Episode 102: Anticholinergic Burden

Karl Wallenkampf, M.A., Kyle Logan, B.S., Adriana Alvarez, B.S., Ryan Holas, B.S., David Puder, M.D.

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There are no conflicts of interest for this episode.

Clinical issue

You are consulted for an "altered" patient whose dysfunctioning cognition and behavior are complicating the patient's clinical care. Or, perhaps you are an outpatient therapist who notices that your patient's attention is waxing and waning, and is drowsy during your interaction. This cognitive impairment could be your patient's new baseline. It could be the progression of dementia but with some decrease in function later in the day due to sundowning. Or, it could be an aggressive derangement of sensorium known as delirium. Today, we consider these three issues. Finally, we discuss a way to approach the medication list and offer a resource we created to improve your treatment of "altered" patients, especially those with delirium precipitated by medications.

A spectrum of sensorium disruptions: from sundown to sunup

Our podcast covered sensorium in a previous series, but to review, we can consider sensorium as referring to "global brain function," including heterogeneous issues that present with a spectrum of severity, such as: sundowning, mild cognitive impairment, dementia, and delirium. Sundowning is a diurnal phenomenon usually experienced in the evenings ("sundown") found in patients with dementia. These patients may experience a group of symptoms including decreased attention, confusion, anxiety, disorientation, and even hallucinations. It can be influenced by pharmacologic, physiologic, and environmental factors (Canevelli et al., 2016). We will be focusing on pharmacologic factors in this podcast.

Sundowning usually occurs within dementia but we all have decreased sensorium mid-day. Dementia is defined as the constellation of symptoms characterized by progressive cognitive decline that interferes with the ability to function independently (activities of daily living) (Duong et al., 2017). Similar, but of lesser degree, is mild cognitive impairment, where patients may have cognitive symptoms and decline, but retain their ability to perform activities of daily living, and will score 18-25 on the Montreal Cognitive Assessment (Langa & Levine, 2015).

Diving deeper: delirium

Episode 102: **Anticholinergic Burden**

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Mild cognitive impairment and dementia may predispose patients to delirium. Delirium, a dangerous derangement of sensorium, has been described by the American Geriatrics Society/National Institute on Aging as “acute brain failure” (2015), analogous to acute heart failure in that there are multiple mechanisms leading to a final common pathway (Marcantonio, 2017). Delirium presents a unique challenge to clinicians, especially those in mental health, given the varied presentation, multitude of etiologies, and substantial morbidity and mortality.

Delirium is common, affecting 30% of patients over 70 years of age admitted to the hospital, and half of that 30% had already become delirious before presentation to the hospital (Marcantonio, 2011). It is the most common postoperative complication in the elderly, affecting as much as 50% of postoperative courses, depending on the severity of the surgery (Marcantonio, 2012). Delirium is also associated with substantial morbidity--and even mortality--in the hospital, with 10 times the risk of death and up to five times the risk for other complications (Marcantonio, 2011). The one-year mortality rate in patients diagnosed with delirium may range from 35-40% (Inouye, 2006).

The high morbidity and mortality may be in part due to how often delirium is missed, or misdiagnosed, in both the inpatient and outpatient. This is largely due to the difficulty of even noticing the symptoms in elderly patients. Patients often have an acute shift--which may have already occurred prior to the hospital stay--toward disturbed attention and awareness, with fluctuations throughout the day. While these changes necessarily must not be explained by a different neurocognitive disorder and are not a part of coma (per the DSM-V), these patients may have dementia as a predisposing factor.

Interestingly, about 50% of all delirium is the hypoactive subtype, about 30% is the mixed subtype and about 20% is the hyperactive subtype (Hosker & Ward, 2017). Hypoactive delirium is characterized by low attention, decreased verbal abilities, and drowsiness to the point of falling asleep during the interview. Hypoactive delirium is more subtle in its presentation compared to hyperactive delirium and can easily be missed. Collecting the patient’s change from baseline could manifest as predominantly drowsy and inactive, and collateral from caregivers and family is very important in teasing out hypoactive delirium, as it can easily be mistaken for depression. A study of 710 hospital admissions found that 75% of the admissions with delirium were not appreciated by the admitting team (Collins et al., 2010).

