

Drug-Induced Dysphagia

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Abstract

Dysphagia is commonly defined as difficulty swallowing. Although the disorder can have several causes, the patient's medication is often overlooked as a source of the problem. This type of dysphagia, one of the most readily corrected, is known as drug-induced dysphagia. A thorough literature search was undertaken to determine the potential for drug-induced dysphagia.

Drug-induced dysphagia can be classified into one of three categories: dysphagia as a side effect, dysphagia as a complication of therapeutic action, and medication-induced esophageal injury. Examples of medications in each category are provided based on therapeutic classification. Specifically, the role of dysphagia in multiple sclerosis and the agents that have been linked with dysphagia are discussed.

The most valuable method of preventing drug-induced dysphagia is obtaining a thorough and accurate medication history from each patient. Other prevention strategies and compensatory techniques are also explored.

Introduction

Dysphagia is defined as the subjective sensation of difficulty swallowing.¹ Dysphagia itself is not a disease; rather, it is a symptom of an underlying disorder. The word dysphagia is derived from the Greek roots *dys* (meaning "with difficulty") and *phagia* (meaning "to eat").¹ It is estimated that up to 15 million people in the United States suffer from some form of dysphagia.²

The seemingly simple act of swallowing is actually a highly complex process. Approximately 30 facial muscles and 8 cranial nerves are involved in a normal swallow.³ Impairment of these muscles or nerves from any mechanism may lead to a swallowing disorder.

Symptoms of dysphagia are widely varied, ranging from difficulty initiating a swallow to the feeling of complete esophageal obstruction.¹ Early symptoms may include frequent throat clearing, drooling, a hoarse or weak voice, choking or coughing while eating, problems with speech, or regurgitation of food.²⁻⁶ The patient may report fullness, pressure or burning in the sternal area after eating, a loss of pleasure in food, or that food is "sticking" in the throat.³⁻⁶ Progressive dysphagia may result in lifestyle changes, such as decreased food intake or alterations in diet.^{5,6} Potentially damaging complications of dysphagia include coughing, choking, dehydration, malnutrition, and bronchitis or other upper airway infections.⁵ In extreme

cases, aspiration of food may result in pneumonia, which can have serious or even fatal consequences.^{2,5}

What Causes Dysphagia?

The most frequent causes of dysphagia are neurologic in origin. Common examples include cerebrovascular accident, Parkinson disease, myasthenia gravis, muscular dystrophy, Alzheimer disease, and multiple sclerosis (MS).^{1,2,5-8} However, dysphagia may also be caused by neuromuscular disorders or by obstruction of the esophagus. These causes include scleroderma, esophageal tumors or strictures, acquired immunodeficiency syndrome (AIDS), and head or neck injuries.^{2,9}

An often overlooked cause of dysphagia is the patient's medication. This is known as drug-induced dysphagia. Drug-induced dysphagia is far more common than reports in medical literature suggest, and it is one of the most readily corrected causes of dysphagia.

Drug-Induced Dysphagia

The first reported case of drug-induced dysphagia occurred in 1970.¹⁰ Through additional reports, 3 major mechanisms have been identified:

1. Dysphagia as a side effect of the drug;⁸
2. Dysphagia as a complication of the drug's therapeutic action;^{8,11} and
3. Medication-induced esophageal injury.^{8,11}

Each of these mechanisms will be discussed in detail, and both prevention strategies and compensatory techniques will be explored. However, it is important to note that the most valuable tool in determining the potential for any type of drug-induced dysphagia is the collection of a thorough and accurate medication history from each patient.^{2,5}

Dysphagia As a Side Effect

The esophagus is composed of both smooth and striated muscle.¹¹ Smooth muscle function and coordination are dependent on both cholinergic and muscarinic innervation. Therefore, drugs with anticholinergic or antimuscarinic activity have the potential to cause dysphagia (Table 1).^{8,11} Management techniques for this type of dysphagia usually include discontinuing the offending agent, if possible. In addition, the use of saliva substitutes or frequent sips of water to facilitate transport may be beneficial.

