Management of attention-deficit/hyperactivity disorder

Management of attention-deficit/hyperactivity disorder is both a challenging and a rewarding experience. Diagnosis is difficult because of the complexities of presentation and lack of biological markers. However, personalized management improves the individual's quality of life and also benefits the family and society as a whole.

Attention-deficit/hyperactivity disorder (ADHD) is a well-defined syndrome with age-inappropriate level of inattention with or without impulsivity and hyperactivity (Mercugliano, 1999). Its impairments affect children and young people in different settings (e.g. home, school and socially) and can cause disability. Although the quantity and quality of behaviour may change over a period of time, a significant number of adults show symptoms and effects of ADHD. Owing to its pervasiveness, functional impairment and impact on self-esteem, its management has to be multimodal and labour intensive. Therefore any management plan must address the impact on the quality of life of the individual and not just focus on reduction of core symptoms of ADHD. The management predominantly consists of a multimodal package including psychoeducation and medication. Although the practice can vary across the country, community paediatricians tend to see the majority of ADHD children for diagnosis and manage them in collaboration with the GP under shared care protocols. When there is a complex presentation or comorbidities are present then help from child and family mental health services is extremely valuable.

ADHD is a common neurobiological, neurodevelopmental disorder. Individuals with ADHD present with an age-inappropriate level of inattention, hyperactivity and impulsivity. The onset is in early childhood by definition before the age of 7 years, nearly always before the age of 5 years and frequently before the age of 2 years. At the time of diagnosis symptoms are present for at least 6 months and are pervasive, affecting the functioning of the child at home, school and socially. These impairments can be disabling and, according to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV), are not explained on the basis of other mental disorders (American Psychiatric Association, 2000).

Dr Saroj Jamdar *is Associate Specialist in Child Health and Clinical Head in the Attention-Deficit/Hyperactivity Disorder Clinic, Wigan Child, Adolescent and Family Mental Health Service, Wigan WN2 2JA and* **Dr Brahan Thara Sathyamoorthy** *is Specialist Registrar in Community Paediatrics, Acute Pennine NHS Trust Manchester*

Correspondence to: Dr S Jamdar

According to the framework elaborated in DSM-IV the subcategories include ADHD (primarily) inattentive type, ADHD (primarily) hyperactive-impulsive type; and ADHD combined type depending upon the pattern of behaviour endorsed. There is also a category of ADHD in partial remission for individuals (adolescents and adults) who might lack the required number of symptoms but experience significant functional impairment. The combined type of ADHD is the most common form and resembles closely the hyperkinetic disorder of ICD-10 (*International Classification of Mental and Behavioural Disorders*, 10th edition; World Health Organization, 1992) criteria requiring that symptoms be present in all three categories.

The prevalence of ADHD varies between different countries; in the UK it is estimated that around 5% of school-aged children and adolescents suffer from ADHD (National Institute for Health and Clinical Excellence (NICE), 2006) but not all are severe enough to require treatment. ADHD has a spectrum and not all children and adolescents will be affected by it to the same degree. Boys are more commonly affected than girls in a ratio of 4:1 (Gaub and Carlson, 1997). Girls commonly present with symptoms of inattention, which may be missed.

The effects of ADHD can be serious for the individual, the family and even society. These children often have low self-esteem, develop emotional and social problems, and frequently underachieve in school. In adolescence and adulthood these difficulties cause continuing social and emotional problems, substance misuse, unemployment and involvement in crime (NICE, 2006). In addition, the symptoms may impact upon the family (Johnston and Mash, 2001), disrupting functioning and causing tension. The quality of life of children with ADHD may be considered to be worse than that of a similar cohort of children with chronic medical conditions, e.g. asthma (Escobar et al, 2005). In addition, the UK SUNBEAM (study into Broader Efficacy of Atomoxetine) study of children with ADHD demonstrated that they have a considerably compromised health-related quality of life across multiple domains (in the region of 2.5 standard deviations below the mean) (Prasad et al, 2007).

Nearly 60% or more of children with ADHD will continue to exhibit debilitating symptoms into adulthood if not the full syndrome (Barkley, 1998).

