The speech-language pathologist/SLP (and all rehab staff/PT & OT) can have a **big impact** in this area of adverse drug reactions and potentially preventing or reducing drug-induced dysphagia & other negative sequelae (confusion, lethargy, falls, etc.)

Part of our job as speech-language pathologists is to **dig** through a patient's medical record to uncover what could potentially be the **underlying** cause(s) of the symptom of dysphagia *(Sheffler, 2014)*.

### Not Just Dysphagia → Big Picture

We need to look at the big picture of nutrition & hydration, enjoyment of eating, meal-time success, as well as related problems that could be due to medications:

- Lethargy
- Drooling
- Dysphonia
- Weak cough
- Cognitive impairments
- Inattention
- Distractibility
- Tremors
- Falls

### Financial Disclosures

- Honorarium for this presentation. Thank you!
- Per diem - Beth Israel Deaconess Medical Center (3 days/week with inpatients/outpatients)
- Dysphagia consultant and presenter for Hormel Health Labs, and she sits on a Hormel Advisory Council with RDNs. Paid positions.
- Karen Sheffler's website, SwallowStudy.com, has affiliate relationships with Medbridge Education and CW (which sells dysphagia products such as thickeners).
- Performed paid peer reviews for MedBridge; Unpaid reviews for ABSSD & DysphagiaGrandRounds.com
- Paid by MedBridge, Trudell Medical International (regarding Abilex), and Arkray USA, Inc (regarding “Slide” & “Phazix”) for blogs and dysphagia consultation services.
- Paid by MedBridge to assist in creating their dysphagia platform of patient education/exercises.
- Consulting fees for her expert witness work from law firms.
- The Center for Medicine in the Public Interest paid for my transportation & lodging related to my unpaid talk on underserved populations of people with dysphagia at their conference: “A Summit Exploring 3D Printed Pharmaceuticals” in November 2018.
Areas of Focus for Today:

1. Medications in the elderly and polypharmacy
2. Dysphagia as a direct impact or side-effect of a drug:
   - Anticholinergics, Benzo’s, Muscle relaxants
   - Antipsychotics / Extrapyramidal side-effects / Delirium
   - Esophageal issues (LES relaxation, GERD, esophageal injury, motility issues)
3. Dysphagia as a secondary complication of side-effects:
   - Xerostomia
   - Central Nervous System (CNS) depression
   - Immunosuppression
4. What medications may help? & Look into the future...

Why worry about medications?

- 82% of adults in US take at least 1 medication.
- 29% take 5+
- 17-19% of adults >65 take at least 10 medications. (Sloan)
  http://www.bu.edu/slone/research/studies/slone-survey/
- Polypharmacy = Use of 5 or more prescription medications.
  (Increased from 6.3% to 12% in 2000 to 2006 per Sloan Survey).
- Polypharmacy = increased risk for Adverse Drug Reactions (ADRs) like falls, cognitive impairment, dysphagia, sedation and delirium

Why worry about medications?

Adverse Drug Reactions (ADR):

- Estimated 99,628 emergency hospitalizations for ADRs for US adults >65 y/o each year.
  Note: bias toward acute events documented.
- However, many cognitive and functional changes go under-reported in the ED.

Why worry about medications?

Polypharmacy: Predictor for Aspiration Pneumonia

In Langmore’s 1998 and 2002 studies regarding predictors of aspiration pneumonia, the “number of medications” was a significant predictor of aspiration pneumonia in both studies.


Pneumonia is an example of an iatrogenic complication:

Unintended adverse complication or side effect of a treatment, invasive procedure, or medication(s).
Medications: Drug-Induced Dysphagia, Complications & Potential Treatments

11/17/19

Karen Sheffler, MS, CCC-SLP, BCS-S

Potential Patient Scenario:

- SLP: “The patient is very agitated and drooling a lot. He cannot manage his secretions. How about that patch that goes behind the ear that can dry up secretions?”
- MD: “We could consider a Scopolamine patch, but I am worried about potential anticholinergic side-effects.”
- SLP thinking: “Anticholi-what!”
- MD: “We could try Haldol for agitation since I don’t want to put him on a Benzo.”
- SLP thinking: “??BENZO??”

HELP! I need resources so I look like I know what I’m talking about!

RESOURCES: https://www.swallowstudy.com/drug-induced-dysphagia-resources-safe-practices/

Resources

- Text: Drugs and Dysphagia: How Medications Can Affect Eating and Swallowing, by Lynnette L. Carl & Peter Roy Johnson
- Think ➔ This is a MUST for seniors
  (MUST = Medication Use Safety Training)
  - https://bemedwise.org/medication-safety/medication-therapy-management-for-seniors
  - https://bemedwise.org/health-education-resources/older-adults
- ISMP.org (Institute for Safe Medication Practices)

Resources

- GeriatricsCareOnline.org (by American Geriatrics Society/AGS)
  - Beers Criteria: drugs that are best avoided in older patients. Updated by AGS 2015.
    “…the 2015 AGS Beers Criteria work best not only when they identify potentially inappropriate medications, but also when they educate clinicians and patients about the reasons those medications are included and the situations in which their use may be more or less problematic.”