Table 1. Drugs That Have Anticholinergic or Antimuscarinic Effects¹¹⁻¹⁴

Atropine (Atropar)
Benztropine mesylate (Cogentin)
Dicyclomine (Bentyl)
Hyoscyamine (Cytospaz)
Ipratropium (Atrovent)
Oxybutynin (Ditropan)
Propantheline (Pro-Banthine)
Scopolamine (Transderm-Scop)
Trihexyphenidyl (Artane)
Tolterodine (Detrol)

Conversely, a direct effect on striated muscle is seen with neuromuscular blocking agents, used as muscle relaxants during surgery (Table 2).^{8,11} Management techniques for this type of dysphagia are minimal, as the effect typically decreases as the agent wears off.

Table 2. Neuromuscular Blocking Agents¹²⁻¹⁴

<p>Atracurium (Tracrium) Cisatracurium (Nimbex) Doxacurium (Nuromax) Mivacurium (Mivacron) Pancuronium (Pavulon) Pipecuronium (Arduan) Rocuronium (Zemuron) Succinylcholine (Anectine, Quelicin) Tubocurarine (Tubarine) Vecuronium (Norcuron)</p>

Drugs that cause dry mouth (xerostomia) interfere with swallowing by impairing food transport.^{8,11} The medications that most commonly cause xerostomia include tricyclic antidepressants, antihistamines, and diuretics.^{8,15} However, numerous other medications have been implicated (Table 3). Management strategies include changing to another agent, if possible; the use of a saliva substitute;¹⁵ and frequent sips of water between meals.

Table 3. Drugs That Cause Xerostomia^{8,11-15}

Angiotensin-converting enzyme (ACE) inhibitors	Captopril (Capoten) Lisinopril (Prinivil, Zestril)
Antiarrhythmics	Disopyramide (Norpace) Mexiletine (Mexitil) Procainamide (Procan)
Antiemetics	Meclizine (Antivert) Metoclopramide (Reglan) Ondansetron (Zofran) Prochlorperazine (Compazine) Promethazine (Phenergan)
Antihistamines and decongestants	Chlorpheniramine (Chlor-Trimeton) Cyproheptadine (Periactin) Diphenhydramine (Benadryl) Hydroxyzine (Atarax, Vistaril) Pseudoephedrine (Sudafed)

Diuretics	Ethacrynic acid (Edecrin)
Selective serotonin reuptake inhibitors (SSRIs)	Citalopram (Celexa) Fluoxetine (Prozac) Nefazodone (Serzone) Paroxetine (Paxil) Sertraline (Zoloft) Venlafaxine (Effexor)
Tricyclic antidepressants (TCAs)	Amitriptyline (Elavil) Desipramine (Norpramin) Imipramine (Tofranil)

Local anesthetics, commonly used for nasogastric tube insertion, endoscopy, or dental manipulation, may also cause dysphagia (Table 4). These drugs cause a loss of sensory afferent input, which results in a feeling of impaired or uncontrolled swallowing by the patient.^{8,11} This effect resolves as the medication wears off; therefore, management strategies are minimal.

Table 4. Local Anesthetics¹²⁻¹⁴

Benzocaine (Americaine, Dermoplast) Benzonatate (Tessalon) Lidocaine (Xylocaine)

Finally, antipsychotic (or neuroleptic) medications represent a unique class of drugs that may cause dysphagia as a side effect (Table 5). Antipsychotics work by blocking dopaminergic transmission, which can result in an extrapyramidal syndrome similar to Parkinson disease. This pseudo-Parkinsonism can contribute to dysphagia.¹¹ Over time, the resultant dopaminergic supersensitivity may lead to an irreversible syndrome known as tardive dyskinesia (TD).⁹ Clinically significant TD occurs in 10% to 20% of patients who take these drugs for longer than 1 year.¹⁵ Since TD usually involves the orofacial and lingual muscles, the syndrome may progress until the patient is unable to chew or swallow.¹⁵