Individuals with ADHD have many more difficulties than just the core symptoms of ADHD. Coexisting and comorbid conditions make life even more difficult for these individuals and their families. As many as 50% of individuals with ADHD will meet the criteria for at least one psychiatric condition in addition to ADHD (Donnelly, 2006). In children these coexisting conditions include learning disability, dyslexia, dyspraxia, oppositional defiant disorder (nearly 60% of children in the ADHD Observational Research in Europe (ADORE) study had symptoms of oppositional defiant disorder), conduct disorders, mood and anxiety disorder (Jensen et al, 1997). There is also a higher incidence of ADHD in individuals with autistic spectrum disorder, Asperger's and Tourette's syndrome. These impact on the individual's ability to function in academic, social and family environments and on their quality of life, which in turn leads to negative life outcomes.

The ADORE study confirms that these children face difficulties with socialization and bullying (as victim or as perpetrators) (Ralston and Lorenzo, 2004). The 'Lesson for Life' campaign found that children with ADHD face significant social exclusion during their formative years. In research carried out by IPSOS Health on behalf of Eli Lilly and Company, telephone interviews with the parents of 100 children with ADHD and 50 children without ADHD (aged 5–16 years) found that only 3 out of 10 children with ADHD were good at making friends as compared to 8 out of 10 of non-ADHD children. More children with ADHD were likely to play alone. They were also less likely to be invited to a birthday party or to a friend's house when compared with children without ADHD. The ADORE study also demonstrated that only 42% of children attended school without any difficulties. All these findings demonstrate that ADHD affects life outside of school hours and should therefore be viewed as a 24-hour problem.

Making a diagnosis

There are many difficulties in making a diagnosis of ADHD which is based on a description of symptoms and impairments from parents, carers and staff at school. These include:

1. ADHD is a behaviour-based syndrome which can be the subject of bias on the part of those who report the quality and quantity of the behaviour, e.g. parents, carers and staff at school
2. There is no biological marker
3. Although there is increased awareness among professionals in recognizing and diagnosing ADHD, there is still a small number of doctors, psychologists and teachers who tend to view ADHD as a result of poor parenting
4. There is negative media attention which portrays the adverse side effects of stimulant medication, e.g. 'chill pill or kill pill'. This has a great impact on society's views on the condition, which in turn affects decisions made by parents and some professionals
5. Clinicians have to deal with complexities of presentation as 50% of the children have coexisting comorbidities which complicate the issue.

Owing to the above identified difficulties it is important to collect as much information as possible to make a diagnosis. A detailed family, antenatal, perinatal and developmental history including speech and/or language problems, coordination difficulties and learning problems is essential in the assessment of ADHD.

Assessment of the quality of behaviour, that is the behaviour resulting from inattention and impulsivity *vs* non-compliance, is useful. In view of the pervasive nature of the condition, a report from the school including a classroom observation is necessary. Using rating scales, e.g. the Conners' Parent Rating Scale (Conners et al, 1998a) and Teacher Rating Scale (Conners et al, 1998b), SNAP-IV, as devised by Swanson, or the Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997), not only helps the assessment process but is also valuable in monitoring progress.

Plan of management

There should be a clear plan acknowledging that ADHD is likely to be a chronic condition. As mentioned above, use of rating scales is helpful in monitoring the improvement in the core symptoms of ADHD.

1. The family and the child are the key partners in the management and decision-making. Personalizing the plan is important as there is no 'one size fits all' solution
2. The adverse impact on family and functioning throughout the day and not only at school should be recognized including: self-esteem, academic and social functioning and parent/child relationship. Do not just aim to reduce core symptoms
3. Remember there is no 'cure'
4. Consider use of tools to assess quality of life, e.g. Child Health and Illness Profile (Child Edition) (CHIP-CE; Starfield et al, 2000) and Harter's (1985) self-perception scale
5. Do not forget coexisting or comorbid conditions which may require treatment
6. Set achievable targets and review them regularly
7. Plans should be made in discussion with the parents, the child and where possible the teacher
8. Drug management should be part of the plan if behaviour management has failed to reach the target outcome or the severity of the condition demands drug therapy
9. The clinician should periodically review the patient to assess target outcomes, monitor symptoms, blood pressure, pulse and growth, monitor side effects, and adjust drug therapy to optimize symptom control

10. Integrative working with psychologists, psychiatrists, education, community paediatricians, educational psychology and social services is important for individuals with ADHD and comorbid disorders. Ensuring a close link with school is imperative.