Resources

- STOPP: Screening Tool of Older Person’s Prescriptions
- START: Screening Tool to Alert Doctors to Right Treatment
- Better than BEERS criteria?
  - JAMA Network article on STOPP versus BEERS: https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/227481

Pharmacokinetics

What the body does to/with the drug

- Absorption
- Distribution
- Metabolism
- Elimination
Aging: Higher Risk for Toxicity
- Reduced GI motility, causing stasis → more drug absorbed or pill injury.
- GI blood flow & gastric secretion is reduced which can cause elevated gastric pH → leading to decreased absorption.
- Increased fat, decreased muscle mass & increased total body water
  Need to understand how and where is the drug distributed (in muscle tissue, water-soluble, lipid-soluble). I.e., Diazepam/Valium is highly fat-soluble, leading to increased distribution in elderly.
  Elderly may have less albumin, which binds drugs in the bloodstream.
  So elderly may have more free drug concentration reaching receptors.
- Blood/brain barrier more permeable → magnifies distribution
- Liver blood flow & metabolic activity is reduced.
- Decline in renal function (a more standard/common decline than liver).
  Many drugs are completely or partially excreted by the kidneys.
  Slower metabolism & elimination leads to prolongation of the half-life.

Half-Life
Amount of time that it takes for the drug to be reduced to 50% in the body.
- Haldol example: 14-16 hours in IV form; 14-37 hours when given orally - in healthy individuals. (Metabolized in liver, excreted through feces and urine)
- What if you are given more doses within that time?

Pharmacokinetic parameters & Altered physiology with aging (See table in Wooten, 2012)

Absorption
- Gastric secretion
- Gastric pH
- GI motility
- GI blood flow
  Many drugs may diminish in their absorptive ability Time of onset of action may be delayed
  Absorption is the pharmacokinetic parameter least affected by aging

Distribution
- Total body water
- Lean body weight
- Albumin
- Body fat
  Increased Volume of distribution of lipid-soluble drugs
  Increased free fraction of drug

Metabolism
- Enzyme induction
- Hepatic mass
- Hepatic blood flow
  Activity in mixed function oxidase system
  Reduced hepatic clearance of drugs
  Increased potential for drug interactions
  For elderly patients, dosage should be reduced for hepatically cleared drugs

Elimination
- Glomerular Filtration Rate (GFR)
- Renal blood flow
  For elderly patients, drug accumulation will occur for renally cleared drugs

Pharmacodynamics
What the drug does to the body
- Mechanism of action: how the drug works
- Neurotransmitters & hormones bind to receptor sites
- Competing and overlapping meds

In Addition to Pharmacokinetics & Pharmacodynamics, Consider:
- Huge variability in:
  - How people take their meds,
  - Adherence to the plan,
  - Cognition/understanding of the rationale and plan,
  - Comorbidities
  - Polypharmacy
Medications: Drug-Induced Dysphagia, Complications & Potential Treatments

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SECTION 2: Dysphagia* as a direct impact from a drug

*Oropharyngeal & Esophageal Dysphagia - Both are in our Scope of Practice!

Read more: https://www.swallowstudy.com/dysphagia-digest-multiphase-dysphagia-evaluations/

~OVERVIEW~

ABA’s of Drug-Induced Dysphagia

**Anticholinergics** (antimuscarinic agents)
e.g., Cogentin, Scopolamine, Benadryl

**Benzodiazepines** (anticonvulsants, anxiolytic/anxiety, muscle relaxants, and related - sedative-hypnotics)
e.g., Ativan, Xanax, Klonopin, Valium, Lyrica

**Antipsychotics**
e.g., Typical: Haldol; Atypical: Zyprexa, Risperidone

Might as well make that ABAAA…, adding Antidepressants and Antihistamines, when considering all the negative impacts on the hospitalized elderly.

We will cover direct impacts & then side-effects ©

**Anticholinergics**

- **Block neurotransmitter Acetylcholine (which is involved in learning, memory & stimulating autonomic nerves).**
- **Relaxing smooth muscles.** (Spasmolytic/antispasmodic)
- **“Anticholinergic effect”**

Blocking acetylcholine – interrupts “parasympathetic nerve impulses in the central and autonomic nervous system.” (Priff & Harold, 2005)

**Category of Anticholinergics: Antimuscarinic Agents**

- Decrease mucous & saliva production in the nose, mouth, pharynx → **xerostomia** & dental caries (more on that later in side-effects section).
- Can cause paralysis of the diaphragm.
- Direct dysphagia impact could be due to inhibition of smooth muscle action with potential for slowing in smooth muscle of distal esophagus, stomach, and other smooth muscles.

**Anticholinergic Toxidrome**

- Blind as a bat (dilated pupils)
- Red as a beet (vasodilation/flushing)
- Hot as a hare (hyperthermia)
- Dry as a bone (dry skin and mouth)
- Mad as a hatter (hallucinations/agitation)
- Bloating as a Toad (ileus or urinary retention)
- And the heart runs alone (heart racing, tachycardia)

From: Life in the Fast Lane: https://litfl.com/anticholinergic-toxidrome/
Anticholinergics: Not Only Dry Mouth

- Some anticholinergics have antimuscarinic effect, but do not have major cognitive burden (e.g., Lasix/Furosemide).
- However, others have significant negative cognitive side-effects for older adults.
- Fox, et al., 2011 used Anticholinergic Cognitive Burden (ACB) Scale to show risk of cumulative cognitive decline & increased mortality. Worst on ACB Scale: Elavil/Amitriptyline, Chlorotrimeton/Chlorpheniramine, Clozaril/Clozapine, Dimetapp/Brompheniramine, etc.


