creatine kinase, blood gas, and urine and/or blood myoglobin levels. Addressing the precipitant and providing supportive care (hydration, respiratory support, hemodialysis etc.) is important. The mainstay of therapy is careful use of sedatives. Chloral hydrate is recommended as initial therapy (30-100 mg/kg orally every 3-4 hours). Most patients need the addition of clonidine (initial dose 3µg/kg 8 hourly, can be increased up to 3-5 µg/kg/hour given as 3-hourly dose. In unresponsive patients, continuous midazolam infusion may be effective. Besides sedatives, dystonia specific drugs like trihexyphenidyl, pimozide and tetrabenazine are also required. In patients with poor response to drugs, DBS should be offered. The role of ITB is less clear but may be more effective in patients with concomitant spasticity [15-16].

TREMORS

Tremors refer to rhythmic, regular back-and-forth or oscillatory movement of part of the body about a joint axis [23]. Tremors are classified as resting tremors and action tremors.

Resting tremors are quite rare in childhood; however, can be seen in juvenile parkinsonism, Wilson disease, PKAN, Huntington disease and midbrain lesions [24]. Psychogenic and dystonic tremors can also be present at

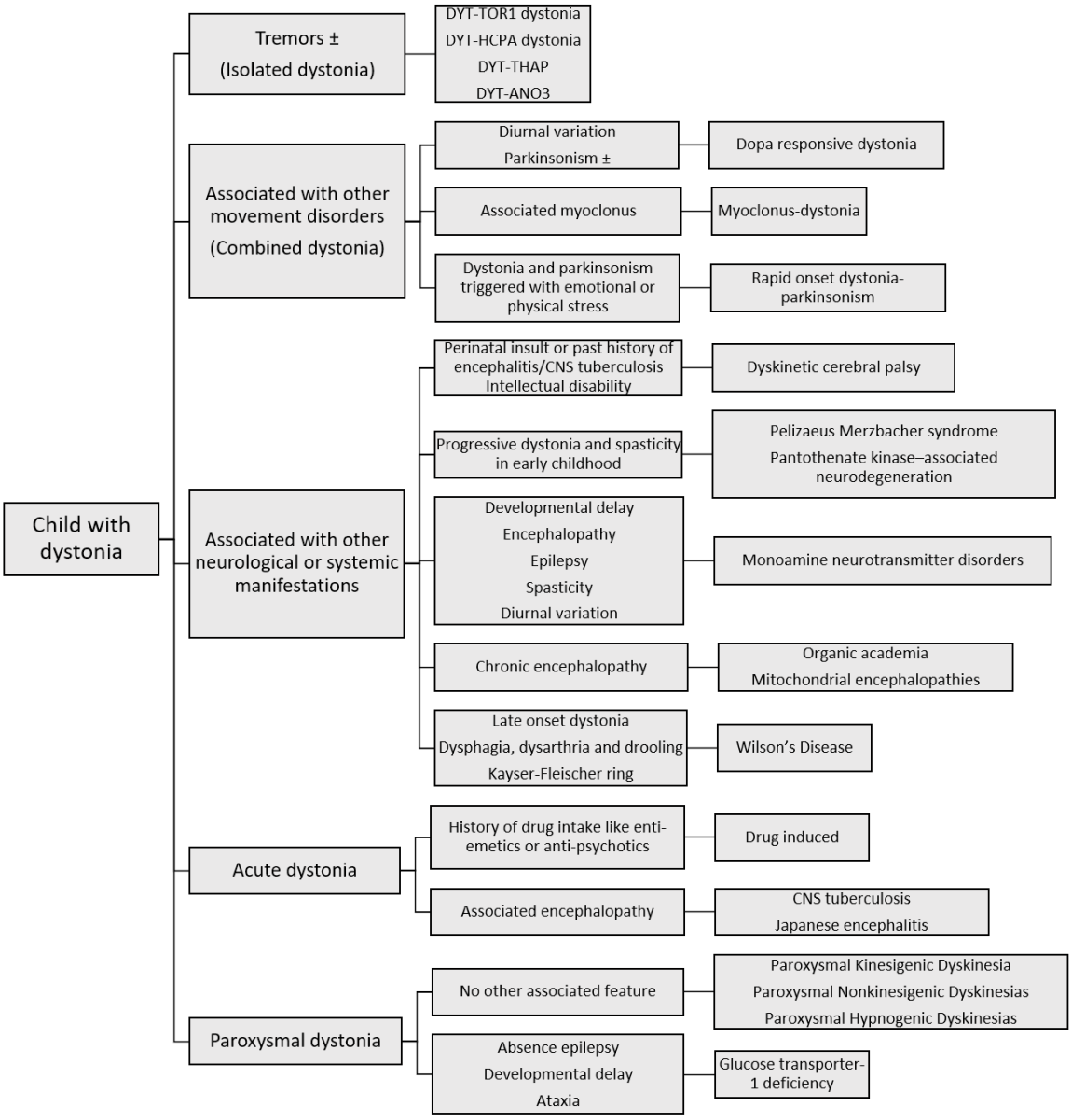

Fig. 2 Clinical approach to diagnosis of dystonia in children.

rest. In context to developing countries, infantile tremor syndrome (ITS) is an important cause. ITS typically manifest in exclusively breastfed infants of vegetarian mothers, with developmental delay/regression, anemia, skin hyperpigmentation, and tremors. Tremors usually start with upper limbs and subside during sleep. Almost all patients have vitamin B12 deficiency and respond to supplementation [25].

Action tremors are further classified as simple kinetic, intention, isometric, task-specific and postural. Simple kinetic tremor is present during simple limb movements. It is typically a feature of essential tremor. Essential tremor affects only the upper limbs and family history is present in many patients. Usually, the onset is in adulthood or later, but can sometimes occur in children. A duration of 3 years is required for diagnosis [24]. Functional and drug-induced tremors can also be simple kinetic. In intention tremor, the amplitude of tremor increases as the body part is reaching a visual target. It is characteristically seen in cerebellar disorders but can also be present in midbrain lesions [24,26].

Postural tremor is seen when a body part is held in a position against gravity. Each individual has some physiological postural tremor, best appreciated in an