Aims of treatment

The management of children with ADHD is complex and needs comprehensive multimodal and multidisciplinary assessment and management. The aims of treatment are to:

- Reduce core symptoms
- Improve disruptive behaviour
- Improve social behaviour with better relationships with teacher and other children
- Improve academic performance
- Improve self-esteem
- Improve independence in future goal-directed tasks
- Address sleep problems as around 30% of children may have sleep difficulties.

There are two approaches to managing ADHD: non-pharmacological (psychosocial) and pharmacological treatment. The treatment package must include a systematic approach with both incorporated to suit the family's and the child's needs. It also should not be forgotten that siblings of children with ADHD may require attention as well (*Figure 1*).

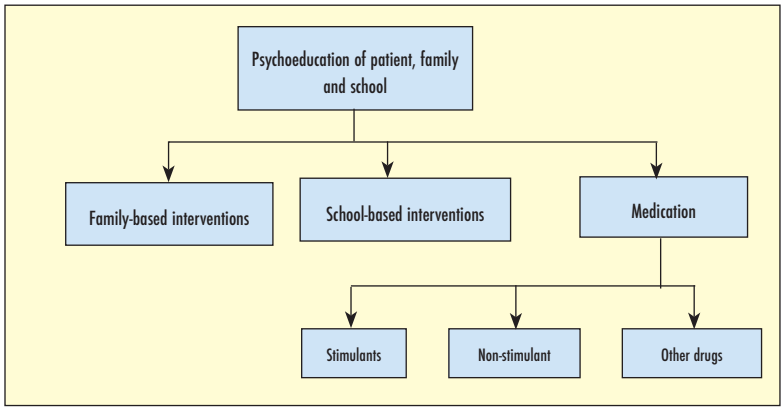
Non-pharmacological (psychosocial) management of ADHD

Psychosocial education involves educating parents, teachers and individuals about ADHD, dispelling myths about ADHD, updating knowledge about the biological basis of the disorder, and providing information about parent support groups, websites and relevant literature.

Ness and Price (1990) say that 'the best non-medical interventions for ADHD are practical, commonsense adjustments to an impulsive and disorganised style'. The aim of behaviour intervention is to improve functioning for the child at home, at school and socially. The main components of non-pharmacological treatment are discussed below.

Up to 20% of children will not respond to medication. Many more will experience only partial remission of their symptoms and can still have secondary morbidity in the form of low self-esteem and social skills deficits; these form the basis of psychotherapeutic interventions (American Academy of Pediatrics, 2001). There is less evidence that psychosocial interventions have a significant effect on the core symptoms of ADHD (Multimodal Treatment Study of ADHD (MTA) Cooperative Group, 1999). Evaluation of the strength of the evidence relating to these interventions is complicated by problems in the research designs. Typical problems are inadequate follow-up in the child's usual environment and short-term evaluation periods.

Figure 1. Management options for children with attention-deficit/hyperactivity disorder. All children, their families and the staff at their school will need psychoeducation. The rest of the management will depend on each individual's need for behaviour-based interventions and/or medication.



Clinic-based psychosocial interventions

Children with ADHD have significant behavioural problems at home and school. Supportive behavioural strategies can reduce conflicts and improve the home situation; however, there is considerable variation between and within individuals (Barkley et al, 1992). This has been found to be particularly true after systematic evaluation in children with comorbid conduct or oppositional behaviour. Some of the most widely relevant behavioural techniques are:

- Give positive responses to appropriate behaviour
- Use of effective method of communication, e.g. make eye contact
- Give simple commands
- Frame commands positively
- Respond to child's compliance
- Immediacy of consequences (this is an immediate response to a behaviour – reward acceptable behaviour but when warranted withdraw a privilege for unacceptable behaviour).