“Benzos” - Benzodiazepines

- Class of meds used for:
  - Anticonvulsants
  - Anxiolytic (reduce anxiety)
  - Muscle relaxants (spasmolytic agents / antispasmodics that work on skeletal muscles)
  - Sedation - Sedatives
  - Insomnia
- Examples: Valium (diazepam), Klonopin (clonazepam), Xanax (alprazolam), Ativan (lorazepam), Zanaflex & Baclofen (spasticity in MS)

Some case reports of chronic use of Benzodiazepines (e.g., Ativan/Lorazepam) causing dysphagia:
- Alvi (1995): pharyngeal phase dysfunction, hypopharyngeal discoordination, cricopharyngeal incoordination, aspiration
- Dantas & Souza (1997): 2mg of lorazepam for 2 yrs causing oropharyngeal dysphagia w/ pharyngeal residue. Resolved 2 weeks after drug discontinued.

“Benzos” - Benzodiazepines

- Serax/Oxazepam has a short half-life (5-15 hrs), but some Benzos have a longer half-life.
- Chlordiazepoxide (5-30 hours) & Diazepam (20-70hrs) - metabolized in liver & half-life up to 100 hours.
- Lorazepam (Ativan) does not depend on liver for metabolism, but half-life still longer 10-20 hrs.

PROBLEM: loading doses are used, which is giving drug every 1-2 hrs until pt shows improvement & then stop. Dangerous for elderly! (Alvi & Gonzalez,1995)

Neuromuscular Blocking Agents

- Muscle relaxants (direct effect on skeletal muscle – will affect swallowing)
  - Decreases tone, pain, spasms, hyperreflexia (example: Botox for spasmodic dysphonia & torticollis causing dysphagia – temporary collateral damage)
  - Neuromuscular blockers: at neuromuscular junction / end plate, NOT at CNS. (i.e., paralysis for surgery/anesthesia, ventilator)

Benzos may be highly effective to prevent complications such as seizures and “DTs” (Alvi & Gonzalez,1995; Mirijello, et al., 2015)
Sedative-hypnotics vs Benzos for procedure sedation
- Diprivan (Propofol) → Sedative-hypnotic/anesthetic. Also used for people on ventilators. Single dose is short acting. Excreted through liver.
- Versed (Midazolam) → Benzodiazapine & central nervous system depressant. Short acting with effects lasting 2 hours. Amnesia effect up to 1 hour. Broken down in liver & excreted within a day from urine and feces.
- Twardowski, et al. (2019): people who regularly use cannabis require higher dosages of both sedatives (as well as Fentanyl) for procedures (i.e., dental, EGD, etc.).

Antipsychotics/Neuroleptics
- Typical / Conventional / 1st Generation
  - Haldol (Haloperidol)
  - Thorazine (Chlorpromazine)
  - Loxapine
- Atypical / Novel / 2nd Generation
  - Risperdal (Risperidone), Geodon (Ziprasidone)
  - Zyprexa, also under tongue Zydis (Olanzapine)
  - Clozeril (Clozapine), Latuda (Lurasidone), Abilify (Aripiprazole), Seroquel (Quetiapine)

Antipsychotics/Neuroleptics
- Class of meds used for: psychotic symptoms (such as those in schizophrenia), bipolar, major depressive disorders, delusions, hallucinations, severe agitation, movement disorders (Tourette’s Syndrome, Huntington’s Chorea, intractable hiccups)
- Neuroleptics block dopamine receptors in basal ganglia → May cause dyskinesias & extrapyramidal symptoms (EPS)

Increased Pneumonia Risk
Knol & colleagues (2008) studied over 22,000 elders, and noted that people who receive antipsychotics were 60% more likely to develop pneumonia. Authors noted: drug-induced dysphagia often goes under-reported, but it may explain this greater risk of pneumonia (p. 664).
Sliwa & Lis (1993), Dziewas, et al. (2007), and Hughes, et al. (1994), Hatta, et al. (2014) & Herzig, et al. (2017): found similar increased risk for aspiration pneumonia on antipsychotics, in addition to issues such as: weight loss, arrhythmias, extrapyramidal symptoms.

Increased Choking Risks
Aldridge, K.J. & Taylor, N.F. (2012): systematic review showing people with mental illness have an increased dysphagia & risk to die of choking asphyxiation deaths.
Sokoloff & Pavlakovic (1997): patient with dementia on Haldol – changed to Loxapine. VFSS showed: reduced mastication, tongue pumping, reduced tongue range of motion, reduced tongue base movement (likely due to rigidity), reduced bolus control, delayed initiation of pharyngeal swallow, reduced laryngeal movement, residue in valleculae and pyriforms after the swallow with penetration on this residue, and silent aspiration on thin liquids.

Haldol should not be “Vitamin H”
- Food and Drug Administration warns against the use of haloperidol in people with dementia-related psychosis. 1.6-times increased mortality. FDA 2005 warning: https://www.accessdata.fda.gov/drugsatfda_docs/label/2008/015923s082,018701s057lbl.pdf
- Park, et al. (2018): small increased risk of death on Haldol vs atypical antipsychotics in people admitted with acute MI.
- Agar, et al. (2017): studied inpatient hospice & palliative care → more severe delirium, more EPS (per EPS Rating Scale/ESRS) in people who took Haldol or Risperidone versus placebo. Authors noted (in page 3/Procedures): “study drug was discontinued if adverse effects became unacceptable, the treating clinician deemed the treatment ineffective, or at onset of dysphagia.”
Extrapyramidal Symptom Rating Scale (ESRS)

- Assesses: Parkinsonism, akathisia (can't stay still), oral/facial/limb dyskinesia, dystonia, tardive dyskinesia (TD)
- Problem: IT DOES NOT ASSESS EATING AND SWALLOWING!!
- Many studies do not include instrumental evaluations either. Therefore, research is incredibly lacking in Haldol-Induced and antipsychotic-induced dysphagia!