In distinguishing hypoactive delirium from depression, remember that depression does not present with reductions in consciousness, pronounced poor focus, or abrupt onset (e.g. depressed patients will be able to spell “world” backwards and draw a clock). An observational study on 60+ year-old inpatients found that 42% of the 67 patients referred for evaluation of a

depressive episode were found to be delirious (Farrell, 1995). If you see someone who seems depressed in a medical hospital, consider first and foremost you might be seeing someone with hypoactive delirium.

Assessing delirium

If suspected, clinicians can screen using the Confusion Assessment Method (CAM) (Inouye et al., 1990) or the 3-Minute Diagnostic Interview for Delirium Using the Confusion Assessment Method (3D-CAM) (Marcantonio et al., 2014). Both of these are brief assessments any clinician may use during their interview. Screening is key, even in the outpatient environment, as delirium may be the presentation of an acute and serious medical problem. Urgent attention should be given to the diverse etiologies that could cause it. A useful mnemonic which spells “Delirium:” “Drugs,” “Electrolyte disturbances,” “Lack of drugs,” “Infection,” “Reduced sensory input,” “Intracranial disorders,” “Urinary and fecal disorders,” and “Myocardial and pulmonary disorders” (Marcantonio, 2017). Prompt diagnostic steps should be taken, but our focus today will be on the actions mental health professionals should take, specifically a review of the medication list. Dr. Puder mentioned his favorite screening is watching patients draw a clock and having them spell “world” backward.

Moving into the med list - how we made our medication table

Numerous papers (Ancelin et al., 2006; Han et al., 2008; Sittironnarit et al., 2011; Ehrt et al., 2009; Rudolph, 2008; Chew et al., 2008; Carnahan et al., 2006; and Boustani et al., 2008, see below for discussion) describe the anticholinergic burdens and effects of different medications. A few systematic analyses and meta-analyses (e.g. Duran et al., 2013 and Salahudeen et al., 2015) have also compared studies, combining their data to create tables that score the burdens and allow some comparison among scales. While these tables were systematically formed, they were not as conducive for clinician review, so we prepared our own table based on their work.

Our table uses the basis of Duran et al. (2013) and subdivides the table into both cognitive impairment and anticholinergic-specific effects, based on the above papers. We also added Boustani et al. (2008) to the table, expanding on the work in Duran et al. (2013), and numerous further medications from the work of Carnahan et al. (2006). Then, we added conditional formatting (green for 0, yellow for 1, orange for 2, and red for 3), allowing ease of visual comparison. Each paper was hyperlinked through its DOI for reference, and brief methods were added for improved comparison to the patient population, with a short definition of what scoring system was used. Also, some common drug names, classes, and indications were inserted for improved searching.

Episode 102: Anticholinergic Burden

Karl Wallenkampf, M.A., Kyle Logan, B.S., Adriana Alvarez, B.S., Ryan Holas, B.S., David Puder, M.D.

Review of the included papers

First, we assessed a systematic review (Salahudeen et al., 2015) seeking to compare anticholinergic burden quantified through risk scales, and assess the adverse outcome associations in older populations (Salahudeen et al., 2015, para 3). This analysis included studies in English using an expert opinion anticholinergic burden quantitative scale, with a study population age of 65 or older. Their study identified seven scales (Ancelin et al., 2006; Han et al., 2008; Sittironnarit et al., 2011; Ehrt et al., 2009; Rudolph, 2008; Carnahan et al., 2006; and Boustani et al., 2008, see below for discussion) and used them to form their own table of low, medium, and high anticholinergic burden, which was the theoretical basis of our own.

We adapted the tables from Duran et al. (2013)., as noted above, and formed our table. This paper is a detailed, systematic review of anticholinergic burden, somewhat differently organized from Salahudeen et al. (2015) .