These form the basis of behaviour modification. It is important to include the child in discussing this therapeutic process. Token systems, response cost and time out can be effective in managing behaviour difficulties. Behaviour management in preschool nursery and school has shown to reduce hyperactivity and promote social behaviour (Taylor et al, 2004).

Family-based psychosocial interventions for behaviour management are recommended for the treatment of comorbid behavioural problems based on the current evidence, but the evidence for individual psychosocial intervention is weak and not routinely recommended.

School-based psychosocial interventions

Individualized school intervention programmes including academic and behavioural interventions are proven to show benefit in the short term only (Abikoff and Gittelman, 1984), and are not proven to significantly

reduce the core symptoms. The class teacher will be the main manager of educational intervention in most cases. The programme should involve problem-solving skills along with coping strategies for children with ADHD as well as children who interact with them regularly (Whalen and Henker, 1991).

At school, time management and self instruction can be taught to teenagers. Contingency contracting can be more productive than a token system or response cost scheme – this involves negotiating a contract with the teenager where the reward or negative consequence of a behaviour is negotiated beforehand.

Meta-analysis has shown that contingency management strategies and academic interventions are more effective for behaviour change than cognitive-behavioural strategies (DuPaul and Eckert, 1997).

Dietary interventions

There is little evidence of benefit in ADHD from taking mineral supplements containing iron, magnesium and zinc (Bekaroglu et al, 1996; Sever et al, 1997). There is some evidence which suggests that lower urinary and hair zinc levels are associated with poorer response to methylphenidate (Arnold et al, 1990) although there are no studies of the efficacy of zinc supplementation. Several double-blind placebo-controlled studies have failed to support a benefit of dietary manipulation on behaviour except in a very small number of children (Bekaroglu et al, 1996).

A few small studies have reported behavioural improvement with hypoallergenic restriction diets but these studies require further larger scale and more rigorously controlled replication. Given the minimal evidence of efficacy and extreme difficulty of inducing children with restricted diet, they should not be recommended routinely.

There is a widely held belief that the presence of refined sugar and artificial additives in the diet of children can adversely influence behaviour, but there is conflicting evidence on the effects of these products. Perhaps the greatest attention has been focused on omega 3 fatty acids. In a double-blind randomized controlled crossover trial in a mainstream school, supplementation of omega 3+6 and vitamin E showed a statistically significant improvement in teacher-rated ADHD-related symptoms and age-standardized measures of reading and spelling achievement in children (Richardson and Montgomery, 2005). This study did not focus specifically on children with ADHD although teachers reported on ADHD-related symptoms.

Complementary and alternative interventions

There is only limited evidence to support Chinese herbal medicines, electromyography and electroencephalography biofeedback as well as chiropractic intervention.

Social and community intervention

Children with ADHD and their families are under significant stress on most days because of the associated morbidity. An extended support network from family, friends and society is considered useful but there is no research to support this. Financial assistance, respite and self-help groups are available. This may form an important part of a multimodal treatment package.

Pharmacological management of ADHD

Medications should be considered when ADHD shows pervasive moderate to severe disability and psychological interventions including behaviour modifications have not been fully effective. Many medications have a significant evidence base. Medications have been extensively studied with good safety profiles and robust effect sizes in the range of 0.6–1.0, among the highest in psychiatry.

A single drug should be initiated first. If the effect of the drug is not optimum or there are unmanageable adverse effects, then an alternative monotherapy should be considered before deciding to use combination treatment. The drug and side-effect profile should be discussed thoroughly with the child and family.

Psychostimulants

The initiation of pharmacological treatment for children with ADHD should only be undertaken by a specialist in either child and adolescent psychiatry or paediatrics who has training in the use and monitoring of psychotropic medications in children and adolescents (Scottish Intercollegiate Guidelines Network, 2001).