EPS: There is a drug for that too?

The medical team frequently looks to Cogentin (Benzotropine) as an antiparkinsonian medication to alleviate the extra-pyramidal symptoms or parkinsonian side-effects of antipsychotics.

However, may need to consider how Cogentin has significant anticholinergic side-effects!

BONUS SECTION: Delirium & Antipsychotics

Delirium

- Acute brain dysfunction → causing inattention, disorganized thinking, altered consciousness, acute cognitive changes that are not due to dementia or another source. (American Psychiatric Assoc, DSM-5, 2013)
- 25% of hospitalized people develop delirium, but up to 89% of people in the ICU.
- Not all hyperactive. Also mixed and hypoactive. Hypoactive = harder to detect, may be more common in ICU, and with worse outcomes. (Barbateskovic, 2019)

Delirium

- Costs: $38 Billion in United States due to reported cases of delirium/complications. (Oh, et al., 2019)
- Over ½ of cases of delirium go unrecognized, even though 1/3rd of our hospitalized elders and 3/4th of our elders in the ICU or on palliative care are experiencing delirium!
- People used to view confusion as a expected “nuisance” to be solved with “10mg of Vitamin H (Haldol),” (editorial by Marcantonio, 2019)
- 10-30% of patients receive antipsychotics during their hospitalization, usually related to their delirium (Pahwa, 2019)
**Do Antipsychotics prevent delirium post-op or improve outcomes in hospitalized adults?**

Researchers in 2016 found no association between antipsychotic use and:
- Incidence of delirium
- Delirium duration and severity
- Length of stay in hospital or ICU
- 30-day mortality

“Antipsychotic pharmacotherapy does not improve outcomes when used for prevention or treatment of delirium in hospitalized adults.”

“There is insufficient evidence to support the routine use of…”


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**Improved efficacy & cost efficient too!**

**Clinician’s Decision could be Non-Pharma Methods:**

**American Geriatric Society 2015 Recs**
- Recent often, Family/Friends: Early mobility, Therapy
- Nutrition focus: Gastro. motility
- Quiet time: Sleep
- Beneficial distractions: Reminiscing, Sensory vests
- Manage pain: Avoid opioids
- Avoid benzos: But treat alcohol withdrawal

Add early communication, early SLP referral!

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**Hot off the Press**

New Research - Johns Hopkins @ICUrehab

- Current evidence does not support routine use or haloperidol or second-generation antipsychotics to prevent or treat delirium in adult inpatients, per systematic reviews comparing the two classes versus placebo. (Prevention article: Oh et al., 2019, Sept https://jama.jamanetwork.com/chapter/2749494/antipsychotics-preventing-delirium-in-postoperative-adults-a-systematic-review. Treatment: Nicoso, et al., 2019 https://jamanetwork.com/chapter/2749495/antipsychotics-treating-delirium-treatment-approaches-a-systematic-review)

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**Do Antipsychotics prevent delirium post-op or improve outcomes in hospitalized adults?**

Systematic review found that use of pharmacological measures do not decrease mortality or prevent delirium. (Barbateskovic, et al., 2019)

Barbateskovic, et al. (2019) summarizes:
- The American College of Critical Care Medicine & the Society of Critical Care Medicine “no longer recommend managing delirium with Haloperidol due to lack of evidence (page 2).” (cited Devlin, et al., 2018; Barr, et al., 2018)
- “The lack of evidence & poor quality of the present evidence on the use of pharmacological agents for delirium leave clinicians to decide which pharmacological intervention to use (pg 8).”

**HOW ABOUT NONE!**

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**Despite recommendations for non-drug delirium prevention**

- Haldol (Haloperidol) still used 46% of the time in ICU patients
- Precedex (Dexmedetomidine) used 21% of the time. (Collet, et al, 2018)
- Per AGS (2015), Pharmacological interventions should only be considered if severe agitation and need to prevent harm to oneself or others, starting with lowest possible dose, after all other strategies have failed. (AGS 2015)

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**Antipsychotics for the Prevention and Treatment of Delirium**


**Key Messages**
- Haloperidol or second-generation antipsychotics used to prevent or treat delirium did not decrease length of stay in hospital.
- There was little or no evidence to determine the effect of antipsychotics on cognitive function, delirium severity, or caregiver burden, or for sedation when used for prevention.
- Second-generation antipsychotics may lower the occurrence of delirium in postoperative patients (but limited evidence).
- Haloperidol or second-generation antipsychotics used to prevent or treat delirium may lead to little or no difference in sedation or extrapyramidal side effects (problems with muscles such as spasms or restlessness). Heart-related side effects tended to occur more frequently with the use of antipsychotics, in particular QT interval prolongation (a type of heart rhythm problem) in second-generation antipsychotics.
- Future studies are needed to assess the effects of using antipsychotics on patient agitation and distress, subsequent memories of delirium, caregiver burden and distress, inappropriate continuation of antipsychotic therapy, and long-term cognitive and functional outcomes.

