Warning! For Mature Audiences Only:
An Explicit Look into the Management of Inappropriate Sexual Behaviors in Dementia

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Objectives
1. Define inappropriate sexual behavior (ISB) and identify common causes
2. Describe behavioral interventions available for treatment of ISB
3. Review evidence of pharmacologic interventions for ISB
4. Discuss major risks of pharmacologic interventions in elderly patients with ISB
5. Recognize ethical dilemmas to consider in treatment decisions for ISB
Background

I. Dementia Overview
   a. Prevalence\(^1\)
      i. Affects 5% of adults > 65 years old and 20% of adults >85 years old
   b. Common Etiologies\(^1\)
      i. Alzheimer’s disease (AD)
      ii. Dementia with Lewy bodies (DLB)
      iii. Vascular dementia (VaD)
   c. Less common etiologies include Parkinson’s Disease, alcohol, traumatic brain injury (TBI)
   d. Alzheimer’s Disease\(^2\)
      i. Hypothesized pathology – multiple proposed pathologies
         1. Neuritic plaques and neurofibrillary tangles develop in cortical areas and temporal lobe structure of the brain
         2. Degeneration of neurons and synapses
         3. Marked destruction of cholinergic pathways
      ii. Clinical characteristics
         1. Cognitive
            a. Memory loss, aphasia, apraxia, agnosia, disorientation, impaired executive function
         2. Noncognitive
            a. Depression, psychosis, behavioral disturbances
         3. Functional
            a. Inability to perform activities of daily living
   e. Dementia with Lewy bodies\(^1,3\)
      i. Hypothesized pathology
         1. Presence of Lewy bodies in specific brainstem nuclei, substantia nigra, amygdala, cingulate gyrus and neocortex
            a. Lewy bodies = histopathologic marker for Parkinson’s disease
      ii. Clinical characteristics
         1. Dementia – Perform worse on tests evaluating attention, frontal lobe function, psychomotor speed, and visuospatial
         2. Cognitive Fluctuations – usually affects alertness or attention
         3. Hallucinations
            a. Occur in 25%-83% of patients
            b. Typically well-formed and persistent
            c. Frequently describe seeing people, children, and animals
         4. Parkinsonism – stooped posture, shuffling gait, reduced arm swing, and tendency to trip and fall
         5. Delusions – commonly secondary to hallucinations
            a. Occur in 33%-60% of patients
            b. Common types – paranoid and “phantom boarder” living in home
   f. Neuroleptic Sensitivity
      a. Treatment with neuroleptics for hallucinations and delusions commonly leads to severe adverse reactions
f. Vascular Dementia\textsuperscript{1,4}
   i. Hypothesized pathology
      1. Associated with cerebral vascular disease
      2. History of strokes
         a. Subtypes include large-vessel and small-vessel disease
      3. Dementia depends on total volume of damaged cortex
   ii. Clinical characteristics
      1. Onset of cognitive loss can be sudden or gradual
      2. Onset of dementia within 3 months of a symptomatic stroke
      3. Progression is slow and stepwise
         a. Increase in severity with each ischemic event
      4. Early and severe decline of executive function (disorganized thought)
      5. Early presence of gait disturbances (shuffling with short steps)
      6. History of unsteadiness and/or frequent, unprovoked falls
      7. Early urinary frequency, urgency, and other urinary symptoms not explained by urologic disease
      8. Pseudobulbar palsy
      9. Personality and mood changes