Table I Drugs Used for Dystonia [19-21]

Drug name	*Mechanism*	*Dose*	*Side effect*	*Comments*
Levodopa (used in combination with carbidopa)	Dopa agonist	Start at 1 mg/kg/d divided TID. Increase weekly by 1 mg/kg/d to a target dose of 5-10 mg/kg/d	Nausea, diarrhea	3-4 wk trial (at target dose) recommended in all children with dystonia. Effective only in Monoamine neuro-transmitter disorders.
Trihexyphenidyl	Anti-cholinergic	Start at 0.2 mg/kg/d divided TID. Increase weekly by the same dose till a maximum dose of 2 mg/kg is reached or side effects appear	Constipation and dry mouth	Effective in most forms of dystonia
Baclofen	GABAergic	Start at 0.3mg/kg/d divided TID. Titrate weekly by 0.1-0.3 mg/kg/day. Maximum dose 40 mg/d in <2 y and 60 mg/d in ≥2y	Sedation, axial hypotonia	Also effective in spasticity
Clonazepam	GABAergic	Start with 0.25 mg BD. Increase by 0.25-0.5 mg/day every 3-4 d to maximum dose of 0.1-0.2 mg/kg/d	Sedation, confusion	
Tetrabenazine	Block vesicular monoamine trans-porter type 2	Start with 6.25-12.5 mg once/twice daily. Increase by same dose weekly to maximum of 50 mg/d divided BD	Nausea, parkinsonism	Effective in a variety of movement disorders
Botulinum toxin injection	Neuromuscular blockage	Depends on muscles injected		Used for focal dystonia like cervical or upper limb dystonia
Diphenhydramine	H1-antagonist	Initial: 1-2 mg/kg/dose (max 50 mg) IV/IM; may repeat if necessary Subsequent: 5 mg/kg/d in 3-4 divided doses Oral/IV (max 50 mg/dose) for 1-2 d	Sedation	Used for drug induced dystonia

outstretched hand. This can be exaggerated by stress, fasting, illness, strenuous exercise, thyrotoxicosis and drugs like salbutamol and valproate. Isometric dystonia occurs during sustained muscle contraction against stationary objects like while holding a book. Exaggerated physiological tremor and essential tremor can be isometric. Task-specific dystonia is related to specific tasks like writing or playing an instrument [24,26].

Clinical Approach and Management

While evaluating a child with tremors, note the onset, aggravating and relieving factors, drug history and family history. Examine for tremors along with muscle tone and gait pattern. Presence of associated dystonia points towards conditions like PKAN and Wilson disease. Sudden onset and offset and marked variation in the semiology favours psychogenic tremor. Some patients with only dystonia may show tremulous limb movements, referred as dystonic tremors. Other conditions that mimic tremors include jitteriness, seizures, myoclonus, shuddering attacks, and stereotypic movements.

