REVIEW

Neurological disorders presenting mainly in adolescence

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The aim of this review is to discuss some of the neurological diseases that present mainly in the adolescent period. The article focuses on the usual presentation and course of the more common, and some uncommon, epilepsies, neuromuscular disorders, neurodegenerative disorders, inflammatory disorders of the central nervous system and some other, miscellaneous conditions. The article ends with a very brief and general discussion about management issues in this age group.

Recent medical publications, including two from the National Health Service,[1 2] have focused on adolescent health issues, and specifically the transition from paediatric to adult services. A recent review in *Archives of Disease in Childhood* outlined some of the major issues at this time of life, and highlighted the important differences between traditional paediatric practice and adolescent medicine.[3] The Oxford dictionary defines adolescence as the process of developing from a child to an adult, and the word itself is derived from the Latin word adolescere, meaning to come to maturity. The age at which a child enters and completes adolescence is therefore difficult to characterise and depends on many variables including sex, health, sociocultural values and economic factors. For the purposes of this review, adolescence will refer to children aged ⩾12 years.

The aim of this review is to describe the common and many of the less common neurological disorders that may have an onset or are present in adolescence; it is not possible to provide a comprehensive and detailed account of all the neurological disorders that may present in the teenage years—for example, head injury, brain tumour, stroke or Guillain–Barré syndrome, partly because these conditions may present throughout childhood, including adolescence. It is also not within the remit of this review to discuss in detail either the diagnostic process or the management of these disorders.

NORMAL NEURODEVELOPMENT IN ADOLESCENCE

Adolescents show significant neuropsychological progress in the years leading up to adulthood, although this may lack the dramatic effect of a toddlers taking their first steps or uttering their first words.[4] Structurally, the brain continues to increase in total volume until the age of approximately 14 years. A longitudinal magnetic resonance imaging (MRI) study showed that the total white matter volume continues to increase into the early 20s, frontal and parietal grey matter volume peaks at approximately 14 years of age before declining, and the grey matter in the occipital and temporal lobes continues to increase until 20 years of age.[5] The decrease in frontal grey matter volume is probably due to massive synaptic loss during this period; data from primate models have estimated that up to 30 000 synapses may be lost per second over the entire cortex, particularly from the frontal regions. Although the precise reason for this is unknown, it is speculated that the brain is developing on the basis of experience and pertinent environmental needs—the ''use it or lose it'' theory. Finally, there seems to be much more focal activation of the brain in adolescence compared with early childhood, with a marked increase in the degree to which each hemisphere can process information independently.

NEUROLOGICAL DISORDERS

Epilepsy

Epilepsy is the most common neurological disorder of adolescence.[6 7] Epilepsy may have an onset at this time or pre-existing epilepsy may continue to remit or deteriorate. Accurate history taking is crucial to the diagnosis. As teenagers usually attend clinic with parents who have not witnessed the paroxysmal events, it may be necessary to talk to their friends and schoolteachers to obtain useful, and even diagnostic, information. Investigations are used to classify epilepsy syndromes in order to guide treatment and inform on prognosis and to identify any underlying cause. There are some important epilepsy syndromes commonly present in adolescence.

Juvenile myoclonic epilepsy

The most common epilepsy syndrome presenting in adolescence is juvenile myoclonic epilepsy (JME).[8] The syndrome is characterised by myoclonic seizures (typically on awakening, but also at other times) in all patients, generalised tonic–clonic seizures (GTCS) in approximately 90% and brief absence seizures in approximately 60% of patients. Presentation is typically with a tonic–clonic seizure, often on wakening after a late night or sleep deprivation (common at this age). Another frequent presentation is when the child/teenager has been playing on a video game, often late at night and in a dark room, indicating probable photosensitivity, a