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**Summary on Antipsychotics to PREVENT delirium** (Oh, et al., 2019)
- 14 RCTs in systematic review.
- Haldol vs placebo -> No difference in:
  - Incidence of delirium
  - Duration of delirium
  - Hospital length of stay (LOS)
  - Mortality
- Limited evidence for use of atypicals to prevent post-op delirium
- No evidence available re changes in cognitive fx, delirium severity, sedation, associated "neuro harms."*
- 1 study showed cardiac issues w/ antipsychotics

*My Opinion: Studies have not looked at neurological harms such as drooling, dysarthria, dysphagia. When talking about EPS, they are not covering these "neuro harms."

**Summary on Antipsychotics to TREAT delirium** (Nikooie, et al., 2019)
- 16 RCTs & 10 observational studies in systematic review
- Haldol vs placebo -> No difference in:
  - Duration of delirium
  - Hospital length of stay (LOS)
  - Mortality
- Re sedation: Low to moderate evidence showing no difference in amount of sedation.
- Re treating severity and cognition: When comparing Haldol vs 2nd generation (Atypicals), limited evidence of low strength. No evidence favoring antipsychotics vs placebo.

**Dysphagia as Direct Esophageal Impact**
- **Drugs that can cause GERD:**
  - Bronchodilators, Anti-angina Meds (Nitroglycerin, Isosorbide, Mononitrate), Calcium Channel Blocker (Diltiazem), Anxiolytic (Alprazolam)
- **Drugs that decrease LES pressure:**
  - Atropine, Dopamine, Butylscopolamine (antispasmodic for smooth muscle spasms; aka, Buscopan), Theophylline, Nitrates, Calcium Antagonists
- **Substances that decrease LES pressure:**
  - Chocolate, alcohol, fatty/fried foods, peppermint oil (antispasmodic), hormones of glucagon & progesterone.

**Dysphagia as Direct Esophageal Impact**
- **Esophagitis / Esophageal Injury, including thrush and ulcers** (e.g., NSAIDS, steroids, antibiotics)
  - Risks elevated if: enlarged L atrium compressing esophagus, hx of cirrhosis & portal hypertension, thoracic surgery, hx of esophageal dysmotility or strictures
- **Tips on how to reduce risk in elderly:**
  - Bronchodilators (e.g., Advair) need to be rinsed out of mouth w/ water to prevent candida/thrush and sores
  - Prevent Esophageal Pill Injury:
    - Careful w/ evening meds: Take pills at least 1 hr before bed
    - Take meds in upright position
    - Take with plenty of fluids (prevent pill injury in esophagus)
    - Cut/crush (if you can) large pills that might get stuck
  - Bronchosch & Allescher, 1993; Akhtar, 2003

**Hard Pill to Swallow!**
See SwallowStudy YouTube videos of VFSSs:
- Pill dysphagia due to pharyngeal and esophageal issues. Risk for aspiration & pill injury to esophagus: [https://youtu.be/no4AQm982Jk](https://youtu.be/no4AQm982Jk)
- Trouble getting pill out of the mouth, tossing head back, penetration on thin liquid with aspiration risk: [https://youtu.be/sC4qPz_HGho](https://youtu.be/sC4qPz_HGho)
- Embedding pill in viscous gel ("Assure Slide/Phazix"): [https://youtu.be/bAK6SumKXRc](https://youtu.be/bAK6SumKXRc)
SECTION 3:
Dysphagia as a secondary complication of the drugs’ side-effects

1. Xerostomia – Dry mouth

- National Institute of Dental and Craniofacial Research in the US state that over 400 medications can cause dry mouth.
- Gallagher and Naidoo (2009) audited the medications of 153 adults in a rehab facility (221 medications in total):
  - Side-effect of xerostomia in 24.8% of meds.
  - Randomly selected 10 people who had dysphagia identified with videofluoroscopy: 6 out of 10 had xerostomia, and each person was using 3-9 drugs that could cause dry mouth.

2. Central Nervous System depression

- Anticholinergics & Antispasmodics with antimuscarinic effects (inhibits parasympathetic nervous system). See chart. Examples: Cogentin, Scopolamine, Levsin, Benadryl, Atropin, Ditropan.
- Antidepressants: older Tricyclic Antidepressants (TCAs), like Elavil/Amitriptyline, caused greater antimuscarinic effects than the second generation, but still about 25% with xerostomia w/:
  - Selective Serotonin Reuptake Inhibitors (SSRIs)
  - Serotonin-Norepinephrine Reuptake Inhibitors (SNRI)
  - Norepinephrine Reuptake Inhibitor (NRI)
2. CNS - Anticholinergic Side-Effects (Review of ACB)

- Decreased coordination
- Memory loss
- Confusion/disorientation
- Inattention, illogical thinking, visual disturbances
- Long-term use can increase risk for:
  - Mental & physical decline,
  - Increased risk for falls (sudden drops in BP/orthostatic hypertension),
  - Death. (However, the studies are not RCTs & do not prove causation.)