Investigations will depend on the suspected etiology. Thyroid function should be done for enhanced physiological tremors. Neuroimaging and other relevant workup should be done for suspected cerebellar disorder or a neurodegenerative condition. For ITS, vitamin B12 levels should be obtained.

Propanolol is recommended in severe cases of essential tremors and patients with physiological tremors who have functional or social limitations. Other drugs that are effective in essential tremors include primidone and benzodiazepines [24,26].

CHOREA

Chorea refers to involuntary, irregular, non-repetitive dance-like movements of the body parts that appear to flow from one muscle group to another without following any pattern. Children with chorea appear hyperactive or fidgety. The ability to perform voluntary movements remains unimpaired. Many grown-up children with chorea transform the choreiform movement into a voluntary act in order to mask it, referred to as parakinesia [27]. Patients with chorea have motor impersistence, which refers to the inability to maintain sustained postures like keeping tongue protruded or arms outstretched [28]. Like all movement disorders, chorea also disappears during sleep.

Chorea with large amplitude, rapid flinging movements, usually affecting the proximal joints is referred as ballism [23]. Some patients have slower continuous, involuntary writhing movements affecting the distal upper extremities, referred to as athetosis. Athetosis is a distinct movement disorder; however, it co-exists with chorea and ballism, and represents a clinical spectrum [23].

Chorea due to a known or presumed genetic cause is referred as primary chorea. Chorea resulting from infections, injuries, infiltrative conditions or immune mediated disorders affecting the brain is called as secondary chorea.

Primary Chorea

Huntington disease: It is an autosomal dominant disorder that manifest in late adulthood with chorea, dystonia, psychiatric disturbances, and dementia. Juvenile Huntington disease is rare and more commonly present with dystonia, parkinsonism, behavior problems, and cognitive deterio-ration, rather than chorea [29].

Ataxia-telangiectasia: Choreoathetosis involving the upper extremities is an early feature of Ataxia-Telangiectasia, however; it is often mild. Ataxia that develops by 3-6 years of age is the prominent manifestation and brings the child to medical attention [30].

Benign hereditary chorea: It is an autosomal dominant condition with median age of onset of 2.5-3 yrs. The intelligence is normal and the condition tends to become static after the first decade with improvement in adulthood. Some patients have accompanying hypothyroidism and pulmonary disease [31].

Others: In some conditions like spinocerebellar ataxia type 17, ataxia with oculomotor apraxia and Friedreich ataxia, chorea may be an early feature, though ataxia predomi-nantes as the disease progresses. Paroxysmal movement disorders present with intermittent episodes of chorea and dystonia [13]. There is a growing list of genetic etiologies of chorea, with mutation in *ADCY5* and *PDE10A* being important cause of childhood onset movement disorders [32].

Secondary Chorea

Sydenham chorea: This is the most common cause of acute-onset chorea in children. It is a late manifestation of acute rheumatic fever and affects children aged 5-15 years. The chorea mainly involves the upper extremities and at times there may be wide flinging movements (ballism) [27]. The other manifestations include hypotonia, personality changes, emotional lability, obsessive-compulsive symptoms and attention-deficit [33]. Diagnosis is mostly clinical as the laboratory evidence of recent streptococcal infection is often lacking.

Other immune-mediated conditions: Chorea may be the presenting or associated feature in children with systemic lupus erythematosus associated with anti-cardiolipin antibodies. Chorea may be a feature of autoimmune encephalitis, the other manifestations being seizures, encephalopathy and neuropsychiatric disturbances [34].

Chorea associated with brain injury: Children with dyskinetic cerebral palsy may have chorea, besides dystonia. Chorea may be a part of neurological sequelae after viral encephalitis or stroke.

Drug-induced chorea: Certain drugs like trihexyphenidyl, levodopa, phenytoin and carbamazepine can precipitate chorea in a child with other types of movement disorders or brain injury [27].

Clinical Approach and Management

The history should include perinatal events, previous infections and associated symptoms. The child should be examined in a distraction-free environment to note the presence of chorea and any other movement disorder. Video recording of movements by parents at home help in characterization of movements. Child should be examined for motor impersistence, including inability to keep tongue protruded (darting tongue), maintain sustained arm grip on examiners fingers (milkmaid's grip) and keep upper limbs extended above the head with palms facing inwards [28]. A clinical approach to diagnosis is discussed in **Fig. 3**. Diagnostic work-up depends on the suspected etiology.