Anticholinergic Burden Classification (ABC)
Ancelin et al., (2006)
Four-point scale (0-3)
Basis: serum anticholinergic activity and expert opinion
Outcomes:

- Cognitive performance was measured by ECO (Examen Cognitif par Ordinateur, a computerized neuropsychometric examination)
- Mild cognitive impairment was diagnosed according to the Stockholm consensus group (Winblad et al., 2004) criteria

Results: *cognitive performance*. Users of anticholinergics (n=297) scored lower than non-users (n=30) in the following facets of cognitive performance: reaction time, attention, delayed non-verbal memory, narrative recall, visuospatial construction, and language tasks. There was no statistical difference seen between the groups in reasoning, immediate and delayed recall of wordlists, and implicit memory. *Mild cognitive impairment*. MCI was found in 80% of users of anticholinergics, and 35% of non-users (odds ratio 5.12; P=0.001). Upon follow-up in 8 years, no difference in dementia development was found.

Clinician-rated Anticholinergic Score (CrAS)
Han et al., (2008)
Four-point scale (0-3)
Basis: pre-existing published anticholinergic scales (Han et al., 2001) and expert opinion
Outcomes: short term memory and executive function at baseline and during follow-up

- Short-term memory was measured by the Hopkins Verbal Recall Test (HVRT)

Episode 102: **Anticholinergic Burden**

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- Executive function was measured by the Instrumental Activity of Daily Living scale (IADLs)

Results: cumulative anticholinergic exposure over the last 12 months was associated with pooper performance in both memory and executive function. “On average, a 1-unit increase in the total anticholinergic burden per 3 months was associated with a 0.32-point and 0.10-point decrease on the HVRT and IADLs, respectively” (p. 1).

Anticholinergic Cognitive Burden (ACB)

Boustani et al., (2008)

Four-point scale (0-3)

Basis: published data and expert opinion

- Searched the Medline database from 1966 to 2007 for any study that both measured the anticholinergic activities of a drug, as well as evaluated the association between this anticholinergic activity and the cognitive function in older adults (including delirium, MCI, dementia or cognitive decline)
- A multidisciplinary panel of geriatricians, geriatric pharmacists, geriatric nurses, and aging brain researchers categorized these medications into mild, moderate, and severe cognitive anticholinergic negative effects

Anticholinergic Loading Scale (ACL)

Sittironnarit et al., (2011)

Four-point scale (0-3)

Basis: pre-existing published anticholinergic scales (Ancelin et al., 2006, Han et al., 2008, Chew et al., 2008, Rudolph, 2008)

Outcomes: psychomotor speed and executive function

Results: in the healthy control, the anticholinergic load was associated with slower response speeds for the Stroop color and incongruent trials. No other relationships were noted.

Ehrt et al., (2009)

Basis/Methods: a cohort study of a community-based cohort of 235 patients with Parkinson’s Disease, which were cognitively assessed over 8 years. Additionally, anticholinergic activity in medication was assessed and classified according to a standardized scale of 0 to 4. The scores from every agent used by each patient were aggregated to calculate the total AA (anticholinergic activity) load for each assessment point. The duration of treatment was scored from 0 to 3.

Outcomes: the study described the relationship between cognitive decline and AA load and duration of treatment.

Episode 102: **Anticholinergic Burden**

Karl Wallenkampf, M.A., Kyle Logan, B.S., Adriana Alvarez, B.S., Ryan Holas, B.S., David Puder, M.D.

Results: the results showed associations between decline on MMSE and total AA load (B = 0.229, p= 0.04) as well as duration of AA drug use (B = 0.231, p = 0.032) (Ehrt et al., 2009).

Rudolph, (2008)
Basis/methods: a cohort study that retrospectively reviewed medical records of 132 geriatric evaluation and management (GEM) patients looking for anticholinergic medications. They also prospectively enrolled 117 primary care patients 65 years or older and performed medication reconciliation, then asked about anticholinergic adverse effects.
Outcomes: they developed the *Anticholinergic Risk Scale*, or ARS, a ranked categorical list of the 500 most commonly prescribed medications with possible anticholinergic effects. The medications were ranked on a scale from 0 to 3 based on anticholinergic potential. The patient's ARS score was then calculated using the sum of the ARS rankings assigned for each of the medications the patient was taking.
Results: higher ARS scores increased the risk of anticholinergic adverse effects in both the GEM (adjusted RR, 1.3; *c* statistic, 0.74) and the primary care cohorts (adjusted RR, 1.9; *c* statistic, 0.77) (Rudolph, 2008).

