Surgery for Psychiatric Disorders

Part Two

Neurosurgical Approaches to Intractable Obsessive-Compulsive Disorder
S. Rasmussen, B. Greenberg, P. Mindus, G. Friehs, and G. Noren

Electrical Stimulation of the Brain for Psychiatric Disorders
B. Nuttin, L. Gabriëls, P. Cosyns, and J. Gybels

Vagus Nerve Stimulation: A New Form of Therapeutic Brain Stimulation

GRAND ROUNDS
SSRI Reduction of Nonparaphilic Sexual Addiction
J. L. Elmore
In mild to moderate Alzheimer's disease

You see it as maintaining cognitive

* Individual responses to ARICEPT® may include improvement, stabilization, or decline.

† The most common adverse events in pivotal clinical trials with ARICEPT® were nausea, diarrhea, insomnia, vomiting, muscle cramps, fatigue, and anorexia. Pivotal clinical trials of ARICEPT® have shown no increase, relative to placebo, in the incidence of either peptic ulcer disease or gastrointestinal bleeding. Nevertheless, cholinesterase inhibitors may be expected to increase gastric acid secretion. Therefore, patients (especially those at increased risk for developing ulcers—eg, having a history of ulcer disease, receiving concurrent nonsteroidal anti-inflammatory drugs) should be monitored closely for gastrointestinal bleeding. In pivotal clinical trials, syncopal episodes have been reported in association with ARICEPT® (2% vs 1% for placebo).
function.

She sees it as a bedtime story.

ARICEPT®. Helping to make a difference for people living with Alzheimer's

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- Proven to maintain cognition in placebo-controlled studies
- Well tolerated†
- Proven safety profile
- Once-daily dosing
- 3 years of real-world use

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5-MG and 10-MG TABLETS
THERAPY TO REMEMBER™

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Frequency estimates may not apply, as the conditions of use, reporting behavior, and the kinds of patients treated may differ from those in the controlled clinical trials and were comparable to those seen in patients on 5 mg/day. See Table 2 for a comparison of the most common adverse events following one and six week titration regimens.

Patients Randomized

<table>
<thead>
<tr>
<th>Dose Group</th>
<th>Placebo</th>
<th>5 mg/day ARICEPT*</th>
<th>10 mg/day ARICEPT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients randomized</td>
<td>355</td>
<td>350</td>
<td>315</td>
</tr>
</tbody>
</table>

Most Frequent Adverse Events Leading to Withdrawal from Controlled Clinical Trials

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Placebo</th>
<th>5 mg/day ARICEPT*</th>
<th>10 mg/day ARICEPT*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose Group</td>
<td>355</td>
<td>350</td>
<td>315</td>
</tr>
<tr>
<td>Patients randomized</td>
<td>1%</td>
<td>1%</td>
<td>3%</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>0%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Most Frequent Adverse Clinical Events Seen in Association with the Use of ARICEPT* The most common adverse events, as defined those occurring at a frequency of at least 5% in patients receiving 10 mg/day and twice the placebo rate, are largely preceded by ARICEPT* cholinomimetic effects. These include naso-sinus, diarrhea, vomiting, mumps, fatigue, and anorexia. These adverse events were often of mild intensity and transient, resolving during continued ARICEPT* treatment without the need for dose modification. There is no evidence to suggest that the frequency of these adverse events is increased for patients treated for the long-term than those seen in patients treated for a shorter period of time. These adverse events were not related to patients receiving placebo in the 15- and 30-week studies. These patients were titrated to a dose of 10 mg/day over a 6-week period. The common rate of adverse events were lower than those seen in patients titrated to 10 mg/day over one week in the controlled clinical trials and were comparable to those seen in patients treated for longer periods of time. See Table 2 for a comparison of the most common adverse events following one and six week titration regimens.
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. 
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- Extensive drug dispersion, dissolution, and absorption
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- BID dosing
- No generic equivalent

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.