Atypical antipsychotics like olanzapine or risperidone are effective in the management of acute onset chorea or

acute exacerbation. Tetrabenazine and anti-epileptics like valproic acid and carbamazepine are alternatives. Valproic acid can be tried in patients who fail to respond to anti-psychotics. Patients with severe forms of Sydenham chorea or those unresponsive to antipsychotics may respond to intravenous immunoglobulin or corticosteroids [35,36]. In patients with Huntington disease, the preferred drugs are tetrabenazine, olanzapine, risperidone, and recently, deutetranenazine [37].

TIC DISORDER

Tics refer to repeated, individually recognizable, intermittent movements, movement fragments, or sounds that are almost always briefly suppressible and are usually associated with awareness of an urge to perform the movement [23]. The premonitory urge to carry out the movement is often distressing to older patients. Tics can manifest after 5-6 years of age; however, adolescents are most severely affected. Tics may affect the social functioning of an individual and cause embarrassment. Tics are presumed to be genetic because of the high concordance rate between twins (53%); however, the genetic loci are not known. Mostly, tic is a primary problem, rarely it may be part of other neurological disorders [38,39].

Tics are classified based on type (motor or vocal) and duration. A tic can be simple (like eye blinking, head jerking, facial grimacing, brief vocalization, throat clearing, and sniffing) or complex (like obscene gestures or copropraxia, posturing, echolalia, and coprolalia). A tic disorder that has been there for less than a year or subsides within a year is labelled as transient tic disorder. Those lasting more than a year are called chronic and include Tourette syndrome and persistent motor or vocal tic disorder [38,39].

Tourette syndrome is defined by presence of multiple motor tics (at least two distinct ones) and one or more vocal tics which wax and wane, but have persisted for more than one year [39]. It is commonly associated with behavioral disorders like attention-deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), anxiety, mood disorders and disruptive behavior disorders. About two-third of individuals meet the criteria of ADHD or OCD at some time during the course of disease [40]. Persistent motor or vocal tic disorder is defined as having a single or multiple motor or vocal tics which may wax and wane but have persisted for more than one year. Tics may sometimes be part of autism spectrum disorder and neurodegenerative disorders.

Management

Comprehensive behavioral intervention for tics (CBIT) is efficacious in reducing tics and is recommended as the initial treatment. CBIT program consists of habit reversal therapy, relaxation training, and functional interventions to address situations that sustain or worsen tics. If CBIT is ineffective or unavailable, pharmacotherapy can be used. A variety of drugs are effective including alpha-agonists like clonidine and guanfacine, anti-psychotics like haloperidol, pimozide and risperidone and anti-epileptics like topiramate. Alpha-agonists have lower efficacy than anti-psychotics but are preferred due to favorable side effect profile. Alpha-agonists also improve the behavioral comorbidities [41,42].

MYOCLONUS AND STARTLE SYNDROMES

Myoclonus is a sudden, brief, shock-like involuntary movement of the body. It can involve a single body part, one half of body or whole body. Myoclonus is mostly spontaneous, but in some conditions it can be induced by an action or sensory stimuli like light, sound or touch [1]

Hiccups and sleep starts are considered as physiological forms of myoclonus. Sleep starts occur during sleep initiation, manifesting with a sense of falling [1]. Benign neonatal sleep myoclonus and benign myoclonus of early infancy are viewed as developmental conditions (detailed later) [47]. Many young children manifest myoclonus during febrile episodes. Myoclonus can be epileptic as in some epileptic syndromes (like West syndrome and juvenile myoclonic epilepsy) and neurodegenerative disorders [1].

Opsoclonus-myoclonus syndrome (OMS) is a rare immune-mediated condition that manifests acutely or sub-acutely in toddlers with chaotic multi-directional conjugate eyes movements (opsoclonus), myoclonus, ataxia, irritability and sleep disturbance. Approximately half of the patients have associated neural crest tumors (mostly a neuroblastoma). A combination of pulse corticosteroids or ACTH and intravenous immunoglobulins are recommended as the initial treatment. Surgical tumor resection has no effect on the symptoms in the majority [43,44].