2. Central Nervous System depression

- Benzodiazepines (“Benzos”) increase risk:
  - Delirium, Cognitive Impairment
  - Falls, accidents
  - Sedation; Amnesia
  - Slurred speech
  - Respiratory depression
  - In patients with liver disease: greater neuro side-effects -- confusion, drowsiness, dizziness, dysarthria, tremor, nystagmus, vertigo (Priff & Harold, 2005)

2. Central Nervous System depression

- Sedatives & Antiemetics (i.e., Dramamine)
- Antiepileptics/Antiepileptics
- Steroids (i.e., Prednisone)
- Opiods (Narcotics) (e.g., Fentanyl/Duragesic, Dilaudid, Oxycodeone plus Paracetamol = Percocet/Roxicet, Morphine, MS Contin, Oxycodeone, OxyContin)
- Antiparkinsonian (i.e., Sinemet can cause dry mouth & dyskinesias, but also mental status changes)

3. Immunosuppression & Immunosuppressive drugs

- Less able to fight off infection
  - Which came first? The dysphagia or infection?
  - May have been an unrelated infection → generalized weakness → dysphagia started → additional infection of the pneumonia.
  - Opportunistic oral infections (i.e., leukoplakia and thrush/candidiasis). Keep this in mind when patient has odynophagia.
  - Oral hygiene!

4. ACE Inhibitors

(Angiotensin-Converting Enzyme)

- Very Common. Examples: Lisinopril, Enalapril, Captopril.
- Treat HTN, CHF, kidney problems due to DM, and may improve survival after an MI.
- Side-effects: bothersome dry cough (differentiate from cough due to aspiration)
- Adverse Drug Reaction: dangerous angioedema - mild to severe swelling in lips, face, oropharyngeal, larynx. More common in African-Americans. Can happen years after being on drug or weeks after drug stopped!
  - Angioedema is most often seen in acute care with Lisinopril.
  - However, Freire, et al. (2017) presented case study of Captopril causing oropharyngeal and glottic edema.
  - Radiographic imaging important to determine urgency of risk.

SECTION 4: What medications may help swallowing?
Can Medications Help?

- **Parkinson’s Medication**: Sinemet can improve the safety and efficiency of the swallow? When taken 30-60 minutes before the meal, on an empty stomach for absorption in small bowel (can’t compete with food proteins in stomach) (Stroschus & Allescher, 1993; Fonda, 1996)
  - Fonda (1995) & Bushmann et al. (1989) found significant improvements in VFSS “on.”
  - Are we evaluating patient “on” or “off” Sinemet? Do they feel an “off” effect?
  - Are they eating often “off” the med?
  - Ask the nurse, patient or caregiver when the last dose was taken and how.

Case: Person with Parkinson’s

- Pt came to 10am session “off” Sinemet, as he took it at 9:55am. Very “stuck,” difficulty w/ transfer, unintelligible, falling asleep…
  - We started the study “off” Sinemet to see how bad the swallow gets.
  - He had significant difficulty & penetration to aspiration of mildly thick liquid/nectar thick by spoon, so we then decided to wait to test him “on” Sinemet.
  - Then sudden change at 10:20 with improved movement, facial expression, talking, etc.

Characteristics of Swallow “OFF” Sinemet:

- Poor tongue base propulsion w/ wide column of contrast between tongue base & posterior pharyngeal wall.
- Decreased velopharyngeal closure w/ escape
- Decreased hyolaryngeal excursion w/ no epiglottic deflection -> incomplete laryngeal vestibule closure (LVC)
  - Therefore, penetration during the swallows, not ejected.
- Bilaterally reduced pharyngeal constriction, leaving the majority of the bolus diffuse in oropharynx. Only 1/8th of bolus cleared on first swallow, leading to more penetrations during reswallows and after the swallows. Tried to swallow 12 times!
- Aspiration during swallow along inferior surface of VC and high risk after the swallow. No response. Cued cough – not able.

Video “Off” Sinemet

Nectar thick/ Mildly thick by spoon. 12 swallow attempts. Very poor cued coughs. Material along inferior surface of vocal cords.

Case: Person with Parkinson’s

- Complaint: “I can’t swallow water & even my saliva sometimes.” Trouble swallowing pills, especially in the morning. Food stuck; scared he is choke. EAT-10: 27/40.
- Meds: Carbidopa/Levodopa increased 1 month prior to exam due to disease progression. Also Comtam 10pm, Mirapex 1 tab 4 times a day – allowing for symptom reduction & comfort at night. Takes Tramadol for pain, Clonazepam for anxiety. When having anxiety, he “can’t swallow anything until taking a sip of hot tea.”

Videos “On” Sinemet

Nectar thick/ Mildly thick by spoon. Improved cued cough to eject penetration.
Medications: Drug-Induced Dysphagia, Complications & Potential Treatments

Can Medications Help?

Have you heard of Substance P?

- Neuropeptide that regulates and may enhance the cough and swallow reflexes, secreted in pharynx/trachea. (Nakashima, et al., 2011)
- The secretion of Substance P can be stimulated by dopamine (Yamaya, et al., 2001).

Can pharmacologic therapy increase Substance P, improve swallowing, and lower risk of pneumonia?

- Drug Sermion/Nigergoline may improve dysphagia because it enhances dopaminergic neurotransmitter function, as well as increases substance P. (Nishiyama, et al., 2010)

When Substance P Is Reduced

- Substance P production was more reduced in patients on Haldol, versus when on an atypical antipsychotic-Risperidone (Risperdal). Correlated with an inhibition of the swallow & cough reflexes. Researchers concluded: patients on Haldol are at increased risk for aspiration, aspiration pneumonia and mortality, especially among elderly patients with dementia and neuropsychiatric illness. Nagamine (2008)

Can Products Found in Food Help?!