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200 mg capsule ~ 300 mg capsule
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(carbamazepine extended-release capsules)
200 mg and 300 mg

**Brief Summary of Prescribing Information**

**WARNING**

APLASTIC ANEMIA AND AGRANULOCYTOSIS HAVE BEEN REPORTED IN ASSOCIATION WITH THE USE OF CARBAMAZEPINE. THE RISK OF DEVELOPING THESE REACTIONS IS 5-6 TIMES GREATER THAN IN THE GENERAL POPULATION. HOWEVER, THE OVERALL RISK OF THESE REACTIONS IN THE UNRELATED GENERAL POPULATION IS LOW. AGRANULOCYTOSIS MAY OCCUR AT ANY TIME DURING THERAPY. THE RISK OF DEVELOPING AGRANULOCYTOSIS IS HIGHER IN PATIENTS TAKING 15-20 GRAMS/day OF WHITE BLOOD CELL COUNTS ARE NOT COMMON IN ASSOCIATION WITH THE USE OF CARBAMAZEPINE. DATA ARE NOT AVAILABLE TO ESTIMATE ACCURATELY THEIR INCIDENCE OR OUTCOME. HOWEVER, THE VAST MAJORITY OF PATIENTS WHO DEVELOP AGRANULOCYTOSIS HAVE A HISTORY OF DRUG ALLERGY. CARBAMAZEPINE AND AGRANULOCYTOSIS

The occurrence of agranulocytosis is associated with other anticonvulsant drugs, particularly phenytoin and phenobarbital. Induction of anticonvulsant metabolism may increase the risk of neutropenic effects. Alterations of thyroid function have been reported in combination therapy with other anticonvulsants, including carbamazepine and phenytoin. The incidence of agranulocytosis is unknown.

**INDICATIONS AND USAGE**

**Epilepsy**

Carbamazepin is indicated for use as an anticonvulsant drug. Evidence supporting efficacy of carbamazepine as an anticonvulsant was derived from active drug-controlled studies that enrolled patients with the following seizure types:

1. Partial seizures with complex symptomatology (psychomotor, temporal lobe). Patients with these types of seizures usually have a different initial clinical picture from those with other types.
2. Generalized tonic-clonic seizures (grand mal).
3. Migraine seizures which include the above, or other partial or generalized seizures. Absence seizures (petit mal) do not appear to be controlled by carbamazepine (see PRECAUTIONS, General).

**Trigeminal Neuralgia**

Carbamazepin is effective in the treatment of the pain associated with trigeminal neuralgia. Beneficial effects have also been reported in glosopharyngeal neuralgia. This drug is not a simple analgesic and should not be used to treat chronic, casual aches or pains.

**CONTRAINDICATIONS**

Carbamazepine should not be used in patients with a history of previous bone marrow depression, including agranulocytosis, aplastic anemia, or myelosuppression. Administration of carbamazepine to patients with these conditions is contraindicated.

**Usage in Pregnancy**

Carbamazepin can cause fetal harm when administered to a pregnant woman. Epidemiological data suggest that there may be an association between the use of carbamazepine during pregnancy and the occurrence of birth defects. Carbamazepine should not be used with caution in patients with a history of cardiac, hepatic, or renal damage; adverse hematologic reaction to other drugs; or interrupted courses of therapy with carbamazepine.

**Information for Patients**

Doctors are aware of the early toxic signs and symptoms of a potential hematological risk, such as fever, sore throat, rash, ulcers in the mouth, easy bruising, petechial or purpuric hemorrhage, and should be alert to the possibility of life-threatening events. Immediate withdrawal of treatment should be undertaken if symptoms suggestive of thrombocytopenia are noted.

Since dullness and dizziness may occur, patients should be cautioned about the hazards of operating machinery or automobiles or engaging in other potentially dangerous situations.

**PRECAUTIONS**

**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 inducers can increase the rate of carbamazepine metabolism and can thus decrease plasma carbamazepine levels. Drugs that are potent inhibitors of CYP 3A4 may decrease the amount of carbamazepine that is cleared. Examples include:
  - CYP 3A4 inducers that increase the rate of carbamazepine metabolism and can thus decrease plasma carbamazepine levels. Drugs that are potent inhibitors of CYP 3A4 may decrease the amount of carbamazepine that is cleared. Examples include:
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**Labor and Delivery**

The effect of carbamazepine on human labor and delivery is unknown.