Startle syndromes are conditions characterized by exaggerated startle in response to a sound, movement and touch. Hereditary hyperekplexia is an autosomal dominant disorder that manifest in infants and young child with exaggerated startle associated with tonic stiffness of the body, with repeated falls. A bedside test involves demonstration of non-habituating head retraction in response to repeated tapping of the tip of the nose. With increasing age, the severity improves; however, it can be precipitated by stress or fatigue. Most children respond to clonazepam in the dose range of 0.01 - 0.1 mg/kg/day [45,46].

Other conditions associated with exaggerated startle

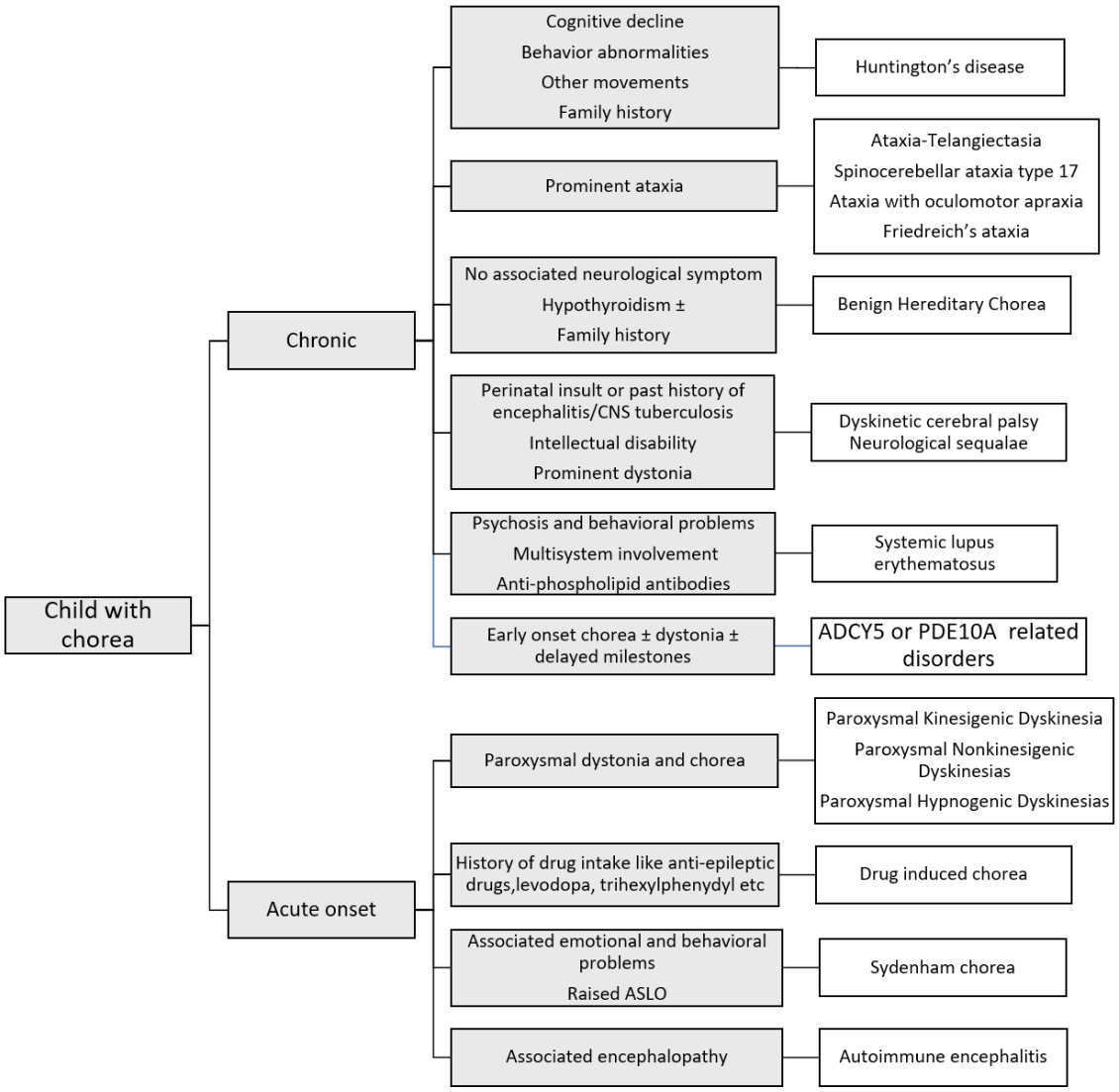

Fig. 3 Clinical approach to diagnosis of chorea in children.

are other forms of hyperekplexia, post-hypoxic and post-traumatic encephalopathy, encephalitis, brainstem dysfunc-tion and neurodegenerative disorders like GM1 ganglio-sidosis and Tay-Sach disease [46].