The psychostimulants available in the UK are methylphenidate and dexamfetamine. Dexamfetamine is licensed for use in patients aged 3 years or above. Methylphenidate is presently licensed for patients aged 6 years and over. The aim is to start small and build to the level of best clinical effect with the least side effects. They are generally considered safe medications with very few contraindications (e.g. seizure disorders, cardiovascular problems).

Methylphenidate hydrochloride is a CNS stimulant with more prominent effects on mental than motor activities. It is a dopamine reuptake inhibitor. Its role in ADHD is well described especially in reducing the core symptoms. The effect lasts for 3–5 hours.

Longer-acting sustained release preparations of methylphenidate have the advantage of removing the stigma of having medicine at school, improving compliance, avoiding the school having responsibility for dispensing a controlled drug, preventing rebound and providing cover for late afternoon and early evening.

Dexamfetamine is also a useful stimulant. The effects and side-effect profile are similar to methylphenidate, and the dose is half that of methylphenidate. It is a useful alternative for patients who do not respond to methylphenidate.

Evidence of efficacy

A large number of short-term (less than 3 months) double-blind placebo-controlled studies demonstrate a 70% response to a single stimulant (methylphenidate, dexamfetamine) (Swanson, 1993), resulting in improvement in the core symptoms of ADHD with effect sizes of 0.8–1 on rating scales. Cognitive and behavioural improvements included increased on-task behaviour; reduced fidgeting, finger tapping and interrupting; reduced impulsive responding and increased accuracy of performance; reduced aggression; improved compliance; improved parent/child interactions; and increased peer status.

A review of extended controlled trials with treatment periods ranging from 3 to 7 months indicates that psychostimulant treatment is superior to placebo or non-pharmacological treatment in ameliorating the core symptoms of ADHD. Longer-term studies with treatment periods between 12 and 24 months demonstrate persistence of positive psychostimulant medication effects over time.

There is evidence for the effectiveness of psychostimulants in preschool children who demonstrate developmentally inappropriate levels of hyperactivity, inattention and impulsivity.

The National Institute for Mental Health Collaborative MTA study (MTA Cooperative Group, 1999) showed that the effects of methylphenidate alone were equal to those of psychosocial intervention and methylphenidate combined although the combined group needed a significantly lower dose of medication.

Side effects

The most frequent psychostimulant side effects in short-term studies are insomnia, reduced appetite, abdominal pain, headache and dizziness; less frequently, anxiety, irritability, or proneness to crying. Some side effects may, on further analysis, represent part of the underlying ADHD condition and be noted in the pre-treatment or placebo states. Guidelines are issued for management of common side effects (Scottish Intercollegiate Guidelines Network, 2001). Psychostimulant side effects are more commonly seen in preschool children.

When psychostimulants are first introduced and being titrated, regular contact between the family and the clinician is important to deal with questions and to make any necessary adjustments.

Once an effective dose has been determined regular review is important. This enables necessary checks of behavioural rating and side effects, along with checks of height, weight and blood pressure.

Blood testing should be carried out at the discretion of the supervising clinician and only when clinically indicated.

Prescribing and monitoring

Since psychostimulant side effects are dose-related, the aim should be to determine the lowest effective dose which produces the maximum therapeutic effect while keeping adverse effects to a minimum. Dose recommendations, notably the advised maximum daily dosage, have not been determined by research. Traditionally a cautious approach to drug scheduling has been advocated, with regimens determined empirically in the light of clinical experience. Response to both methylphenidate and dexamfetamine is variable and cannot be predicted on a dose/body weight basis.

The European guidelines recommend beginning methylphenidate at a low dose (0.2 mg/kg per dose) and increasing the dose in light of the response. The amount should be increased until either a good result is achieved, adverse effects appear or a ceiling of methylphenidate 0.7 mg/kg per dose is achieved – whichever comes first.

In most cases, medication should be continued 7 days per week to obtain maximum benefit with respect to behavioural control problems, which occur at home and in the community as well as in school. Weekend or vacation drug holidays may be required, but only if there are serious concerns about growth.

When a specialist considers that a patient's condition on psychostimulant medication is stable, he/she should seek the agreement of the patient's GP to share the patient's care on the basis of a shared-care protocol.