**Nursing Mothers**

Carbamazepine and its metabolites are excreted in breast milk and during lactation. The risk to the nursing infant of adverse effects associated with maternal administration of carbamazepine is unknown. Because of the potential for serious adverse reactions in nursing infants from carbamazepine, a decision should be made whether to continue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**Pediatric Use**

Substantial evidence of carbamazepine effectiveness in use in the management of children with epilepsy (see CLINICAL PHARMACOLOGY). Carbamazepine is contraindicated in infants and children, since safety and efficacy have not been established in these populations.

**Hemorrhagic System**

Aplastic anemia, agranulocytosis, hypopigmentation, bone marrow depression, the effect of male, leukaemia, leukocytosis, leukophagy, acute interstitial.

**Skin:** Purpura and erythematous rashes, urticaria, toxic epidermal necrolysis (Lyell's syndrome) (see WARNINGS). Stevens-Johnson syndrome (see WARNINGS), photosensitivity reactions, alterations in skin pigmentation, pigmentation of the nail apparatus, and alopecia.

**Psychiatric System:** Depression, agitation, anxiety, confusion, dizziness, drowsiness, excitement, insomnia, nystagmus, myalgia, nervousness, nervousness, paresthesia, rash, tremor, vertigo, weakness, weight loss, weight gain, weight gain, weight gain, weight gain.

**Genitourinary System:** Urinary frequency, acute urinary retention, oliguria with elevated blood pressure, azotemia, renal failure, and impotence. Albuminuria, glycosuria, elevated BUN and microscopic deposits in the urine have also been reported. Torsade de pointes atrial arrhythmia may occur in rats receiving carbamazepine orally from 4-5 weeks at doses of 50-400 mg/kg/day. Additionally, rats receiving carbamazepine in the diet for 2 years at doses of 25, 75, and 250 mg/kg/day had a dose-related incidence of tachyarrhythmia and aspermatogenesis. In the long-term study, carbamazepine produced a rare form of adenocarcinoma, the urine bladder and the day of 50 mg/kg/day and higher. Relevance of these findings to humans is unknown.

**Metabolism:** Blood, liver, and brain. Changes in liver function tests, cholesterol, and leucopenia, anemia, eosinopenia, and neutropenia, decreased white blood cell count, and decreased platelet count, decreased serum electrophoretic patterns, increased serum transaminase levels, increased serum alkaline phosphatase levels, increased serum gamma-glutamyl transferase levels, increased serum bilirubin levels, and decreased serum albumin levels.

**Other:** Isolated cases of a lupus erythematosus-like syndrome have been reported. There have been occasional cases of photosensitivity and antinuclear antibodies. A case of aseptic meningitis, accompanied by mycoplasma and peripheral eosinophilia, has been reported in a patient with carbamazepine-induced interstitial nephritis. Other cases of drug-induced liver injury have been reported. The patient was successfully discharged, and the meningitis reappears with recurrent rash on carbamazepine treatment.

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This month we present part two of our survey of new procedures and surgical techniques that are used for the treatment of neurological disease and under study for the treatment of psychiatric illness. Within neurology and neurosurgery, many of these techniques are already part of regular clinical procedures when more conventional measures fail, but for psychiatry the idea of invasive procedures often seems provocative. This is particularly the case when we remember the suspect past of psychosurgery. There are even some very misguided critics who cast aspersions at the most effective treatment for depression, electroconvulsive therapy.

The three reviews in this issue, however, should reassure the neurologist, neurosurgeon, and psychiatrist that these procedures are well worth investigating for psychiatric illness. Rasmussen and colleagues begin their discussion of surgical procedures for refractory obsessive-compulsive disorder (OCD) by reviewing what is known about the neuroanatomy of the condition. Clearly, modern neuroimaging technology has for the first time made it possible to trace brain circuits that are activated during a variety of human emotions and behaviors and to show when activity in these networks is abnormal. This paves the way for studying surgical and other invasive procedures to treat illnesses like OCD.

Similarly, deep brain stimulation (DBS), as reviewed by Nuttin and colleagues, is a fascinating procedure used to some extent in neurology and now being tested for the treatment of some psychiatric illnesses. The technique has the advantage of being reversible; unlike psychosurgery, if the results are not positive or side effects too bothersome, DBS can be stopped immediately. Clearly, this technique will require careful research before it can be recommended as an approach to even the most severely afflicted patients with mood and anxiety disorders.