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Abbreviations: ADEM, acute disseminated encephalomyelitis; CAE, childhood-onset absence epilepsy; CPT-2, carnitine-palmitoyl transferase type II; EEG, electroencephalogram; GTCS, generalised tonic–clonic seizures; HMSN, hereditary motor and sensory neuropathy; JAE, juvenile absence epilepsy; JME, juvenile myoclonic epilepsy; MRI, magnetic resonance imaging; PKAN, panthotenate kinase-associated neurodegeneration; PME, progressive myoclonic epilepsy

commonly observed phenomenon in this syndrome, occurring in 40% and possibly up to 80%[9] of patients and with a female predominance. It is important to ask the teenager presenting with a first GTCS about it and, if necessary, mime the myoclonic and absence seizures, which may not be recognised as seizures by either the teenagers or their friends and carers. Seizures are usually well controlled with appropriate drugs (usually sodium valproate) in up to 90% of patients; it is relatively common that some teenagers will be prescribed carbamazepine, which, although it controls the tonic–clonic seizures, usually exacerbates the myoclonic and absence seizures. This again emphasises the need to always ask about ''jerks'', ''twitches'' and ''blank periods'' when initially assessing these teenagers. Seizure recurrence rate after drug withdrawal is high in JME, with approximately 80% of patients relapsing, even after a 2–3-year period of seizure freedom.

Juvenile absence epilepsy

Juvenile absence epilepsy (JAE) is another idiopathic generalised epilepsy that may present in adolescence, usually between 10 and 13 years of age.[10] The absence seizures tend to occur every day, but not as frequently as those in childhood-onset absence epilepsy (CAE). In addition, the absences in JAE are more prolonged, last for 30–40 s or even for over a minute and are usually accompanied by more purposeful automatisms; in addition, speech may not be completely lost. This has often resulted in an initial (wrong) diagnosis of complex partial seizures and the prescription of carbamazepine, which exacerbates the absences and may even precipitate absence status. The electroencephalogram (EEG) shows spike and slow wave activity, but, in contrast with CAE, typically at a higher frequency (3.5–4 Hz) and with a bifrontal accentuation. At least 80% of patients have GTCS and 20% have occasional myoclonic seizures. Seizure control tends to be more difficult than in CAE, but can still be achieved in approximately 60% of patients. Unfortunately, spontaneous remission occurs in $<$50% and, although seizures may be life-long, the absences tend to become less frequent by the third or fourth decade.

Epilepsy with generalised tonic–clonic seizures on awakening

Epilepsy with generalised tonic–clonic seizures on awakening is the other recognised and relatively common idiopathic generalised epilepsy to occur in adolescence, with a peak age of onset in the mid-teens, often around puberty.[11] Individuals usually present with a GTCS invariably occurring at or within 2 h of waking from sleep (nocturnal or diurnal sleep). There is an overlap between this syndrome and JME, JAE and CAE; predictably therefore, some patients with epilepsy with generalised tonic–clonic seizures on awakening have been reported to have juvenile-type absence and myoclonic seizures. Seizure control is relatively easy.

Isolated partial seizures of adolescence

Isolated partial seizures of adolescence (also occasionally known as benign focal seizures of adolescence) is a rare and idiopathic seizure susceptibility syndrome with a peak age of onset at 13–15 years of age.[12] It presents with a single or cluster of focal onset seizures (usually no more than 2–5), often occurring over a period of no more than 36 h. Seizure manifestations include motor (often with a ''Jacksonian march'', suggesting a frontal origin for the seizures), somatosensory and visual manifestations, but without auditory, olfactory or gustatory symptoms. Approximately 50% of patients will experience a secondarily GTCS. Neuroimaging with MRI is normal, and treatment is not usually required as most patients have only a single seizure or a cluster of seizures over a finite period.