STEREOTYPIC MOVEMENT DISORDERS

Stereotypies refer to repetitive, non-functional, patterned movements and/or vocalizations that can be suppressed by distraction. Simple stereotypies like leg shaking, hair twirling, body rocking, head banging, and humming are considered as part of normal behavior. Complex stereotypies like hand flapping, oro-facial movement and eye-poking, which interfere with functions or are self-injurious are considered as abnormal [47]. Complex stereotypies are sometimes seen in typically developing children, but tend to remain stable or regress with age. More commonly, they are associated with conditions like autism spectrum disorders, intellectual disability, Rett syndrome, Down syndrome, phenylketonuria, visual or auditory impairment, and acquired brain injury [47,48]. In children with blindness, stereotypies are seen in more than two-third of patients, the common ones are body rocking, repetitive handling of objects, hand and finger movements, eye pressing and eye poking [49]. Behavior therapy (habit reversal therapy) is the mainstay of treatment for stereotypies. Drugs like risperidone and fluoxetine have role in patients with autism [47,48].

PARKINSONISM

Parkinsonism is a hypokinetic movement disorder,

characterized by presence of resting tremors, bradykinesia (paucity or slowness of movements), rigidity (lead pipe type) and postural instability. It can occur in conditions like Huntington disease and Wilson disease, or can be an adverse effect of tetrabenzine. Juvenile Parkinson disease is a rare genetic disorder that manifest with parkinsonism and leg dystonia [50].

FUNCTIONAL MOVEMENT DISORDERS

It refers to involuntary movements that result from abnormal mental state or condition, and are incompatible with recognized neurological and medical conditions. The common presentations in children are tremors, dystonia and myoclonus; others being gait disturbances, tics, chorea and tetany. Many children have identifiable precipitating factors like school examination, bullying, injury, illness, sexual abuse of the child or family member, parental discord or domestic violence, and death of a close relative [51-53]. It is mostly seen in children above 6-7 years and is more common in girls.

The diagnosis is suggested by a history of sudden onset, marked variability of symptoms, and sustained spon-taneous remissions. Examination often shows symptom variation, incongruous movements, distraction during spontaneous speech and behavior, the appearance of symptoms, or worsening during attention and production or suppression of symptoms on examiner's suggestion [51]. In psychogenic tremor, entrainment or alteration with rhythmic tapping of another body part is seen. For management, behavior therapy and relaxation techniques are usually employed. Parental education and counseling are important [53].

DEVELOPMENTAL AND BENIGN MOVEMENT DISORDERS

These are a group of conditions that manifest during specific developmental phases of childhood in absence of associated neurological features. They are considered as manifestation of subtle modification in the developing brain and have a favorable outcome [54]. The common disorders are detailed in **Table II**.

CONCLUSION

Movement disorders in children comprise of a heterogeneous group of conditions with diverse etiologies. The predominant conditions are dystonia, chorea, tics and tremors. Multiple movement disorders coexist in many conditions and often create diagnostic confusion. Presence of other neurological and systemic manifestations helps in narrowing the differential diagnosis. Neuroimaging and genetic studies enables accurate diagnosis. The management of these conditions is often challenging. One should always look for easily treatable conditions like dopa-responsive dystonia and infantile tremor syndrome.

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REFERENCES

1. Delgado MR, Albright AL. Movement disorders in children: definitions, classifications, and grading systems. J Child Neurol. 2003;18:S1-8.
2. Fahn S. Classification of movement disorders. Mov Disord. 2011;26:947-57.
3. Wichmann T. Pathophysiologic Basis of Movement Disorders. Prog Neurol Surg. 2018;33:13–24.