Another novel technique involving direct interaction with the central nervous system is nicely reviewed in this volume by George and colleagues. They are among the leaders in developing the technique of vagus nerve stimulation (VNS) to treat depression. VNS is already an important procedure for the treatment of medication-resistant epilepsy and given the successful use of anticonvulsant medications for several mood disorders, it was logical that sooner or later it would be tried for depression as well. As George and colleagues note, the procedure appears to be remarkably safe, but its efficacy is still not known. One problem is that it is only currently attempted in research studies involving patients who have not responded to multiple trials of antidepressant medications. No novel treatment, regardless of how effective, is likely to show robust results in such a group of refractory patients. Hence, the bar for deciding whether VNS is helpful in treating depression is set very high.

These are exciting developments and we are grateful to our guest editor, Ali R. Rezaia, MD, for assembling this group of distinguished scientists and clinicians to present a comprehensive overview of an emerging field. As I mentioned last month in my first column as editor of CNS Spectrums, we welcome your comments and suggestions for future themes as well as your original research articles for rapid review and, if accepted, publication.

Dr. Gorman is professor of psychiatry and vice chair for research at Columbia University College of Physicians & Surgeons in New York City. He is also the editor of this journal.
ANSWERING THE NEED FOR NEW THERAPEUTIC APPROACHES TO OCD

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“Despite significant progress over the last decade in the treatment of OCD, current behavioral therapies and pharmacologic treatments provide substantial benefit to only 50% to 70% of patients. In addition, side effects of current drug therapies limit long-term treatment adherence. More than 50% of those patients who respond to a 12-week trial of a serotonin reuptake inhibitor (including clomipramine, fluoxetine, sertraline, fluvoxamine, and paroxetine) stop taking the medication before completing 2 years of maintenance treatment due to sexual dysfunction, weight gain, or sedation. It is, therefore, not surprising that a recent conference of experts in the field highlighted the need for new therapeutic approaches to OCD. An estimated 20% of OCD patients are refractory to current medication and behavioral treatments. Half of this treatment-refractory group suffers from incapacitating illness, with tremendous suffering and overall functional impairment. For clinicians who are familiar with the devastating consequences of the malignant form of this disorder, it is not surprising that these severely ill OCD patients have turned to neurosurgical intervention for any possibility of relief, however remote, from their daily distress and suffering.

In this article, the authors review prior studies of the efficacy and safety of neurosurgical procedures for intractable OCD. Recent data that are relevant to the hypothetical neuroanatomic pathophysiology of OCD are discussed as they relate to future prospects in this field.”

REVERSIBLE INTERVENTIONS: OFFERING RELIEF AND AUTONOMY

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“A lesioning procedure is irreversible. In the field of functional and stereotactic neurosurgery, however, there is currently a trend towards reversible interventions. The reversibility is usually not an advantage in terms of the beneficial effects that are obtained, but it is an advantage if unwanted side effects occur. The lesioning procedure has the advantage of a long-lasting beneficial effect, but with the disadvantage of irreversibility should unwanted side effects occur.

A parallel can be drawn between surgical treatments in PD and severely ill patients suffering from OCD. Lesioning or electrically stimulating the ventral intermediate nucleus leads to similar results (i.e., tremor reduction). The same is true for the globus pallidus and even the subthalamic nucleus. This cannot, however, be applied to every target. For example, electrical stimulation of the posterior limb of the internal capsule leads to a tonic contraction of contralateral muscles, whereas a stroke involving the same brain region leads to paralysis.

Patients can decide for themselves whether they will actually take medication or not. They can try a certain compound, and if it is not working or if they suffer too many adverse effects, they can opt to stop it and to change to another compound. Capsulotomy, being a lesioning technique, is irreversible both in its effects and side effects. Electrical stimulation, therefore, may provide patients with some autonomy. When the current is switched off, the effects of capsular stimulation disappear. If side effects are unacceptable and do not outweigh therapeutic efficacy, patients can decide to stop stimulation. Moreover, after an adaptation period, one of our patients learned to adjust stimulation parameters (especially amplitude and pulse width) herself, based on the necessities and therapeutic outcomes she preferred in a given situation.