Symptomatic focal epilepsies

Symptomatic focal epilepsies may also present in the mid-to-late teenage years. Characteristically, the initial seizures often occur during sleep or on waking, when the partial onset of the seizures may not have been witnessed. Neuroimaging (with MRI) should be undertaken in these teenagers unless the electroclinical features are entirely consistent with benign focal seizures of adolescence. In addition, children with mesial temporal epilepsy may also present at this age with obvious complex partial and secondary GTCS. They may have previously experienced complex febrile seizures with or without subsequent simple and complex partial seizures in mid-childhood that may not have been recognised.[13 14]

Late-onset childhood occipital epilepsy

Late-onset childhood occipital epilepsy (also known as Gastaut syndrome) is a relatively uncommon and presumed idiopathic (possibly genetic) epilepsy syndrome with a peak age of onset at 9 years, but which may present up to the age of 15 or 16 years.[15] Seizure manifestations are typically visual, with either simple (elementary) hallucinations or blindness, or both, lasting typically for 1–5 min. The simple hallucinations may progress into more complex visual hallucinations and may terminate in either a hemi-convulsion or a generalised tonic–clonic convulsion. Importantly, consciousness may be lost without any accompanying tonic–clonic movements, which may occasionally make episodes difficult to differentiate from vasovagal syncope. Deviation of the eyes with or without ipsilateral deviation of the head is the most common motor symptom and occurs during or after the visual hallucinations. Postictal headache occurs in approximately 50% of patients and is often associated with nausea and vomiting. The interictal EEG typically shows occipital spike discharges that are usually (but not invariably) bilateral; occasionally these may only be seen in a sleeping record, and rarely the EEG may be normal. Neuroimaging is normal; however, in view of the relative rarity of this epilepsy syndrome, and because occipital spikes on EEG are not specific to this syndrome, there should be a low threshold for undertaking cerebral MRI. The visual seizures occur often and although the hemi-seizures and generalised tonic–clonic seizures may occur infrequently, epilepsy drugs are always considered and usually prescribed (sodium valproate or carbamazepine). Spontaneous remission is reported to occur in approximately 60% of patients, usually within 4 years from onset.

Progressive myoclonic epilepsies

These are a rare group of both sporadic and genetic epilepsies, which may either have an onset or deteriorate in adolescence.[16] The key feature is that they may initially present as and follow an early course that is typical of an idiopathic generalised (or less likely focal), epilepsy and specifically JME. This is well illustrated by Lafora disease, an autosomal recessive disorder which presents in the early teens with seizures, usually myoclonic, clonic and focal, and often with predominant occipital paroxysms on the EEG. A relentless cognitive decline with associated development of extrapyramidal signs ensues after a delay of months to years. Clues to the possibility of an underlying PME include the fact that seizure control in PME is nearly always poor (and considerably worse than that seen in the idiopathic generalised epilepsies) and, importantly, additional features invariably develop, including cognitive stagnation and dementia, ataxia, non-epileptic (action) myoclonus, pyramidal and extrapyramidal dysfunction (usually chorea), and visual failure. These additional features, together with the age at which they develop, depend on the specific PME (table 1). It is relatively common for the additional features of cognitive stagnation, ataxia, chorea and myoclonus to be

Epilepsy

- Juvenile myoclonic epilepsy
- Juvenile absence epilepsy
- Epilepsy with tonic–clonic seizures on awakening
- Isolated partial seizures of adolescence
- Symptomatic partial epilepsy (eg, mesial temporal epilepsy)
- Late onset childhood occipital epilepsy
- Idiopathic photosensitive occipital epilepsy
- Progressive myoclonic epilepsies
  - Unverricht–Lundborg disease
  - Lafora disease
  - Juvenile neuronal ceroid lipofuscinosis
  - Neimann–Pick disease type C
  - Myoclonic epilepsy with ragged red fibres on muscle biopsy
  - Sialidosis type 1
  - Juvenile Huntington's disease
  - Subacute sclerosing panencephalitis