Chew et al. (2008)
Basis/methods: this study measured the anticholinergic activity of 107 medications commonly used by older adults. They then measured the AA on rodent forebrain and striatum at six clinically relevant concentrations of each medication.
Results: psychotropic medications had higher AA and Nortriptyline is dose-dependent (Chew et al., 2008).

Carnahan et al., 2006
Basis/methods: this cross-sectional observational study of delirium attempted to replicate a pilot study that associated anticholinergic drug scale scores (ADS scores) with serum anticholinergic activity (SAA).
Outcomes: the anticholinergic action of each drug was rated on a scale of 0 to 3 using the Anticholinergic Drug Scale scores. Then, the total anticholinergic scores were calculated based on the sum of the scores of each medication the subject received.
Results: ADS scores were significantly associated with and predicted serum anticholinergic activity (SAA) ($P < 0.0001$ for each). However, the modifications did not appear useful in optimizing the ADS (Carnahan et al., 2006).

Episode 102: Anticholinergic Burden

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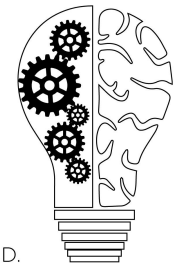
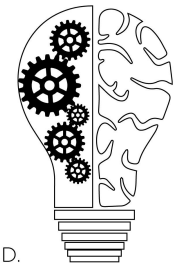


Example medications

- **Hydroxyzine (e.g., Vistaril, Atarax)**
  - Hydroxyzine is an H1-histamine antagonist (1st gen) often used as an antiemetic, anxiolytic, antipruritic, or perioperative drug. The studies we reviewed noted that it has a score of 3/3 in decreasing cognitive performance, 3 on frequency of anticholinergic events (confusion, dizziness, falls), and 3 on serum anticholinergic activity. However, we believe this is in error, due to a study Orzechowski 2005, which showed it had in humans an affinity to the acetylcholine receptor (1/Ki) estimated as 1/800 to 1/6000 nM, which means it is only an antihistamine. In patients with dementia, Dr. Cummings said he would be hesitant to use, because of the potent affinity for H1 which could cause idiosyncratic agitation.

- **Amitriptyline (e.g., Elavil)**
  - A tricyclic antidepressant with many off-label uses including chronic fatigue, fibromyalgia, tension headache, interstitial cystitis, neuropathic pain.
  - Tricyclic antidepressants cause serotonin and norepinephrine to build up in the synaptic cleft.
  - Amitriptyline's side effects are much more commonly established, however its anticholinergic burden is notable, with every study we reviewed, all eight, giving it a 3/3 score for anticholinergic burden.
  - For this drug, alternatives are more difficult to assess.
  - Amitriptyline is heavily metabolized by CYP2D6.
- **Nortriptyline (e.g., Pamelor)**
  - Nortriptyline is a tricyclic antidepressant.
  - Some studies found amitriptyline to have a higher anticholinergic burden at a given dose compared to nortriptyline (Chew et al., 2008).
  - Han 2008 - 3
  - Ehrt 2010 - 2
  - Rudolph 2008 - 2
  - Chew 2008 - 2
  - Carnahan 2006 - 3
  - Boustani 2008 - 3
- **Diphenhydramine (e.g., Benadryl)**
  - H_1-receptor antagonist
  - Allergy symptom relief, motion sickness, insomnia
  - Han 2008 - 3
  - Rudolph 2008 - 3
  - Chew 2008 - 2
  - Carnahan 2006 - 3
  - Boustani 2008 - 3
- **Promethazine (e.g., Phenergan)**
  - H_1-receptor antagonist, dopamine receptor antagonist