Electrical stimulation of the brain is, in a way, comparable to drug treatment. Like an antidepressant, stimulation may alter mood. Both act as long as they are administered. Many drugs, such as baclofen for spasticity, require the implantation of a drug-administration device. For electrical stimulation, a stimulation device needs to be implanted.”

VNS AND THE UNDEREMPHASIZED AFFERENT ROLE OF THE VAGUS NERVE

page 43

“There has long been interest in whether and how autonomic functions modulate activity in the limbic system and higher cortex. For reasons that are unclear, most people are more familiar with the vagus nerve’s efferent functions, where it serves as the messenger for signals from the brain to control the viscera. Traditionally, the vagus nerve has been considered a parasympathetic efferent nerve, controlling and regulating autonomic functions, such as heart rate and gastric tone. However, it is actually a mixed nerve, composed of about 80% afferent sensory fibers carrying information to the brain from the head, neck, thorax, and abdomen.

It is this afferent role that has been underemphasized in the traditional literature. Despite this bias toward viewing the vagus nerve as an efferent carrier of signals from the brain to the body, several astute researchers over the past 100 years have studied the afferent role of the vagus nerve. Numerous studies have identified extensive projections of the vagus nerve via its sensory afferent connections in the nucleus tractus solitarii (NTS) to diverse brain regions. For example, in 1938 Bailey and colleagues reported that VNS in the cat elicited synchronized activity in the orbital cortex. In 1949, MacLean and colleagues stimulated the vagus nerve and recorded electroencephalographic (EEG) activity from the cortical surface of anesthetized monkeys, finding inconsistent slow waves generated from the lateral frontal cortex. In 1951, Dell and colleagues found that VNS evoked a slow-wave response in the anterior rhinal sulcus, as well as in the amygdala, in awake cats with high cervical spinal sections. More recently, in 1980 MacLean used single-unit recordings to show that VNS results in specific activity in the cingulate and other limbic regions.”
APHTHEMPTINES HAVE A HIGH POTENTIAL FOR ABUSE. ADMINISTRATION OF APHTHEMPTINES FOR PROLONGED PERIODS OF TIME MAY LEAD TO DRUG DEPENDENCE AND MUST BE AVOIDED. PARTICULAR ATTENTION SHOULD BE PAID TO POTENTIAL SUBJECTS OBTAINING APHTHEMPTINES FOR NON- THERAPEUTIC USE OR DISTRIBUTION TO OTHERS, AND THE DRUGS SHOULD BE PRESCRIBED OR DISPENSED SPARINGLY.

INDICATIONS: Attention Deficit Disorder with Hyperactivity: ADDERALL is indicated as an integral part of a total treatment program which typically includes other remedial measures (psychological, educational, social) for a stabilizing effect in children with behavior disorders. The following symptoms: moderate to severe distractibility, short attention span, hyperactivity, emotional liability, and impulsivity. The diagnosis of this syndrome should not be made with frivolity when these symptoms are only of comparatively recent origin. Nonlocalizing (soft) neuropsychological tests are not appropriate here. A detailed history of the patient's life and a careful diagnosis of central nervous system dysfunction may or may not be warranted. In Narcolepsy: CONTAINING: Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, locomotor hypersensitivity or idiocyndra to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crises may result). WARNINGS: Clinical experience suggests that in psychotic children, administration of amphetamine may exacerbate symptoms of behavior disturbance and thought disorder. Data are inadequate to determine whether chronic administration of amphetamine may be associated with growth inhibition. Puberty may be delayed. A child's sexual development should be monitored during treatment. Usage in Pregnancy: Mothetrs: Amphetamines are excreted in human milk. Mothers taking amphetamines should be advised to refrain from nursing.

PRECAUTIONS: General: Caution is to be exercised in prescribing these drugs to patients with a history of cardiac disease; MAO inhibitors should be discontinued at least 14 days before starting amphetamines, unless a long period of time has elapsed since the last MAO inhibitor dose. A child's sexual development should be monitored during treatment. WARNINGS: Clinical experience suggests that in psychotic children, administration of amphetamine may exacerbate symptoms of behavior disturbance and thought disorder. Data are inadequate to determine whether chronic administration of amphetamine may be associated with growth inhibition. Puberty may be delayed. A child's sexual development should be monitored during treatment. Usage in Pregnancy: Mothetrs: Amphetamines are excreted in human milk. Mothers taking amphetamines should be advised to refrain from nursing.