Neurodegenerative disorders

- Diabetes insipidus, diabetes mellitus, optic atrophy and deafness (DIDMOAD)
- GM1 gangliosidosis
- Juvenile Huntington's disease
- Metachromatic leucodystrophy
- Mitochondrial cytopathies
- Juvenile neuronal ceroid lipofuscinosis
- Adrenoleucodystrophy
- Variant Creutzfeldt–Jakob disease
- Wilson's disease

Neuromuscular disorders

- Becker muscular dystrophy
- Facio-scapulo-humeral dystrophy
- Myotonic dystrophy
- Juvenile (autoimmune) myasthenia
- Hereditary motor and sensory neuropathy type Ia
- Metabolic myopathies

Inflammatory disorders

- Multiple sclerosis
- Acute disseminated encephalomyelitis

initially ascribed to the side effects of epilepsy drugs, substance misuse, non-concordance with drugs or persisting seizure activity, thereby leading to a considerable delay in diagnosis of the specific PME.

NEURODEGENERATIVE DISORDERS

Neurodegenerative disorders, although individually rare, are collectively an important group of disorders to consider at this age. Regression, whether cognitive, motor or a mixture of both, poses a specific diagnostic challenge. The first question that must be dealt with in the adolescent presenting with an apparent loss of skills is whether this reflects a genuine neurodegenerative disorder or a pseudoregression due to some other aetiology. The first symptoms of a neurodegenerative disorder may be a change in personality or a declining school performance, or often a combination of both. The change from a primary school, single classroom environment to the secondary school with large varied classrooms as well as the increasing academic and organisational demands can often unmask pre-existing static difficulties.

In a child with pre-existing neurological difficulties it can be difficult to differentiate between a plateauing of skills, a pseudoregression (important as the cause may be reversible) and real onset of a neurodegenerative condition. In these situations, it is vital to consider the validity of the original diagnosis. The progressive myoclonic epilepsies are an excellent example of this problem, as discussed above. Other examples of this particular problem include the child with erroneously diagnosed ''diplegic cerebral palsy'' who has in fact a genetic disorder such as dopa-responsive dystonia[17] or idiopathic torsion dystonia, hereditary spastic paraplegia or pantothenate kinase-associated neurodegeneration (PKAN). Causes of pseudoregression include depression, which is becoming increasingly recognised (and often overlooked) in teenagers, and other non-neurological conditions including acquired hypothyroidism and substance misuse. Poorly controlled and subtle epileptic seizures or frequent spike and wave activity on the EEG represent other potentially treatable causes of pseudoregression.

If it becomes clear that the adolescent does have an acquired neurodegenerative disorder, it may be helpful to consider such conditions in terms of:

- whether it appears to be a multi-system disorder;
- whether the symptoms suggest mainly a peripheral or a central nervous system disorder (in addition, there are many rare disorders where both may be involved); and
- whether the grey or white matter is predominantly involved if it exclusively or predominantly involves the CNS.

Grey matter disorders more typically present with seizures (often myoclonic), a change in behaviour/personality and dementia. Symptoms more suggestive of a white matter disorder include focal neurological deficits, spasticity, and visual symptoms and signs. However, there may be considerable overlap. Data on disorders with progressive intellectual and neurological decline have been collected since 1997 and reported recently.[18] In this rare group of confirmed progressive intellectual and neurological decline disorders, the more common ones either diagnosed or occurring in adolescence included:

- diabetes insipidus, diabetes mellitus, optic atrophy and deafness (DIDMOAD)
- G_M1 gangliosidosis
- juvenile Huntington's disease
- metachromatic leucodystrophy
- mitochondrial cytopathies
- juvenile neuronal ceroid lipofuscinosis
- subacute sclerosing panencephalitis
- adrenoleucodystrophy
- variant Creutzfeldt–Jakob disease
- Wilson disease

Subacute sclerosing panencephalitis (SSPE)