Table II Common Developmental and Benign Movement Disorders [45]

Disorders	*Age at onset*	*Age at resolution*	*Clinical features*
Jitteriness	<2 wk	< 1 mo	Paroxysmal, bilateral, high frequency tremor involving the extremities and chin, often exaggerated by startle or cry. Sometimes, can be a manifestation of drug withdrawal, hypocalcemia, hypoglycemia or encephalopathy.
Benign neonatal sleep myoclonus	<2 wk	< 6 mo	Myoclonic jerks in sleep, which disappear completely on waking up.
Benign myoclonus childhood	< 1 y	< 3 y	Upper body myoclonus occurs in absence of other neurological of features.
Spasmus nutans	4-18 mo	3- 4 y	Triad of paroxysmal head nodding (usually of no-no type), nystagmus (asymmetric, dysconjugate and horizontal) and torticollis (head tilting).
Benign paroxysmal torticollis	<3 mo	< 4 y	Recurrent episodes of painless rotation and inclination of head, often alternating from side to side. Sometimes associated with lateral incurvation of spine.
Shuddering attacks	< 1y	< 4 y	Brief, paroxysmal episodes characterized by shivering of head, shoulders and sometimes the trunk. Each episode last for few seconds and a child may have up to 100 episodes per day.

4. Albanese A, Bhatia K, Bressman SB, et al. Phenomenology and classification of dystonia: a consensus update. Mov Disord. 2013;28:863-73.
5. Meijer IA, Pearson TS. The twists of pediatric dystonia: Phenomenology, classification, and genetics. Semin Pediatr Neurol. 2018;25:65-74.
6. Zorzi G, Zibordi F, Garavaglia B, et al. Early onset primary dystonia. Eur J Paediatr Neurol. 2009;13:488-92.
7. Segawa M. Autosomal dominant GTP cyclohydrolase I (AD GCH 1) deficiency (Segawa disease, dystonia 5; DYT 5). Chang Gung Med J. 2009;32:1-11.
8. Balint B, Bhatia KP. Isolated and combined dystonia syndromes - an update on new genes and their phenotypes. Eur J Neurol. 2015;22:610-617.
9. Kurian MA, Gissen P, Smith M, et al. The monoamine neurotransmitter disorders: an expanding range of neurological syndromes. Lancet Neurol. 2011;10:721-33.
10. Hayflick SJ, Kurian MA, Hogarth P. Neurodegeneration with brain iron accumulation. Handb Clin Neurol. 2018;147:293-305.
11. Roberts EA, Socha P. Wilson disease in children. Handb Clin Neurol. 2017;142:141-56.
12. Goraya JS. Acute movement disorders in children: experience from a developing country. J Child Neurol. 2015;30:406-11.
13. Waln O, Jankovic J. Paroxysmal movement disorders. Neurol Clin. 2015;33:137 152.
14. Koch H, Weber YG. The glucose transporter type 1 (Glut1) syndromes. Epilepsy Behav. 2019;91:90-93.
15. Allen NM, Lin JP, Lynch T, et al. Status dystonicus: a practice guide. Dev Med Child Neurol. 2014;56:105-112.
16. Lumsden DE, King MD, Allen NM. Status dystonicus in childhood. Curr Opin Pediatr. 2017;29:674-82.
17. Maas RPPWM, Wassenberg T, Lin JP, et al. l-Dopa in dystonia: A modern perspective. Neurology. 2017;88:1865-1871.
18. Powis Z, Towne MC, Hagman KDF, et al. Clinical diagnostic exome sequencing in dystonia: Genetic testing challenges for complex conditions. Clin Genet. 2020;97:305-11.
19. Luc QN, Querubin J. Clinical Management of Dystonia in Childhood. Paediatr Drugs. 2017;19:447 61.
20. Fehlings D, Brown L, Harvey A, et al. Pharmacological and neurosurgical interventions for managing dystonia in cerebral palsy: a systematic review. Dev Med Child Neurol. 2018;60:356-66.
21. Hegenbarth MA; American Academy of Pediatrics Committee on Drugs. Preparing for pediatric emergencies: drugs to consider. Pediatrics. 2008;121:433-43.
22. Elkaim LM, De Vloo P, Kalia SK, et al. Deep brain stimulation for childhood dystonia: current evidence and emerging practice. Expert Rev Neurother. 2018;18:773-84.
23. Sanger TD, Chen D, Fehlings DL, et al. Definition and classification of hyperkinetic movements in childhood. Mov Disord. 2010; 25:1538-549.
24. Miskin C, Carvalho KS. Tremors: Essential Tremor and Beyond. Semin Pediatr Neurol. 2018;25:34 41.