Table 5. Antipsychotic/Neuroleptic Medications^{9,12-14,16,17}

Chlorpromazine (Thorazine) Clozapine (Clozaril) Fluphenazine (Prolixin) Haloperidol (Haldol) Lithium (Eskalith, Lithobid) Loxapine (Loxitane) Olanzapine (Zyprexa) Quetiapine (Seroquel) Risperidone (Risperdal) Thioridazine (Mellaril) Thiothixene (Navane) Trifluoperazine (Stelazine)
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Management of these patients is difficult, because use of the medication is imperative in many patients. Decreasing the dosage may also prove a challenge: drug-induced Parkinson-like dysphagia usually resolves on decreases in dosage, whereas the opposite is true for TD due to dopaminergic supersensitivity.⁹ However, several strategies can still be employed to manage dysphagia from an antipsychotic drug. First, use an atypical antipsychotic agent (such as risperidone, quetiapine, or olanzapine), which has less association with pseudo-Parkinsonism and TD.¹⁵ The patient should be observed carefully for pseudo-Parkinsonism; a reversing agent such as diphenhydramine, benztropine, or amantadine can be administered if such symptoms occur. Finally, monitoring the patient for TD is of utmost importance. The drug must be discontinued at the first signs of TD; if the drug is still given after the development of TD, the only treatment is to administer larger doses of the antipsychotic.^{9,15}

Dysphagia As a Complication of Therapeutic Action

Agents used to treat cancer or suppress the immune system may cause dysphagia through 2 different mechanisms. First, chemotherapy directly injures the esophageal mucosa due to cytotoxic effects on the rapidly dividing cells of the gastrointestinal tract. Second, prolonged use of immunosuppressants predisposes the patient to viral and fungal infections of the esophagus.^{8,11} Because these mechanisms often occur in combination, dysphagia in the oncology or transplant patient may be quite severe. A list of such medications is provided in Table 6. Management techniques for this type of dysphagia are twofold: using a therapeutic mouthwash to prevent infection and anesthetize the area, and treating the underlying infection, if present.¹¹

Table 6. Antineoplastics and Immunosuppressants¹¹⁻¹⁴

<p>Azathioprine (Imuran) Carmustine (BiCNU) Cyclosporine (Sandimmune, Neoral) Daunorubicin (Daunomycin) Lymphocytic immunoglobulin (Atgam) Paclitaxel (Taxol) Porfimer (Photofrin) Vinorelbine (Navelbine)</p>

The therapeutic effects of corticosteroids can also contribute to dysphagia. When used over a long period of time and in high doses, steroids can cause skeletal muscle wasting (Table 7).¹⁵ Although not usually the primary sight of deterioration, the skeletal muscles of the esophagus may be affected, resulting in dysphagia. Unfortunately, at this stage of muscle wasting, compensatory techniques may be the only viable option for dysphagia management. In such cases, a speech-language pathologist can offer suggestions beyond the scope of this discussion.

Table 7. High-Dose Corticosteroids¹²⁻¹⁴

<p>Dexamethasone (Decadron) Methylprednisolone (Medrol, Solu-Medrol) Prednisolone (Delta Cortef) Prednisone (Deltasone)</p>
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Medications that depress the central nervous system have been cited as a serious potential cause of dysphagia. Agents such as antiepileptics, benzodiazepines, narcotics, and skeletal muscle relaxants place the patient at greater risk for dysphagia due to decreased awareness, decreased voluntary muscle control, and difficulty initiating a swallow.^{8,15} A list of such medications is provided in Table 8. Approaches to managing this type of dysphagia involve advising the patient to take other medications prior to taking the offending agent, if possible. If this is not a realistic option, stress the importance of using caution when swallowing and to do so under close supervision.