In the UK, SSPE is rare (four patients (aged 11–15 years) have been diagnosed in the past 15 years at Alder Hey), but this condition is likely to increase in the next 10–15 years, with the reduced uptake of measles immunisation in the second year of life. The onset is usually insidious, often with a decline in school performance (poor concentration and short-term memory) and behavioural disturbances, which may be initially ascribed to psychological problems or depression. Rare presentations include visual failure and frequent atypical absences, occasionally with myoclonic seizures. Progression varies from child to child, but characteristically includes clumsiness, myoclonic and tonic–clonic seizures. Over the ensuing weeks, months or years, dysphagia, dysarthria, involuntary movements and cortical visual impairment develop, eventually leading to coma and death. The EEG is characteristic (often suggesting the diagnosis) and shows very high-amplitude and periodic triphasic slow wave complexes; diagnosis is confirmed by finding an increased anti-measles antibody titre in the cerebrospinal fluid.

Variant Creutzfeldt–Jakob disease

Variant Creutzfeldt–Jakob disease is important, although fortunately its incidence would not seem to be as high as predicted when first identified a decade ago.[19–21] The vast majority of paediatric cases have either had an onset around, or have presented after, 12 years of age. The most common presentation is with psychiatric symptoms (depression, anxiety or social withdrawal); cognitive involvement occurs early, but may be masked and initially overlooked because of the psychiatric symptoms. Sensory symptoms (paraesthesiae/painful dysaesthesiae) usually develop within 6 months of the onset, followed by ataxia and involuntary movements, typically dystonia, chorea and myoclonus. The EEG does not show the characteristic periodic paroxysms seen in sporadic Creutzfeldt–Jakob disease, but brain MRI usually shows symmetrical high signal in the posterior thalamic (pulvinar) regions. Death occurs usually at a median of 14–18 months from disease onset.

Wilson's disease

In children with Wilson's disease (hepatolenticular degeneration), presentation after 10 or 12 years of age is typically neurological although this may initially be subtle and limited to a single symptom (eg, dysarthria or gait disturbance). Psychiatric features ranging from behavioural disturbance to a paranoid psychosis may precede any neurological manifestations in up to 20% of patients. Neurological deterioration occurs in the late teenage years with worsening dysarthria, dystonia, a fixed pseudosmile, tremor, postural abnormalities and rigidity; dementia is a later complication and epilepsy is uncommon. The Kayser–Fleisher ring, an orange–brown discolouration at the limbus of the cornea, will be seen in most teenagers with neurological symptoms and, although usually visible with an ophthalmoscope, are far better visualised on slit-lamp examination. Diagnosis can be confirmed by low serum caeruloplasmin and copper levels and high 24-h urinary copper excretion; the defective gene is on chromosome 13q. The diagnosis of Wilson's disease is important as it is one of the very few treatable neurodegenerative disorders.

Friedreich's ataxia

The most common progressive disorder affecting primarily motor function in adolescence is Friedrich's ataxia, an autosomal recessive disorder.[22] It has a mean age at onset of 11–12 years (range 4–16 years) and presentation is usually with clumsiness, ataxia and dysarthria; these children may initially be diagnosed as having dyspraxia. Presentation in the teenage years may also be with pes cavus, or less commonly with scoliosis or cardiomyopathy. The ataxia is relentlessly progressive, but the rate of progression varies between (and occasionally within) families. Ambulation is lost between 6 and 10 years after onset. A hypertrophic cardiomyopathy is very common and may be shown early in the course of the disease by echocardiography in asymptomatic individuals. Muscle stretch/deep tendon reflexes are absent and plantar responses are extensor. Diagnosis is confirmed by finding the mutation of the frataxin gene on chromosome 9q, which is present in approximately 90% of affected individuals. Vitamin E-responsive ataxia may present with a very similar clinical phenotype although the cardiomyopathy is rare; the Friedrich's ataxia mutation is negative and the ataxia improves with high-dose vitamin E supplementation.