Why make the switch to ADDERALL®?

- On average, ADDERALL is more effective than Ritalin® ($p<0.001$)\(^1\)
- ADDERALL was favored 3 to 1 over Ritalin by clinical staff for continued medication\(^1\)
- Ritalin patients were rated more deviant than ADDERALL, particularly on lower doses\(^1\)
- ADDERALL scored better than MPH on Clinical Global Impression (CGI) improvement ($p<0.05$)\(^2\)
- There were significantly more responders in the ADDERALL group than the MPH group ($p<0.01$)\(^2\)
- ADDERALL showed better scores than MPH for both inattention and hyperactivity ($p<0.05$)\(^2\)
- Clinical staff clearly preferred ADDERALL over MPH for continuation of treatment\(^3\)
- ADDERALL is dispensed for more ADHD patients than Ritalin\(^4\)
- ADDERALL is safe—low incidence of spontaneously reported adverse events\(^5\)

ADDERALL is generally well tolerated—adverse reactions have seldom been reported (most frequently reported adverse reactions include anorexia, insomnia, stomach pain, headache, irritability, and weight loss). As with most psychostimulants indicated for ADHD, the possibility of growth suppression and the potential for precipitating motor tics and Tourette’s syndrome exist with ADDERALL treatment and, in rare cases, exacerbations of psychosis have been reported. Since amphetamines may have a high potential for abuse, ADDERALL should only be prescribed as part of an overall multimodal treatment program for ADHD with close physician supervision.

**References**

2. There were significantly more responders in the ADDERALL group than the MPH group.
3. ADDERALL showed better scores than MPH for both inattention and hyperactivity.
5. ADDERALL is dispensed for more ADHD patients than Ritalin.

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This continuing medical education series gives the reader the opportunity to test his/her understanding and recall of clinical material presented in this issue. Approved for 3.0 credit hours in Category 1.

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In two 6- to 8-week placebo-controlled clinical trials, spontaneously reported, treatment-emergent adverse events with an incidence of 5% or greater in at least one of the RISPERDAL groups and at least twice that of placebo were: anxiety, somnolence, extrapyramidal symptoms, dizziness, constipation, nausea, dyspepsia, rhinitis, rash, and tachycardia.

EPS with RISPERDAL, while dose-dependent, are comparable to placebo at doses ≤6 mg/day and differ significantly from placebo at doses >6 mg/day. Prescribing should be consistent with the need to minimize the risk of tardive dyskinesia; if its signs and symptoms appear, discontinuation of RISPERDAL should be considered.

Orthostatic hypotension was reported infrequently (<1%) in clinical trials; its risk may be minimized by following the recommended RISPERDAL dose titration regimen.

Reference:
1. IMS America, 12/99.

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Reference:
1. IMS America, 12/99.

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The #1 prescribed antipsychotic

01-RS-708 July 2000

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Risperidone (RISPERDAL*) is contraindicated in patients with a known hypersensitivity to the product.


drug interactions

The concomitant use of RISPERDAL* and other drugs in patients with severe hepatic impairment has not been studied. However, cross-reactivity among the cytochrome P450 enzyme systems is expected, and caution should be exercised when Risperidone is coadministered with other drugs that are metabolized by the same enzyme systems.


drug interactions

Concomitant use of RISPERDAL* and other drugs with various mechanisms of action should be used cautiously because of the potential for adverse events. Cross-reactivity among the cytochrome P450 enzyme systems is expected, and caution should be exercised when risperidone is coadministered with other drugs that are metabolized by the same enzyme systems.


drug interactions

Concomitant use of RISPERDAL* and other drugs with various mechanisms of action should be used cautiously because of the potential for adverse events. Cross-reactivity among the cytochrome P450 enzyme systems is expected, and caution should be exercised when risperidone is coadministered with other drugs that are metabolized by the same enzyme systems.


drug interactions

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drug interactions

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