Attention-deficit/hyperactivity disorder (ADHD) is a condition that is characterized by developmentally high levels of inattention, overactivity, and impulsivity, although the extent and distribution of symptoms often varies across individuals. ADHD often begins very early in childhood. Children with this condition are often unable to focus their attention on tasks, are easily distracted, fail to complete assignments, and shift from one play activity to another. They may also be extremely overactive and aggressive. 

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, groups ADHD symptoms into two domains: inattention and hyperactivity/impulsivity. Some children only manifest symptoms in one of these domains, although the majority have impairments in both. ADHD co-occurs with other psychiatric and cognitive conditions in approximately two thirds of cases. Most common among these are oppositional and conduct problems (up to 50% of some samples), anxiety disorders (often approximately 25% of cases), mood disorders (5% to 15%), and learning disorders (at least 20%). Children with ADHD are at risk for development of conduct and antisocial disorders, substance use disorders, academic underachievement, poor educational and vocational attainment, and secondary mood and anxiety disorders. Moreover, ADHD symptoms frequently persist into adulthood, with the majority of individuals showing some evidence of residual symptomatology or impairment, and a somewhat lower percentage having the full disorder.

Although ADHD has long been well known to pediatricians and specialists in child mental health, it was often unfamiliar to other disciplines. However, as information about the range of impairments associated with ADHD and its persistence over the lifespan have become more available, ADHD has attracted considerable interest. Not all of this attention has been positive; there have been concerns regarding the possibility of over-diagnosis and over-treatment, with particular focus on the large increase in stimulant medication use over the past decade. Some have alleged that ADHD is better conceptualized as a problem of temperament, rather than a psychiatric disorder, or a reflection of a mismatch between the developmental needs of children and those of an increasingly achievement-oriented society. The public dialogue regarding these issues has led to several comprehensive reviews of ADHD diagnosis and treatment. The American Medical Association Council on Scientific Affairs concluded that there was little support for the suggestions of over-treatment, and epidemiological data indicate that under-treatment is at least as serious problem as over-treatment. Nevertheless, the results of other studies suggest that stimulant use is quite high in selected school districts or geographic regions. Concerns persist, despite the fact that medications for ADHD have been shown to be quite effective and well-tolerated in a large, long-term randomized multicenter trial. As a result of continuing controversy in this area, the Consensus Conference on Diagnosis and Treatment of ADHD was convened in November, 1998. Jensen provides a summary of the conference.

Other papers review key areas in the literature and present new data on questions of interest. Schulz et al summarize what is known regarding the neurobiology of ADHD, describing several models that have been presented and examining the degree to which these models are supported by the results of neuropsychological, neurochemical, imaging, and genetic studies. Solanto reviews the empirical basis for the distinction between ADHD combined and primarily inattentive subtypes, raising the question of whether apparently related symptoms of inattention in the two subtypes are driven by different mechanisms. Marks et al present longitudinal data related to the development of aggression in children with ADHD, suggesting that severity of verbal aggression, rather than physical aggression, may be a more potent predictor of the persistence and escalation of aggression over time. Finally, Himmelstein presents pilot data on neuropsychological functioning in adults with ADHD, suggesting that organization of motor output may be more important than inattention over the lifespan.

The goal of this issue of CNS Spectrums is to offer a glimpse into key issues in the field, focusing primarily on neurobiology, developmental psychopathology, and neuropsychology. Despite all that is known about ADHD, there is still much work to be done. Hopefully, the papers in this issue identify fruitful areas for future research.
Why expose your patients to the “ups and downs” of traditional carbamazepine therapy?

Peak-to-trough fluctuations in patients receiving immediate-release carbamazepine three times daily can be as great as 2.5 fold\(^1\)
Switch to Carbatrol®—Second-generation delivery system design that targets the limitations of conventional carbamazepine

• Bioequivalent to immediate-release carbamazepine dosed rigidly Q6h
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Absence seizures (petit mal) do not appear to be controlled by carbamazepine. The most frequently reported adverse events (particularly during the initial phases of therapy) are dizziness, drowsiness, unsteadiness, nausea, and vomiting. Adverse events can be minimized by initiating therapy at the lowest possible effective dose.

**CARBATROL®**
(carbamazepine extended-release capsules)
200 mg and 300 mg

**Brief Summary Precautions Information**

**WARNING**

APLASTIC ANEMIA AND AGRANULOCYTOSIS HAVE BEEN REPORTED IN ASSOCIATION WITH THE USE OF CARBAMAZEPINE. FROM ITS INCEPTION CARBAMAZEPINE HAS BEEN ASSOCIATED WITH THE RISK OF HEPATIC TOXICITY WHICH MAY OCCUR AS A SYMPTOMATICALLY SILENT LIVER DISEASE. THE RISK OF DEVELOPING THESE REACTIONS IS ABOUT 5-6 TIMES GREATER THAN THE BASE RISK OF THE GENERAL POPULATION.

Hepatic toxicity manifested by elevations of hepatic transaminase, alkaline phosphatase, or bilirubin has been reported in up to 15% of patients receiving carbamazepine. In approximately 5% of patients, these abnormalities have led to discontinuation of the drug. The drug should be discontinued if hepatic transaminase elevations to two times the upper limit of normal are observed. A liver biopsy should be performed in patients who continue to receive the drug despite persistently elevated liver enzymes, particularly if the duration of therapy is prolonged. When discontinuing the drug, patients should be observed closely for at least 3 months after discontinuation.

**Drug Interactions**

Clinically meaningful drug interactions have occurred with concomitant medications and include, but are not limited to:

- **Agents that may affect carbamazepine plasma levels:**
  - CYP 3A4 inhibitors inhibit carbamazepine metabolism and can thus increase plasma carbamazepine levels. Drug interactions include, but are not limited to:
    - **CYP 3A4 inducers** increase the rate of carbamazepine metabolism and can thus decrease plasma carbamazepine levels. Drugs that have been shown, or would be expected, to decrease plasma carbamazepine levels include:
      - dexamethasone, diltiazem, fluoxetine, flecainide, indinavir, nelfinavir, nevirapine, ritonavir, and saquinavir.

**Effect of carbamazepine on plasma levels of concomitant agents:**

Carbamazepine induces CYP 3A4, which can affect the plasma levels of concomitant medications.

**Geriatric Use**

No systematic studies in geriatric patients have been conducted.

**Adverse Reactions**

Adverse reactions of such severity that the drug must be discontinued, the physician must be notified, and the patient monitored, include, but are not limited to:

- **Hepatic**
  - Portal hypertension, hepatic failure.

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