Pantothenate kinase–associated neurodegeneration

PKAN (previously known as Hallervorden–Spatz disease) is a rare autosomal recessive disorder that usually presents after 10–12 years of age with extrapyramidal dysfunction as manifest by rigidity (not spasticity), dystonia and, subsequently, choreoathetosis and dementia.[23] A pigmentary retinopathy is commonly found. Initial diagnoses in these young teenagers include cerebral palsy, dyspraxia and suspicion of substance abuse. The reported pathognomic brain MRI feature (the eye of the tiger sign) is not always seen in affected individuals, even with progressive neurological symptoms and signs, and may also disappear during the course of the disease.[24] Identification of the mutation encoding the enzyme pantothenate kinase 2 in approximately 60% of patients has allowed a more accurate diagnosis, but its absence does not preclude a diagnosis of PKAN.

Idiopathic torsion dystonia

Children with idiopathic torsion dystonia usually present between 7 and 12 years of age, but occasionally later. In most cases (80%), the disorder is inherited in an autosomal dominant pattern (but with incomplete penetrance) and present with bilateral (although occasionally asymmetric) lower limb dystonia and an abnormal, frequently bizarre gait that usually becomes more generalised to involve the upper limbs, neck and bulbar muscles. Initial diagnoses in these children may include cerebral palsy and a functional disorder. Generalisation is less probable if the initial presentation is in the upper limbs or trunk. The generalised form tends to progress relatively slowly over 5–10 (or more) years. Neuroimaging is normal and DNA analysis may show the presence of the DYT1 gene on chromosome 9q34 in about 60% of individuals.

NEUROMUSCULAR DISORDERS

Adolescents with recent-onset neuromuscular disorders tend to have specific problems, usually related to self-help skills and activities of daily living (eg, the teenage girl with facio-scapulo-humeral dystrophy or myasthenia who can no longer lift her arms or whose arms fatigue rapidly when brushing her hair).[25] This contrasts with younger children who more typically present with gross motor developmental delay, stumbling or an inability to keep up with their peer group. Although most neuromuscular disorders in adolescence present with weakness or muscle cramps or both, a number of rarer, and predominantly metabolic muscle disorders may present with fatigue.

Most of the neuromuscular disorders involving the muscle or peripheral nerve are inherited (often in an autosomal dominant pattern), and show clinical variation within a family. It is therefore important to always examine the child's biological parents and siblings in detail (including, where appropriate, undressed), as this may be important in identifying a specific neuromuscular disorder. In the authors' experience, this is particularly true for myotonic dystrophy, facio-scapulo-humeral dystrophy, hereditary motor and sensory neuropathy (HMSN) type Ia, and central core disease—all of which are typically

inherited in an autosomal dominant pattern. Diagnosis is confirmed by neurophysiological investigations (nerve conduction studies, electromyography), muscle biopsy, DNA and other analyses (eg, positive anti-acetylcholine receptor antibodies in juvenile auto-immune myasthenia), depending on the specific disorder.

In general, progressive proximal muscle weakness in childhood is usually caused by a myopathy. Included in this group are the dystrophies and the inflammatory, endocrine and metabolic myopathies.

Becker muscular dystrophy

Patients with Duchenne muscular dystrophy always present in the first decade of life, whereas in Becker muscular dystrophy the onset is usually after 5 years of age, but also at any time in childhood or even in early adult life. Boys with Becker muscular dystrophy usually have a history of poor sporting activities and quite severe muscle pains after even moderate exercise, often leading to an initial referral to an orthopaedic surgeon or rheumatologist—with a consequent delay in diagnosis. Marked calf pseudo-hypertrophy is common, and, as with the muscle pains, tends to be more marked than in Duchenne muscular dystrophy. The creatine phosphokinase level is always raised (>10–20 times normal) and echocardiography may show cardiac involvement in the absence of cardiac symptoms.