There are two brands of long-acting methylphenidate available in the UK: Concerta XL (Janssen-Cilag Ltd, High Wycombe) and Equasym XL (UCB Pharma, Slough). Concerta XL uses an osmotic pump system which has a 12-hour duration of effect. Twenty two per cent of the medication is immediate release and 78% is released gradually in an ascending profile for about 10 hours after administration. Concerta's action on behaviour is stated to last about 12 hours but clinical experience suggests that there is considerable inter-individual variation.

Equasym XL capsules comprise both immediate- and extended-release beads such that 30% of the dose is provided by the immediate-release component and 70% of the dose is provided by the extended-release component. Equasym XL has a shorter duration of action than Concerta XL (approximately 8 hours) but a larger effect in the 4–5 hours immediately after dosing given similar total daily doses (Banaschewski et al, 2006).

When to discontinue treatment

In view of the evidence for the persistence of ADHD into adolescence as well as adulthood, and the rapid return of core symptoms when psychostimulants are discontinued, treatment may be required long term.

Accepted practice is to undertake regular (annual) short (up to 2 weeks) trial periods off treatment, obtaining feedback from school as well as parents and child. This is best avoided at the beginning of a new school year. If there is no appreciable difference in the child's behaviour when he or she is on or off medication, it may be discontinued for a longer period.

Non-stimulant medication

Atomoxetine (Strattera, Eli Lilly and Co Ltd, Basingstoke) is a selective noradrenaline-reuptake inhibitor. Atomoxetine has a selective effect in enhancing noradrenaline activity in the frontal cortex (Bymaster et al, 2002), as do stimulants. Unlike stimulants atomoxetine does not increase dopamine activity globally across the brain, an attribute which may be responsible for its lack of abuse potential and low propensity for causing motor or vocal tics. Atomoxetine is approved in the UK for treatment of children aged 6 years and above and into adulthood if there has been a response to the treatment. This drug has been extensively evaluated in children and adolescents, including the SUNBEAM study which is the largest quality of life psychopharmacotherapy study performed in the UK (Prasad et al, 2007).

The full effect of atomoxetine may take 4–8 weeks but responders usually show some changes within 2 weeks. Once full clinical effectiveness is established this appears to persist across the day at a fairly consistent level. The drug is initiated at 0.5 mg/kg/day and gradually increased to 1.2 mg/kg/day in the second week and further if necessary to 1.8 mg/kg/day. It can be given once a day or in two equally divided doses. Atomoxetine is available in 10, 18, 25, 40 and 60 mg capsules.

As atomoxetine has been developed under the more recent stricter surveillance some rarer uncommon side effects have been notified to the regulatory authorities. Common side effects include headache, nausea and fatigue. Rarer side effects include suicidal ideation in 0.44%, aggressiveness, agitation, prolonged QT interval and a rarer hepatic idiosyncratic effect. It is important to be aware of these and advise parents accordingly. Taking atomoxetine with food may help initial stomach pain and nausea. Dividing the dose into twice-daily dosing may help with tolerability issues.

Atomoxetine may be a drug of choice in the following group of patients:

- Patients with history of anxiety or tic disorders
- Patient with history of drug diversion or drug misuse
- Family not keen to use stimulants
- Poor or no response to stimulants.

Other medication

Other unlicensed treatments include: tricyclic antidepressants, buproprion, guanafacin, neuroleptics (e.g. risperidone can be useful especially when there is comorbid pervasive developmental disorder or when there is severe aggressiveness), and clonidine.

Recent developments

A transdermal patch of methylphenidate has been launched which provides up to 12 hours of symptom coverage with once-daily application. Methylphenidate in liquid form is especially useful for individuals, especially young children, who do not want to swallow tablets or capsules (Prasad et al, 2007).