- Capsaicin (chillis):
  Capsaicin is an agonist of Transient Receptor Potential Channel Vanilloid 1 (TRPV1) which increase sensory input to the pharynx & larynx.
  Shin et al. (2016) studied effects of regular, long-term stimulus of 1.5 micrograms of capsacinoids in a 10g portion of pickled Napa cabbage on latency of swallowing response (LSR).
  Faster swallow response time pre- versus post-intervention in young & elderly normal groups

Can Medications Help Drooling? (Sialorrhea)

First: rule-out that it is not coming from medications that can cause drooling (Mato et al., 2010):

- Haloperidol
- Clozapine
- Olanzapine
- Risperidone
- Nitrazepan
- Bethanecol
Can Medications Help Drooling? (Sialorrhea)

- Behavioral Therapies First
  Reynolds, Miller and Walker (2018) noted how drooling in people with Parkinson’s Disease may be a factor of attention. Swallowing frequency decreased when distracted, going down to only 1x/5 min.
- Sometimes medications are needed to gently dry up secretions. Monitor closely for anticholinergic side effects, as antimuscarinics may decrease salivary flow rates, but increase cognitive burden!

ALS Association Recs re Drooling

- 2 meds most commonly used in the ALS:
  (Note: Scopolamine was fifth/last in the list. See entire list here: http://www.alsa.org/als-care/resources/publications-videos/factsheets/saliva.html)
  Glycopyrrolate (Robinul) 1-2 mg. Every four hours. Robinul is also available in injectable form – 0.1 mg: every four hours or 3-4 times/day. Maximum adult dose – 0.2 mg 4 times/day.
  Propantheline (Pro-Banthine) 15 mg. Half hour before meals three times a day.

Banfi, et al. (2015) on drooling in people with ALS

- Warned re anticholinergic contraindications, especially in elderly people with ALS.
- Despite warnings, Banfi and colleagues referred to a 2013 study by McGeachan, Stephenson & Shaw that found:
  85% of people had a positive response w/ scopolamine patches.
- Contraindications: heart diseases, glaucoma, pyloric stenosis, prostatic hypertrophy, and hepatic and/or renal insufficiency.

Can Medications Help in Head & Neck Cancer Population?

Per, Langmore & colleagues work in 2012:
NPO status and over-reliance on tube feedings can cause disuse atrophy and worsen outcomes. When people stay on at least a partial oral intake, they have better long-term swallowing outcomes.

But how can your patient maintain oral intake if they are in so much pain?

Gabapentin (Neurontin) & less need for narcotics?

- Gabapentin can reduce neuropathic pain & help reduce need for narcotics. 2700mg/day early on during radiation before the pain starts (Starmer et al., 2014).
  Neuropathic pain: due to injury to central or peripheral nervous system & may be due to chronic diseases (MS)
  Nociceptive pain: due to trauma or damage to body, arthritis, dental. Narcotics/Analgesics numb/decrease sensation.
Can Medications Help in Head & Neck Cancer Population?

Gabapentin (Neurontin) & less need for PEG?


- See 2017 study re good outcomes when Gabapentin part of a "comprehensive dysphagia prevention strategy, (p 441)," but this 2017 study of 26 pts did not have control or placebo group and no details on swallowing therapy program or adherence. Only side-effect was mild fatigue. Prophylactic PEGs removed 2 months after chemoradiation.
- 2014 study did use matched control group of those not treated prophylactically with Gabapentin.
- NOTE: both studies on young, HPV-associated CA

Gabapentin (Neurontin) 23 participants, mostly male, HPV. Stage IV tumors of the tongue base, tonsil, soft palate w/ lymph node involvement. Gabapentin use was 41.75 days (mean). RESULTS:

- Shorter overall pain duration.
- 13% required no additional pain medications, and those who did use Oxycodone, it was at a lower dose (mean of 7.05mg) and less often.
- Began use of PEG tubes later and had them removed earlier, with some patients never using their PEG tubes for feedings.
- Less weight loss.
- Less time between chemoradiation completion and the repeat videofluoroscopic swallow study.
- Less impairment on the following physiological swallowing parameters: velopharyngeal closure, tongue base retraction, laryngeal elevation, epiglottic tilt, and pharyngeal constriction.
- Less penetration and aspiration.
- More advanced diet levels achieved.

Other articles recommended by Radiation Oncologist:


Can Medications Help?

Gabapentin (Neurontin) (Yang, et al. (2016). Dysphagia, 31, 208-213.)

Predictive Factors for REDUCED prophylactic PEG in Head & Neck CA:

- Good pre-treatment function (KPS score https://en.wikipedia.org/wiki/Performance_status)
- No pre-treatment dysphagia
- No concurrent chemotherapy ("radio-sensitizing tissues")
- Use of prophylactic Gabapentin (2700mg/day)

Notes on Magic Mouthwash

- Have to be careful with Magic Mouthwash compound medication. Discuss what medications are needed and/or contraindicated for your patient:
  - Typical compound may have
  - Analgesias:
    - Diphenhydramine/Benadryl (sedating, anticholinergic effects)
    - Lidocaine (Numbs. Spot treat as needed.)
    - Antacid (thought to coat mucosa)
    - Hydrocortisone (decrease inflammatory response, but don’t use if systemic yeast issue)
    - Nystatin (antifungal & allow for more permeable membranes)
    - Antibiotic – Tetracycline (but may increase action of warfarin)
  - Tetracycline (but may increase action of warfarin)
  - Tetracycline (but may increase action of warfarin)
Medications: Drug-Induced Dysphagia, Complications & Potential Treatments