Facio-scapulo-humeral dystrophy

Facio-scapulo-humeral dystrophy is an autosomal dominant dystrophy presenting in late childhood or early adolescence with progressive facial weakness, scapular winging and weakness of muscles in the shoulder girdle leading to difficulties in raising the arms. Disease progression is variable, with periods of apparent arrest. Many patients do not become disabled and their life expectancy is normal, whereas others become wheelchair dependent in adult life.

Myasthenia gravis

Myasthenia gravis in adolescents (predominantly in females) is usually an autoimmune disease that presents in a similar fashion as the adult disease. Ptosis and diplopia are usually the initial presenting features, but weakness may become more generalised. Affected individuals may only have increasing fatigue as the day progresses. A considerable minority may present acutely over hours or days (often precipitated by an intercurrent illness or infection) in a myasthenic crisis with severe bulbar and respiratory difficulties, which is a medical emergency. The course tends to be slowly progressive.

Myotonic dystrophy

The onset of symptoms in myotonic dystrophy is usually in adolescence or early adult life, although symptomatic myotonia (abnormal muscle relaxation after contraction) may be seen in childhood. Presenting features include muscle weakness, particularly of the face and distal limb muscles, and the teenager may already have been diagnosed with diabetes mellitus. Often, a background of mild to moderate learning difficulties is observed, which together with the presence of motor difficulties may lead to an initial diagnosis of dyspraxia. The affected parent in childhood/teenager-onset myotonic dystrophy is typically the father, in contrast with the congenital form, where the affected parent is the mother. The course is slowly progressive, with severe weakness in the hands and feet in adult life.

Peripheral neuropathies

Most peripheral neuropathies in childhood and adolescence are hereditary; the most important exception is acute inflammatory demyelinating polyradiculoneuropathy (Guillain–Barré syndrome), which commonly presents between 11 and 15 years of age. Of the inherited neuropathies, HMSN type Ia and type II tend to be the most common and usually have a peak incidence in the second decade of life. HMSN type Ia is commonly inherited in an autosomal dominant manner. Weakness begins in the anterior tibial compartment and causes foot drop, pes cavus deformities and, eventually, clawing of the toes. Sensory disturbance may be found on formal examination, but is rarely clinically significant. Muscle stretch reflexes are typically absent at the ankles, but may be reduced or absent elsewhere, depending on the person's age. Symptom progression is slow and significant disability does not develop until middle adult life. Acquired neuropathies are most commonly seen in hospital, particularly in oncology patients receiving antineoplastic drugs and undergoing intensive care (critical illness neuropathy or myopathy).

Metabolic myopathies

A number of rare metabolic muscle disorders may also present in adolescence. Carnitine-palmitoyl transferase type II (CPT-2) has an onset in late childhood/adolescence and usually presents with myalgia, fatigability during or after exercise, and myoglobinuria after sustained aerobic exercise.[26] Respiratory muscles may be involved and fatal rhabdomyolysis has been reported rarely. There is no residual weakness after individual episodes, but repeated episodes over years may lead to a permanent, although mild, myopathy. The CPT-2 concentration can be measured to confirm the diagnosis. Patients with CPT-2 are at risk of malignant hyperthermia syndrome and must be counselled accordingly. Very-long-chain acyl coenzyme A dehydrogenase deficiency also usually presents after the age of 10 years with severe pain and myoglobinuria on exercise. The other important genetic metabolic myopathy is that seen in the mitochondrial cytopathies,[27] a multi-organ group of conditions that can present at any age (commonly in childhood and early adult life) and with any symptoms, depending on the predominant organs involved. A predominant myopathic or neuropathic presentation is seen in myoclonic epilepsy and ragged red fibres (MERRF) (on muscle biopsy), and neurogenic atrophy ataxia and retinitis pigmentosa (NARP), respectively. Diagnosis of both myoclonic epilepsy and ragged red fibres and neurogenic atrophy, ataxia and retinitis pigmentosa may be made by finding the specific mutation on blood DNA analysis, although these mutations may be negative and diagnosis will subsequently be made on muscle biopsy (through histological analysis or finding the specific mutation on muscle DNA).