    - Motion sickness, nausea, vomiting
    - Sitironnarit 0
    - Rudolph 3
    - Carnahan 3
    - Bustani 3
- **Metoclopramide (e.g., Reglan)**
    - D2 and 5-HT3 receptor antagonist
    - Nausea, vomiting, gastroparesis
    - Han 2008 - 3
    - Sittironnarit 2011 - 1
    - Ehrt 2010 - 0
    - Rudolph 2008 - 1
    - Carnahan 2006 - 0
- **Quetiapine/Olanzapine (e.g., Seroquel/Zyprexa)**
    - Decreases delirium, but also has an anticholinergic effect. At least one article argues to use haloperidol for treating delirium, though quetiapine and olanzapine may be used
    - Quetiapine
        - Han 2
        - Ehrt 1
        - Rudolph 1
        - Chew 1
        - Carnahan 0
        - Boustani 3
- **Paroxetine (e.g., Paxil)**
    - Selective serotonin reuptake inhibitor
    - Strong CYP2D6 inhibitor
    - Desipramine increased 360% due to paxil inhibition of CYP2D6. Other tricyclic antidepressants are also increased.
    - Han 2,
    - Sittironnarit 2
    - Ehrt 2
    - Rudolph 1
    - Chew 2
    - Carnahan 1
    - Boustani 3
- **Oxybutynin (e.g., Ditropan)**
    - Smooth muscle muscarinic antagonist
    - Urinary urgency
    - Ancelin 2006 - 3
    - Sittironarrit 2008 - 2
    - Ehrt 2010 - 3
- **Cetirizine (e.g., Zyrtec)**
    - H_1-receptor antagonist
    - Allergic rhinitis, urticaria
    - Han 2008 - 2

    - Sittironnarit 2011 - 2
    - Rudolph 2008 - 2
    - Note that Chew 2008 and Carnahan 2006 noted scores of 0

- **Carbidopa (e.g., Lodosyn)**
    - Peripheral decarboxylase inhibitor
    - Decreases peripheral conversion of levodopa to dopamine
    - Han 2008 - 1
    - Sittironnarit 2011 - 1
    - Rudolph 2008 - 1
    - Chew 2008 and Carnahan 2006 both 0
- **Furosemide (e.g., Lasix)**
    - Loop diuretic
    - Ascites, edema
    - Ancelin 2006 - 3
    - Sittironnarit 2011 - 0
    - Ehrt 2010 - 1
    - Chew 2008 - 1
    - Carnahan 2006 - 1
    - Boustani - 1
- **Baclofen (e.g., Lioresal)**
    - Muscle relaxer
    - Han 2008 -2
    - Rudolph 2008 - 2
    - Chew 2008 and Carnahan 2006 both 0
    - Switch to robaxin
- **Alprazolam (e.g., Xanax)**
    - Anxiolytic
    - Ancelin 2006 - 3
    - Han 2008 - 1
    - Sittironnarit 2011 - 1
    - Chew 2008 - 0
    - Carnahan 2006 - 1
    - Boustani 2008 - 1

Step 3 - look for other causes

While to some extent the primary service should look for other causes, the psychiatric provider should also review the patient's medical history, recent interventions and changes, and recommend (when appropriate) subtle changes in the patient's environment that may bring increased calm and comfort, such as: cessation of overnight vitals, cessation or periodicity of early AM lab draws (e.g. every other day), and the possibility of lighting changes or other

environmental factors. Also, though complicated by the current pandemic, efforts should be made to bring family visitors to bedside to possibly create connections that have been lost.

Where to go from here

It is advisable to review a patient's medications on an ongoing basis. At times, patients may start a medication on an inpatient basis but continue as an outpatient due to absent or miscommunication between the inpatient and outpatient providers, psychiatric or otherwise. Changes made on an inpatient basis may be continued without review, so it may be helpful to assess patients' medication lists on a regular basis, but also immediately after a hospital discharge.

Summary:

There are medications that worsen cognitive function and all mental health providers should be aware, and work on optimizing sensorium.

To download the excel sheet that goes with this episode, go here.