Table 8. Medications That Cause Drowsiness or Confusion^{8,12-15}

Antiemetics	Droperidol (Inapsine)
Antiepileptic drugs	Carbamazepine (Tegretol) Gabapentin (Neurontin) Phenobarbital (Luminal) Phenytoin (Dilantin) Valproic acid (Depakote)
Benzodiazepines	Alprazolam (Xanax) Clonazepam (Klonopin) Clorazepate (Tranxene) Diazepam (Valium) Lorazepam (Ativan)
Narcotics	Alfentanil (Alfenta) Codeine (Tylenol #3) Fentanyl (Duragesic) Hydromorphone (Dilaudid) Meperidine (Demerol) Morphine (Astramorph, MS Contin, Roxanol) Oxycodone (OxyContin, Roxicodone) Propoxyphene (Darvon, Darvocet)
Skeletal muscle relaxants	Baclofen (Lioresal) Cyclobenzaprine (Flexeril) Tizanidine (Zanaflex)

Medication-Induced Esophageal Injury

The first case of medication-induced esophageal injury was reported by Pemberton in 1970.¹⁰ Medication-induced esophageal injury is typically caused by local irritation of the esophageal mucosa by orally ingested drugs.¹¹ Symptoms are quite characteristic, including a sudden onset of dysphagia, retrosternal chest pain, and odynophagia within 4 to 12 hours after ingesting the medication.^{10,11,16} A thorough medication history often reveals one of the agents listed in Table 9. The most common site of esophageal injury from medication is near the level of the aortic arch or left atrium.¹

Table 9. Drugs Associated With Medication-Induced Esophageal Injury^{1,8,10-14,16}

Acid-containing products	Clindamycin (Cleocin) Doxycycline (Vibramycin) Erythromycin (Ery-tabs, E-mycin) Minocycline (Minocin) Pentamidine (NebuPent) Tetracycline (Sumycin)
Antiarrhythmics	Quinidine (Quinaglute, Cardioquin)
Aspirin	Bayer Aspirin, others
Bisphosphonates	Alendronate (Fosamax) Tiludronate (Skelid)
Iron-containing products	FeoSol, Feratab, Slow FE, Fer-Iron, others
Methylxanthines	Theophylline (Theo-Dur, Unidur, Slo-Bid)
Nonsteroidal anti-inflammatory drugs (NSAIDs)	Ibuprofen (Advil, Motrin) Indomethacin (Indocin) Ketoprofen (Orudis) Naproxen (Aleve, Naprosyn)
Potassium chloride	K-Dur, K-Tabs, Klor-Con, Micro-K, Slow-K, others
Vitamin C (ascorbic acid) products	Allbee with C, others

Increased risk of developing medication-induced esophageal injury is associated with several activities. Swallowing medications in a supine position promotes withholding of the medication in the esophagus and prolongs contact between the drug and the esophageal mucosa.^{8,11} Taking medications immediately prior to sleeping also increases risk, because both saliva production and frequency of peristalsis decrease during sleep.^{11,16} Patients who take medication without enough fluid are also at increased risk, as limited or no fluid intake promotes esophageal retention of the drug.^{8,11,15,16}

Elderly patients are at the highest risk for the development of medication-induced esophageal injury.¹¹ This is due to a combination of predisposing factors. First, the elderly are more likely to take an increased number of medications; the sheer volume of drugs ingested makes injury more probable. Second, the elderly have decreased esophageal motility and decreased production of saliva, which both contribute to impaired transport of medication and increased contact time with the offending agent. Finally, the elderly are more likely to have cardiac enlargement from congestive heart failure, which can compress the esophagus and delay the passage of medication.¹¹

Medications that are most frequently implicated in this type of dysphagia include agents containing acid or those with a pH less than 3.^{8,11,16} Other characteristics of caustic medications include those with a prolonged dissolution time, large pill diameter, or circular (versus oval) shape.^{10,15} These types of medications are also listed in Table 9.