Inflammatory disorders of the central nervous system in adolescence

Multiple sclerosis

Multiple sclerosis occurring in the early to late teenage years is reported to represent between 3.6% and 4.4% of all cases of multiple sclerosis, although the figure may be higher with improved diagnostic techniques, including MRI scanners of greater magnetic strength, and an increased awareness that multiple sclerosis can occur in childhood. It is more common in females, particularly after puberty, and follows a relapsing and remitting course in approximately 60% of patients as in adults. The symptoms and signs of childhood multiple sclerosis are similar to those in adults, with visual involvement (optic neuritis or an internuclear ophthalmoplegia) or sensorimotor disturbances representing the most common manifestations.[28 29]

Miscellaneous

Isolated location-specific episodes of demyelination are relatively common in adolescents and include optic neuritis, transverse myelitis and rarely neuromyelitis optica (Devic disease). Acute disseminated encephalomyelitis (ADEM), usually a post-infectious or, rarely, postvaccination disorder, can also present in adolescence and tends to be a monophasic

illness; it is probably the most common demyelinating disorder in children. The presentation of ADEM is more often with an encephalopathic illness than with multiple sclerosis. The MRI changes in multiple sclerosis and ADEM may be similar, although characteristically are more widespread and dramatic in ADEM. However, relapses may occur although the risk is unclear; one recent case series suggested a risk of 57%.[29] Debate continues as to whether such relapses should be labelled as polyphasic ADEM or simply multiple sclerosis.[30]

The diagnosis of both multiple sclerosis and ADEM is made on the basis of the child's presenting symptoms and signs and MRI findings. Importantly, multiple sclerosis should never be diagnosed after a single episode of demyelination. Cerebrospinal fluid analysis is important in both confirming the diagnosis, particularly in multiple sclerosis, with the finding of oligoclonal bands (which may also be present in ADEM and some disorders which involve the breakdown of the blood-cerebrospinal fluid barrier), and excluding other causes including infections and some malignancies.

MANAGEMENT

It is beyond the scope of this review to discuss the approach to an adolescent in general. However, certain points are worth emphasising. The diagnosis of any neurological disorder at this crucial time in development can have profound effects on the patient, particularly in terms of trying to achieve independence from their carers, making career choices, self-esteem, and on establishing and maintaining peer relationships. Discussions on diagnoses demand understanding and sensitivity. The diagnosis of paroxysmal disorders usually relies on witness accounts of the event, and teenagers may find the relaying of such accounts by family members or friends embarrassing or even distressing. Involving adolescents in treatment decisions is also important, and giving choices and finding solutions around potential problems are often helpful approaches. Young people often respond better to facts and information rather than opinions and advice. There remains significant debate regarding the most appropriate approach to managing the transitional period; the two most common approaches include developing a formal specialty of adolescent medicine or developing a shared hand-over service that is supervised jointly by both paediatric and adult specialists (eg, in epilepsy, neuromuscular disorders and neurodisability).

SUMMARY

The considerable overlap between child and adult neurological practice in terms of disease presentation and management should not disguise the fact that adolescent neurology requires a specific approach to the patient. The clinician has to:

- be aware of the range of neurological disorders that may present at this age;
- be aware of the fact that the initial presentation of a neurological disorder may be with behavioural (including psychiatric) or cognitive features, or both;
- be open to reviewing and, if necessary, revising the original diagnosis if the subsequent course of the disorder is atypical or unusual and the response to treatment is unexpected or suboptimal;
- consider the possibility of depression or substance misuse in teenagers who present with what seems to be regression;
- appreciate the complex psychosocial changes at this time of life, the dynamic biological environment and the effect that a chronic disorder may have on the patient (eg, epilepsy[31]); and
- seek appropriate specialist (neurological or psychiatric) advice sooner rather than later.

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