To learn more about Sensorium:
Episode 006: Sensorium Part 1: Total Brain Function Optimization
Episode 009: Diet Optimization for Cognitive Function and Brain Optimization
Episode 010: Sensorium Part 3: Exercise as a Prescription for Depression, Anxiety, Chronic Stress (like Diabetes) and Sensorium
Episode 011: Sensorium Part 4: Medications, Drugs (THC, Alcohol), Medical Issues, Sleep, and Free Will

Reference List

AGS/NIA Delirium Conference Writing Group, Planning Committee and Faculty (2015). The American Geriatrics Society/National Institute on Aging Bedside-to-Bench Conference: Research Agenda on Delirium in Older Adults. *Journal of the American Geriatrics Society*, *63*(5), 843–852. https://doi.org/10.1111/jgs.13406

Ancelin, M. L., Artero, S., Portet, F., Dupuy, A.-M., Touchon, J., & Ritchie, K. (2006). Non-degenerative mild cognitive impairment in elderly people and use of anticholinergic drugs: longitudinal cohort study. BMJ, 332(7539), 455–459. https://doi.org/10.1136/bmj.38740.439664.de

Episode 102: **Anticholinergic Burden**

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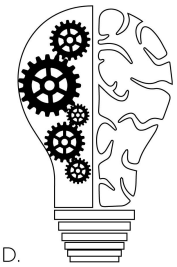

Boustani, M., Campbell, N., Munger, S., Maidment, I., Fox, C. (2008). Impact of anticholinergics on the aging brain: a review and practical application. *Aging health* 4(3):311-320. https://doi.org/10.2217/1745509X.4.3.311

Canevelli, M., Valletta, M., Trebbastoni, A., Sarli, G., D'Antonio, F., Tariciotti, L., de Lena, C., & Bruno, G. (2016). Sundowning in Dementia: Clinical Relevance, Pathophysiological Determinants, and Therapeutic Approaches. *Frontiers in Medicine*, 3, 1–2. https://doi.org/10.3389/fmed.2016.00073

Carnahan, R. M., Lund, B. C., Perry, P. J., Pollock, B. G., & Culp, K. R. (2006). The Anticholinergic Drug Scale as a Measure of Drug-Related Anticholinergic Burden: Associations With Serum Anticholinergic Activity. The Journal of Clinical Pharmacology, 46(12), 1481–1486. https://doi.org/10.1177/0091270006292126

Chew, M. L., Mulsant, B. H., Pollock, B. G., Lehman, M. E., Greenspan, A., Mahmoud, R. A., Kirshner, M. A., Sorisio, D. A., Bies, R. R., & Gharabawi, G. (2008). Anticholinergic Activity of 107 Medications Commonly Used by Older Adults. Journal of the American Geriatrics Society, 56(7), 1333–1341. https://doi.org/10.1111/j.1532-5415.2008.01737.x

Collins, N., Blanchard, M.R., Tookman, A., & Sampson, E.L. (2009). Detection of delirium in the acute hospital. Age and Ageing, 39(1), 131–135. https://doi.org/10.1093/ageing/afp201

Duong, S., Patel, T., Chang, F. (2017). Dementia: What pharmacists need to know. *Can Pharm J (Ott)*. 150(2),118-129. https://doi.org/10.1001/jama.2014.13806

Ehrt, U., Broich, K., Larsen, J. P., Ballard, C., & Aarsland, D. (2009). Use of drugs with anticholinergic effect and impact on cognition in Parkinson's disease: a cohort study. Journal of Neurology, Neurosurgery & Psychiatry, 81(2), 160-165. https://doi.org/10.1136/jnnp.2009.186239

Facts & figures. (n.d.). Loma Linda University Health. Retrieved October 13, 2020, from https://lluh.org/about-us/facts-figures

Farrell, K.R. (1995). Misdiagnosing delirium as depression in medically ill elderly patients. *Archives of Internal Medicine*, 155(22), 2459–2464. https://doi.org/10.1001/archinte.155.22.2459

Han, L., Agostini, J. V., & Allore, H. G. (2008). Cumulative Anticholinergic Exposure Is Associated with Poor Memory and Executive Function in Older Men. Journal of the American Geriatrics Society, 56(12), 2203–2210. https://pubmed.ncbi.nlm.nih.gov/19093918/

Han, L., McCusker, J., Cole, M., Abrahamowicz, M., Primeau, F., & Elie, M. (2001). Use of medications with anticholinergic effect predicts clinical severity of delirium symptoms in older medical inpatients. Archives of Internal Medicine, 161(8), 1099–1105. https://doi.org/10.1001/archinte.161.8.1099