There are several strategies that should be employed to prevent the development of medication-induced esophageal injury. These include the following:

- Having the patient take the medication sitting up at a 45- to 90-degree angle.^{1,10,15,16}
- Taking the medication with at least 100 mL of water or other appropriate carrier.^{10,11,15,17}
- Taking a small sip of water or other appropriate carrier *before and after* taking the medication.^{15,16}
- Taking medications that must be taken "at bedtime" at least 30 minutes before sleeping or 10 minutes before reclining.^{10,15,16}
- Taking one medication at a time.¹⁵
- Consulting a pharmacist before crushing tablets or opening capsules.¹⁵
- Requesting the liquid form of the medication—consult with a pharmacist regarding equivalent doses.^{10,15,16}

Miscellaneous Medications

Several other medications have been cited in the literature as having an association with dysphagia (Table 10). The mechanisms by which these agents cause dysphagia are unknown.

Table 10. *Miscellaneous Agents Associated With Dysphagia*¹²⁻¹⁵

Anti-Parkinson agents	Amantadine (Symmetrel) Bromocriptine (Parlodel) Pergolide (Permax) Ropinirole (Requip) Selegiline (Eldepryl)
Antiretroviral agents	Ritonavir (Norvir) Saquinavir (Invirase) Zalcitabine (Hivid)
Antiviral agents	Foscarnet (Foscavir) Ganciclovir (Cytovene) Rimantadine (Flumadine)
Migraine agents	Zolmitriptan (Zomig)
Multiple sclerosis agents	Interferon -1a (Avonex) Interferon -1b (Betaseron)
Myasthenia gravis agents	Edrophonium (Tensilon)
Rheumatoid arthritis agents	Penicillamine (Cuprimine)
Toxins/toxoids	Botulinum A toxin (Botox) Tetanus toxoids

Management strategies for these miscellaneous medications include changing to another agent (if possible), and educating the patient about the potential for dysphagia with the use of these drugs.

Dysphagia and MS

It is highly unlikely for MS to present as dysphagia. Dysphagia is usually observed in MS patients who already have an established diagnosis, and it is more likely to be evident in the MS patient with prior fluctuations of sensory, motor, visual, or bladder symptoms.⁴ An MS patient with dysphagia will usually have brain stem lesions or bilateral corticobulbar tract

involvement;⁷ this can interfere with muscle control of the lips, tongue, and soft palate.³ Dysphagia in the MS patient is thought to be multifactorial: it may be caused by lack of oropharyngeal control, delayed swallowing, delayed peristalsis, or poor laryngeal closure.⁵

Patients with MS are likely to be on a large number of medications, many of which have the potential to cause or exacerbate dysphagia. A list of MS medications that have been linked to dysphagia is found in Table 11.

Table 11. Multiple Sclerosis Medications Associated With Dysphagia

Anticholinergics and antimuscarinics	Oxybutynin (Ditropan) Propantheline (Pro-Banthine) Tolterodine (Detrol)
Antiepileptics/antineuralgics	Carbamazepine (Tegretol) Gabapentin (Neurontin)
Antipsychotics/neuroleptics	Lithium (Eskalith, Lithobid) Risperidone (Risperdal)
Benzodiazepines	Clonazepam (Klonopin) Diazepam (Valium)
Corticosteroids	Dexamethasone (Decadron) Methylprednisolone (Solu-Medrol) Prednisone (Deltasone)
Disease-modifying agents	Interferon -1a (Avonex) Interferon -1b (Betaseron)
Immunosuppressants	Azathioprine (Imuran)
Selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs)	Amitriptyline (Elavil) Fluoxetine (Prozac) Imipramine (Tofranil) Paroxetine (Paxil) Sertraline (Zoloft)
Skeletal muscle relaxants	Baclofen (Lioresal)

Management of the MS patient with dysphagia will vary with both the offending agent and the patient's symptoms. As expected, the offending agent should be discontinued; however, this may not be possible due to the limited number of medications available to treat MS and the

potential benefits of such drugs. If discontinuation is not realistic, the patient should be thoroughly educated regarding the potential for dysphagia and possible use of the compensatory techniques previously mentioned for each agent. If the dysphagia is especially severe or if the patient is at significant risk, a speech-language pathologist should be consulted.