Future directions

The future of ADHD lies in elucidating the aetiology for a better understanding of its pathophysiology to enable more efficient management of the condition. Improved techniques for early diagnosis should be a goal for the future. Children in the ADORE study waited an average of 4 years from awareness of symptoms by carers to reaching a full diagnosis of the syndrome. It is important to develop tools like CHIP-CE and the Harter's self-perception profile which are validated and easy to administer both in time and content. These will enable clinicians to assess the quality of life of children with ADHD. There is a real shortage of specialist services to diagnose and manage ADHD in adults. Commissioners need to address this issue as soon as possible.

Conclusions

ADHD is a common, chronic childhood disorder with high persistence rates into adulthood. Its management requires a comprehensive, multimodal package of care. Childcare workers should acknowledge that these children have innate difficulties in the areas of inattention, impulsivity and hyperactivity. It is important to recognize that the management is multimodal and medication is but one part of management, albeit an important one. With a proper package of care ADHD is highly treatable especially if the treatment plan is personalized to meet the needs of the individual, optimizing their functioning and improving their quality of life and life outcomes. **BJHM**

Conflict of interest: Dr Jamdar has participated in the SUNBEAM study and has been on the Eli Lilly Advisory Board.

Abikoff H, Gittelman R (1984) Does behaviour therapy normalize the classroom behaviour of hyperactive children? *Arch Gen Psychiatry* **41**: 449–54

American Academy of Pediatrics (2001) Clinical practice guideline: treatment of the school-aged child with attention-deficit/hyperactivity disorder. Subcommittee on Attention-Deficit/Hyperactivity Disorder and Committee on Quality Improvement. *Pediatrics* **108**(4): 1033–44

American Psychiatric Association (2000) *Diagnostic and Statistical Manual of Mental Disorders.* 4th edn. Text revision. American Psychiatric Association, Washington DC

Arnold LE, Votolato NA, Kleykamp D, Baker GB, Bornstein RA (1990) Does hair zinc predict amphetamine response of ADD/hyperactivity. *Int J Neurosci* **50**: 103–7

Banaschewski T, Coghill D, Santosh P et al (2006) Long-acting medications for the hyperkinetic disorders. A systematic review and European treatment guideline. *Eur Child Adolesc Psychiatry* **15**(8):

KEY POINTS

- Assessment of attention-deficit/hyperactivity disorder should be multidisciplinary.
- Management should be multimodal.
- The treatment plan should be individualized, and should address quality of life as well as core symptoms.
- Doctors must ensure that they treat and manage co-morbid conditions.
- Attention-deficit/hyperactivity disorder will persist into adulthood in at least 60% of individuals.