11/17/19

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More Good News: The Future is Here Now! 3D Printed Pharmaceuticals

Think outside the box! 3D Printed Pharmaceuticals

- [https://youtu.be/jG8N9ddst7M](https://youtu.be/jG8N9ddst7M)

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Case Study for Your Review

- **Case Study**
  - 75 y/o male admitted w/ hypoxemia, hypoventilation due to lethargy, acute hypercarbic respiratory failure. Similar episode of hypoxia 3 months prior.
  - Wife reported increased lethargy after his Risperdal injection 1 week prior. Additionally, decreased mobility (not OOB), SOB, decreased appetite, depressed mood, intermittent SI. Pt had recently been objecting to Risperdal. Had been on a typical antipsychotic in past (?)Trilafon per record). No mention of difficulty swallowing. Sleep apnea newly discovered.
  - PMH: Ischemic Cardiomyopathy, CAD w/ multiple stents, EF 55%, HTN, severe pulmonary HTN, diastolic CHF, OSA, Afib, DM2, HLD, GERD, vascular dementia, psychiatric disorders w/ hx of agitation & paranoia (Schizophrenia vs bipolar, dx 1980, many psych hospitalizations in 25 yrs). Non-smoking.

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Case Study

- **MEDS PTA**: Lyrica (Pregabalin) started 3 weeks PTA 75mg BID for spinal stenosis & neuropathy, Percocet (Oxycodone-Acetam.) 5/325 q6h, Risperidone Consta (injections 50mg IM every 2 weeks), Glipizide & Metformin (glucophage/Janumet) for diabetes, Lisinopril, Toprol (Metoprolol), Eliquis (Apixaban), Lasix (Furosemide) 80mg PO, 2 tabs in AM & 1 tab at dinner, Metolazone (another diuretic), Atorvastatin (Lipitor) 80mg PO qHS, ASA, Colace, Protonix (pantoprazole) 40mg.
- **Allergies**: gabapentin
- **ETOH**: Small amount of hard liquor in coffee every night to every other night

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Case Study

- Night 1: Episode of slurred speech. Head CT negative. H&P described him as somnolent, mumbling, slurred, slow rate of speech.
- **Psychiatry evaluated**: Held Lyrica & Oxycodone (switching to TYLENOL). Continued Risperid Consta. Rec to add Haldol 5mg PO q4hr pm. If can’t take po, Haldol 2mg IV q4hours pm (if Qtc, then change to Depakote 250mg po TID pm).
- Coughing with thin liquids per ICU staff on days 1-2.
- Consult for swallow eval received late day 2. Too lethargic to see on day 3.
- **CXR** day 2 & 3: "Lung volumes remain low, accentuating the cardiac silhouette and bronchovascular structures. Interval worsening of left basilar opacification is probably due to atelectasis, although aspiration and developing infectious pneumonia are also possible."
- Bedside Swallow Eval completed day 4 (out of ICU). MD had already put him on regular diet, thin liquid. Fluid RN reported he appeared to be tolerating regular diet, thin liquid, but difficulty with meds -> held pills and liquids in mouth, needing step-by-step cues to swallow. RN noted he had Haldol the night before. Tmax day 4: 99.0; WBC WNL.
Case Study
**Swallow eval findings:** speech/voice now at baseline w/ mild dysarthria per staff who knows him from prior admissions, A&Ox1, communicating basic needs, mild lingual weakness on protrusion. Able to feed self, but noted food all over himself from prior meal.

**PO trials** (Liquids, puree, eggs, cracker, fruit cup): slow bolus formation and oral clearance, slow mastication, but complete recollection of bolus with tongue sweep to clear oral cavity. No anterior escape, but suspected complete recollection of bolus with tongue sweep to clear bolus formation and PO trials food all over himself lingual weakness on protrusion. Able to feed self, but admissions, A&Ox1, communicating basic needs, mild dysarthria per staff who knows him from prior Swallow eval findings (Marks, 2015, October)

**Risk of Polypharmacy** (Kristensen, et al., 2018)

**Main issue is that the patient may be taking more drugs than are indicated.** (Dr Holmes, SIOG 2015)


**Start Low & Go Slow** - or avoid - especially benzos, muscle relaxants, antihistamines, antipsychotics, tricyclic antidepressants in elderly. (Marks, 2015, October)

**Case Study**

**Summary:** Within the constraints of a bedside swallowing evaluation, pt shows overt s/x of aspiration with thin liquid by straw and is deemed at an elevated risk for aspiration and dysphagia due to his baseline of Dementia and his current need for multiple medications that could contribute to dysphagia. Pt appears safer with thin liquids by cup with small/single sips; supervised oral intake. Silent aspiration cannot be ruled-out bedside; therefore, he will benefit from instrumental evaluation (at rehab due to d/c planning). Pt admitted with lethargy, SOB, poor appetite and increased weakness, as well as overt s/x of aspiration on thin liquids when Haldol added. Note: Lyrica and Oxycodone d/c’d, but Haldol has been newly added to his baseline med of Risperidone, which could further increase his risk for dysphagia. His risks for aspiration pneumonia are increased by his dependency for oral care, his bedridden status, multiple medications, his baseline of GERD, and decreased pulmonary clearance.

**Questions? Thank you!**
https://www.swallowstudy.com/drug-induced-dysphagia-resources-safe-practices/
Medications: Drug-Induced Dysphagia, Complications & Potential Treatments

References


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