Conclusion

Dysphagia is a potential side effect of numerous medications. The most valuable tool in identifying drug-induced dysphagia is obtaining a thorough and accurate medication history from each patient. Ideally, the offending agent should be discontinued; however, in the MS patient this may not always be feasible. If it is not possible to discontinue the agent, dysphagia management strategies may include taking the medication with adequate amounts of fluid, ingesting the drug in an upright position, taking the drug at least 30 minutes before sleeping, and spacing the offending agents and other medications to allow for recovery time between doses. Most important, however, is educating the patient regarding his or her medication's potential to cause dysphagia and its avoidance.

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References

1. Trate DM, Parkman HP, Fisher RS. Dysphagia: evaluation, diagnosis and treatment. *Primary Care Clin Office Pract.* Sept 1996;23(3):417-432.
2. Logeman JA. *Dysphagia: A Review for Health Care Professionals.* St. Louis, Mo: Professional Services; 1997.
3. Brown SA. Multiple sclerosis and quality of life: the search for new directions, the role of the speech-language pathologist. Lecture notes. March 11, 1997.
4. Buchholz DW. Neurogenic dysphagia: what is the cause when the cause is not so obvious? *Dysphagia.* 1994;9:245-255.
5. Evans WB, White GL, Wood SD, et al. Managing dysphagia: fundamentals of primary care. *Clinician Rev.* Aug 1998;8(8):47-70.
6. Brown SA. The role of the speech-language pathologist in the treatment of swallowing disorders in the "new health care system." Lecture notes. August 1, 1998.
7. Domenech E, Kelly J. Otolaryngology for the internist: swallowing disorders. *Med Clin N Am.* Jan 1999; 83(1):97-113.
8. Schechter GL. Systemic causes of dysphagia in adults. *Otolaryngol Clin N Am.* June 1998;31(3):525-535.
9. Sliwa JA, Lis S. Drug-induced dysphagia. *Arch Phys Med Rehabil.* Apr 1993;74:445-447.

10. Boyce HW. Drug-induced esophageal damage: diseases of medical progress. *Gastrointestinal Endoscopy*. June 1998;47(6).
11. Stoschus B, Allescher HD. Drug-induced dysphagia. *Dysphagia*. 1993;8:154–159.
12. Burnham T, ed. *Facts & Comparisons*. St. Louis, Mo: Facts & Comparisons; 1999.
13. Gelman CR, Rumack BH, Hutchinson TA, eds. *DRUGDEX® System*. Englewood, Colo: MICROMEDEX, Inc.
14. Lacy CF, Armstrong LL, Goldman MP, Lance LL. *Drug Information Handbook, 1999–2000*. Hudson, Ohio: Lexi-Comp; 1999.
15. Feinberg M. The effects of medication on swallowing. In: Sonies BC. *Dysphagia—A Continuum of Care*. New York, NY: Aspen Publishing; 1994.
16. McLean W, Ariano R. Drug-induced esophagitis (Drug Consult). In: Gelman CR, Rumack BH, Hutchinson TA, eds. *DRUGDEX® System*. Englewood, Colo: MICROMEDEX, Inc.
17. McLean W, Ariano R: Antipsychotic-induced dysphagia (Drug Consult). In: Gelman CR, Rumack BH, Hutchinson TA, eds. *DRUGDEX® System*. Englewood, Colo: MICROMEDEX, Inc.