476–95
Barkley RA (1998) ADHD: Long-term couse adult outcome and co-morbid disorders. In: NIH consensus development conference on diagnosis and treatment of ADHD. November 16–18 1998. National Institute of Mental Health, Bethesda: 57–60
Barkley RA, Guevremont DC, Anastopoulos AD, Fletcher KE (1992) A comparison of three family therapy programs for treating family conflicts in adolescents with ADHD. *J Consult Clin Psychol* **60**: 450–62
Bekaroglu M, Aslan Y, Gedik Y et al (1996) Relationships between serum free fatty acids and zinc, and attention deficit hyperactivity disorder; a research note. *J Child Psychol Psychiatry* **37**: 225–7
Bymaster FP, Katner JS, Nelson DL et al (2002) Atomoxetine increases extracellular levels of norepinephrine and dopamine in prefrontal cortex of brain; a potential mechanism for efficiency in ADHD. *Neuropsychopharmacology* **27**: 699–711
Conners CK, Sitarenios G, Parker JD, Epstein JN (1998a) The revised Conners' Parent Rating Scale (CPRS-R): factor structure, reliability, and criterion validity. *J Abnorm Child Psychol* **26**(4): 257–68
Conners CK, Sitarenios G, Parker JD, Epstein JN (1998b) Revision and restandardization of the Conners Teacher Rating Scale (CTRS-R): factor structure, reliability, and criterion validity. *J Abnorm Child Psychol* **26**(4): 279–91
Donnelly C (2006) Treating patients with ADHD and coexisting conditions. *Behav Healthc* **26**(9): 39–51
DuPaul G, Eckert TL (1997) The effects of school-based Interventions for attention deficit hyperactivity disorder; a meta-analysis. *School Psychology Review* **26**: 5–27
Escobar R, Soutullo CA, Hervas A, Gastaminza X, Polavieja P, Gilaberte I (2005) Worse quality of life for children with newly diagnosed attention-deficit/hyperactivity disorder, compared with asthmatic and healthy children. *Pediatrics* **116**(3): e364–e369
Gaub M, Carlson CL (1997) Gender differences in ADHD; a meta-analysis and critical review. *J Am Acad Child Adolescent Psychiatry* **36**: 1036–45
Goodman R (1997) The Strengths and Difficulties Questionnaire: a research note. *J Child Psychol Psychiatry* **38(5):** 581–6
Harter S (1985) *Manual for the Self-Perception Profile for Children.* University of Denver, Denver, CO
Jensen PS, Martin D, Cantwell DP (1997) Comorbidity in ADHD; implications for research, practice and DSM V. *J Am Acad Child Adolesc Psychiatry* **36**: 1065–79
Johnston C, Mash EJ (2001) Families of children with attention-deficit/hyperactivity disorder; review and recommendations for future research. *Clinic Child Fam Psychol Rev* **4**(3): 183–207
Mercugliano M (1999) What is attention-deficit/hyperactivity disorder? *Pediatr Clin North Am* **46(5):** 831–43
MTA Cooperative Group (1999) A 14 month randomized clinical trial of treatment strategies for attention-deficit hyperactivity disorder. The MTA Cooperative Group. Multimodal Treatment Study of children with adhd. *Arch Gen Psychiatry* **56**: 1073–86
National Institute for Health and Clinical Excellence (2006) *Methylphenidate, atomoxetine, dexamphetamine for ADHD in children and adolescents.* Review of Technology Appraisal 13. Technology Appraisal 98. National Institute for Health and Clinical Excellence, London
Ness J, Price LA (1990) Meeting the psychosocial needs of adolescents and adults with learning disability. *Intervention in School and Clinic* **26**: 16–21
Prasad S, Harpin V, Poole L, Zeitlin H, Jamdar S, Puvanendra K (2007) A multicentre,randomized,open label study of Atomoxetine in comparison to standard current therapy in UK children and adolescents with ADHD. *Curr Med Res Opin* **23**(2): 379–94
Ralston SJ, Lorenzo MJM (2004) Attention-Deficit Hyperactivity Disorder Observational Research in Europe. ADORE study group. *Eur Child Adolesc Psychiatry* **13** (suppl 1): 36–42
Richardson AJ, Montgomery P (2005) The Oxford-Durham study: a randomized, controlled trial of dietary supplementation with fatty acids in children with developmental coordination disorder. *Pediatrics* **115(5)**: 1360–6
Scottish Intercollegiate Guidelines Network (2001) *Attention deficit and hyperkinetic disorders in children and young people.* Scottish Intercollegiate Guidelines Network Clinical Guideline 52. Scottish Intercollegiate Guidelines Network, Edinburgh (http://www.sign.ac.uk/guidelines/fulltext/52/index.html accessed 25 June 2007)
Sever Y, Ashkenazi A, Tyano S, Weizman A (1997) Iron treatment in children with attention deficit hyperactivity disorder. A preliminary report. *Neuropsychobiology* **35**(4): 178–80
Starfield B, Riley A, Ensminger M et al (2000) *Manual for Child Health and Illness Profile – Child Edition.* The John Hopkins University, Baltimore, MD
Swanson J (1993) Effect of stimulant medication on hyperactive children. A review of reviews. *Except Child* **60**: 154–62
Taylor E, Dopfner M, Sergeant J et al (2004) European clinical guidelines for hyperkinetic disorder -- first upgrade. *Eur Child Adolesc Psychiatry* **13** Suppl 1: I7–30
Whalen CK, Henker B (1991) Therapies for hyperactive children; comparisons, combinations and compromises. *J Consult Clin Psychol* **59**: 126–37
World Health Organization (1992) *International Classification of Mental and Behavioural Disorders,* 10th edn. World Health Organization, Geneva