Hosker, C., & Ward, D. (2017). Hypoactive delirium. BMJ, 2047–2052. https://doi.org/10.1136/bmj.j2047

Inouye S.K. (2006). Delirium in older persons. *The New England journal of medicine*, *354*(11), 1157–1165. https://doi.org/10.1056/NEJMra052321

Inouye, S.K., van Dyck, C.H., Alessi, C.A., Balkin, S., Siegal, A.P., & Horwitz, R.I. (1990). Clarifying confusion: the confusion assessment method. A new method for detection of delirium. *Annals of internal medicine*, *113*(12), 941–948. https://doi.org/10.7326/0003-4819-113-12-941

Kalish, V.B., Gillham, J.E., & Unwin, B.K. (2014). Delirium in older persons: evaluation and management. *American family physician*, *90*(3), 150-158.

Langa, K.M., & Levine, D.A. (2014). The Diagnosis and Management of Mild Cognitive Impairment. *JAMA*, 312(23), 2551-2561. https://doi.org/10.1001/jama.2014.13806

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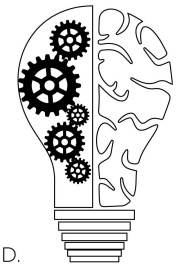

Marcantonio, E.R. (2011). In the clinic. Delirium. *Annals of Internal Medicine*, *154*(11), ITC6-1, ITC6-2, ITC6-3, ITC6-4, ITC6-5, ITC6-6, ITC6-7, ITC6-8, ITC6-9, ITC6-10, ITC6-11, ITC6-12, ITC6-13, ITC6-14, ITC6-15; quiz ITC6-16. https://doi.org/10.7326/0003-4819-154-11-201106070-01006

Marcantonio E.R. (2012). Postoperative delirium: a 76-year-old woman with delirium following surgery. *JAMA*, *308*(1), 73–81. https://doi.org/10.1001/jama.2012.6857

Marcantonio E.R. (2017). Delirium in Hospitalized Older Adults. *The New England journal of medicine*, *377*(15), 1456–1466. https://doi.org/10.1056/NEJMcp1605501

Marcantonio, E. ., Ngo, L. ., O'Connor, M., Jones, R.N., Crane, P.K., Metzger, E.D., & Inouye, S. K. (2014). 3D-CAM: derivation and validation of a 3-minute diagnostic interview for CAM-defined delirium: a cross-sectional diagnostic test study. *Annals of internal medicine*, *161*(8), 554–561. https://doi.org/10.7326/M14-0865

Orzechowski, R.F., et al. Comparative Anticholinergic Activities of 10 Histamine H1 Receptor Antagonists in Two Functional Models. European Journal of Pharmacology 2005; 506(3):257-64.

Rudolph, J. L. (2008). The Anticholinergic Risk Scale and Anticholinergic Adverse Effects in Older Persons. *Archives of Internal Medicine*, 168(5), 508-513. https://doi.org/10.1001/archinternmed.2007.106

Salahudeen, M.S., Duffull, S.B., Nishtala, P.S. (2015). Anticholinergic burden quantified by anticholinergic risk scales and adverse outcomes in older people: a systematic review. *BMC Geriatr* 15, 31. https://doi.org/10.1186/s12877-015-0029-9

Sittironnarit, G., Ames, D., Bush, A. I., Faux, N., Flicker, L., Foster, J., Hilmer, S., Lautenschlager, N. T., Maruff, P., Masters, C. L., Martins, R. N., Rowe, C., Szoeke, C., & Ellis, K. A. (2011). Effects of Anticholinergic Drugs on Cognitive Function in Older Australians: Results from the AIBL Study. Dementia and Geriatric Cognitive Disorders, 31(3), 173–178. https://doi.org/10.1159/000325171

Winblad, B., Palmer, K., Kivipelto, M., Jelic, V., Fratiglioni, L., Wahlund, L.-O., Nordberg, A., Bäckman, L., Albert, M., Almkvist, O., Arai, H., Basun, H., Blennow, K., Leon, M. D., DeCarli, C., Erkinjuntti, T., Giacobini, E., Graff, C., Hardy, J., … Petersen, R. C. (2004).