25. Goraya JS, Kaur S. Infantile tremor syndrome: A review and critical appraisal of its etiology. J PediatrNeurosci. 2016;11:298 304.
26. Prasad M, Ong MT, Whitehouse WP. Fifteen minute consultation: tremor in children. Arch Dis Child Educ Pract Ed. 2014;99:130 134.
27. de Gusmao CM, Waugh JL. Inherited and acquired choreas. Semin Pediatr Neurol. 2018;25:42 53.
28. Kojoviæ M, Bhatia KP. Bringing order to higher order motor disorders. J Neurol. 2019;266:797-805.
29. Roos RA. Huntington's disease: A clinical review. Orphanet J Rare Dis. 2010;5:40.
30. Pearson TS. More than ataxia: Hyperkinetic movement disorders in childhood autosomal recessive ataxia syndromes. Tremor Other Hyperkinet Mov. 2016;6:368.
31. Peall KJ, Kurian MA. Benign hereditary chorea: An update. Tremor Other Hyperkinet Mov. 2015;5:314.
32. Carecchio M, Mencacci NE. Emerging monogenic complex hyperkinetic disorders. Curr Neurol Neurosci Rep. 2017;17:97.
33. Punukollu M, Mushet N, Linney M, et al. Neuropsychiatric manifestations of Sydenham's chorea: A systematic review. Dev Med Child Neurol. 2016;58:16-28.
34. Cardoso F. Autoimmune choreas. J Neurol Neurosurg Psychiatry. 2017;88:412-17.
35. Walker KG, Wilmshurst JM. An update on the treatment of Sydenham's chorea: The evidence for established and evolving interventions. Ther Adv Neurol Disord. 2010;3:301-9.
36. Dean SL, Singer HS. Treatment of sydenham's chorea: A review of the current evidence. Tremor Other Hyperkinet Mov. 2017;7:456.
37. Coppen EM, Roos RA. Current pharmacological approaches to reduce chorea in Huntington's disease. Drugs. 2017;77:29-46.
38. Leckman JF. Phenomenology of tics and natural history of tic disorders. Brain Dev. 2003;25:S24-S28.
39. Fernandez TV, State MW, Pittenger C. Tourette disorder and other tic disorders. Handb Clin Neurol. 2018;147:343-54.
40. Hirschtritt ME, Lee PC, Pauls DL, et al. Lifetime prevalence, age of risk, and genetic relationships of comorbid psychiatric disorders in Tourette syndrome. JAMA Psychiatry. 2015;72: 325-33.
41. Pringsheim T, Okun MS, Müller-Vahl K, et al. Practice guideline recommendations summary: Treatment of tics in people with Tourette syndrome and chronic tic disorders. Neurology. 2019;92:896-906.
42. Quezada J, Coffman KA. Current approaches and new developments in the pharmacological management of Tourette synd-rome. CNS Drugs. 2018;32:33-45.
43. Desai J, Mitchell WG. Acute cerebellar ataxia, acute cerebellitis, and opsoclonus-myoclonus syndrome. J Child Neurol. 2012;27:1482-8.
44. Hero B, Schleiermacher G. Update on pediatric opsoclonus myoclonus syndrome. Neuropediatrics. 2013;44:324-9.
45. Saini AG, Pandey S. Hyperekplexia and other startle syndromes. J Neurol Sci. 2020 Sep 15;416:117051.
46. Bakker MJ, van Dijk JG, van den Maagdenberg AM, et al. Startle syndromes. Lancet Neurol. 2006;5:513-24.
47. Katherine M. Stereotypic Movement Disorders. Semin Pediatr Neurol. 2018;25:19-24.
48. Barry S, Baird G, Lascelles K, et al. Neurodevelopmental movement disorders - an update on childhood motor stereotypies. Dev Med Child Neurol. 2011;53:979-985.
49. Fazzi E, Lanners J, Danova S, et al. Stereotyped behaviors in blind children. Brain Dev. 1999;21:522-28.
50. Niemann N, Jankovic J. Juvenile parkinsonism: Differential diagnosis, genetics, and treatment. Parkinsonism Relat Disord. 2019;67:74-89.
51. Hallett M. Functional (psychogenic) movement disorders - Clinical presentations. Parkinsonism Relat Disord. 2016;22: S149-S152.
52. Harris SR. Psychogenic movement disorders in children and adolescents: an update. Eur J Pediatr. 2019;178:581-585.
53. Pandey S, Koul A. Psychogenic movement disorders in adults and children: A clinical and video profile of 58 Indian patients. Mov Disord Clin Pract. 2017;4:763-67.
54. Bonnet C, Roubertie A, Doummar D, et al. Developmental and benign movement disorders in childhood. Mov Disord. 2010;25:1317-3.