II. Inappropriate Sexual Behavior (ISB)
   a. Definition\textsuperscript{5,6}
      i. Sexual behaviors that cause distress, disturbance, or suffering for close relationships and caregivers
      ii. Persistent uninhibited sexual behaviors directed at oneself or others
      iii. May be further categorized into two types\textsuperscript{7}:
         1. Intimacy seeking – normal behaviors misplaced in social context
            a. Kissing, hugging
         2. Disinhibited – behaviors that would be considered inappropriate in most contexts
            a. Fondling, exhibitionism, vulgarity
   b. Types of Hypersexual Behavior\textsuperscript{5,8}
      i. Sex talk
         1. Most common inappropriate behavior
         2. Use of foul language, dissimilar from resident’s premorbid personality
      ii. Implied sexual acts
         1. Requesting unnecessary genital care
         2. Publicly reading pornographic material
      iii. Sexual acts
         1. Touching, grabbing, exposing, masturbating
         2. In private or in public areas
   c. Etiology and prevalence\textsuperscript{9,10}
      i. ISB is exhibited in 2-17\% of demented patients
      ii. More commonly occurs in men (ratio not determined)
      iii. Rates of ISB differ according to type and severity of dementia
         1. More common in patients with moderate-severe and vascular dementia
      iv. Aliagiakrishnan K, \textit{et al} 2005\textsuperscript{11}
1. Retrospective Cross Sectional Study
2. Reviewed 2,278 charts including long term care psychiatric consulting services, community based geriatric psychiatry, and inpatient dementia behavioral unit
3. Prevalence of ISB: 1.8% (n=41 of 2,278)
   a. Age: 65-80 years 58.5% (n=24); >80 years 41.5% (n=17)
   b. Sex: male 92.7% (n=38); female 7.3% (n=3)
4. Etiology of ISB
   a. Vascular Dementia 54%
   b. Alzheimer's Disease 22%
   c. Alcohol 12.2%
   d. Mild Cognitive Impairment 9.8%
   e. Other 2.5%
5. Type of ISB (overlapping presentation)
   a. Physically inappropriate behavior 87.8% (n=36) – touching inappropriately, fondling, public masturbation, disrobing
   b. Verbal inappropriate behavior 65.7% (n=27) – sexual remarks

Tsai S, et al 1999
1. Retrospective Study
2. 133 demented elderly patients admitted to geropsychiatry unit
   a. VaD (n=40)
   b. AD (n=75)
   c. Dementia not otherwise specified (n=18)
3. Prevalence of ISB: 15% (n=20)
4. Etiology of ISB
   a. Vascular Dementia 45% (n=9)
   b. Alzheimer's Disease 40% (n=8)
   c. Dementia not otherwise specified 15% (n=3)

Causes of ISB
i. Neurobiology of sexual function

![Figure 1: Areas of central nervous system that play a role in ISB](image)
1. Central Nervous System (CNS)\textsuperscript{5,6,8,13,14}
   a. Frontal System
      i. Location: frontal lobe
      ii. Dysfunction: disinhibition; impairs inhibitory sexual self-control mechanisms
   b. Temporo-Limbic System
      i. Location: Left and right sided temporal lobes
      ii. Dysfunction: impairs emotional and intellectual understanding of sexual arousal; hypersexual behaviors
      iii. Right sided > left sided
      iv. Right sided temporal lobe modulates emotions and the understanding of the effect associated with sexual arousal
   c. Striatum
      i. Location: corticostriatal circuits
      ii. Dysfunction: obsessive-compulsive sexual behaviors
   d. Hypothalamus\textsuperscript{16,17}
      i. Dysfunction: increased sexual drive and disinhibition

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Circuit_diagram.png}
\caption{Circuit between pre-frontal-subcortical systems, striatum and thalamus leading to changes in executive function\textsuperscript{16}}
\end{figure}

2. Endocrine Factors\textsuperscript{14}
   a. Hormones related to sexual function include androgens, estrogens, progesterone, prolactin, oxytocin, cortisol and pheromones
   b. Testosterone
      i. Withdrawal of exogenous testosterone has been shown to cause rapid decrease in sexual interest and activity of males
      ii. Influences sexual desire in women

Hannah Sulik, PharmD
c. Estrogen
   i. Research suggests estrogens have little influence on sexual desire in males or females
   ii. High levels of exogenous estrogen inhibit sexual desire in males
   iii. Administration of both estrogen and androgen to menopausal women has shown slight increase in sexual desire (estrogen therapy alone is not effective)

d. Progesterone
   i. Does not have substantial influence on sexual desire in either males or females

3. Neurotransmitters
   a. Neurotransmitters related to sexual function include serotonin, dopamine, nitric oxide, epinephrine, norepinephrine, acetylcholine, histamine, and gamma-aminobutyric acid (GABA)
   b. Serotonin
      i. 95% of serotonin receptors are located in the periphery
      ii. May effect smooth muscle vasodilation and vasoconstriction of sexual organs
      iii. Serotonin_1A receptor = activation facilitates sexual functioning
      iv. Serotonin_2 receptor = activation impairs sexual functioning
   c. Dopamine
      i. Increased dopamine activity increases sexual desire and erection in males
      ii. May have more significant role in males
      iii. Limited research in females suggests role in sexual desire and orgasm
   d. Low CNS serotonin and high dopamine \(\rightarrow\) increases sexual desire
   e. High CNS serotonin and low dopamine \(\rightarrow\) suppresses sexual desire

ii. Medications
   1. Dopamine agonists
      a. Proposed mechanisms
         i. Increased dopamine levels
         ii. Reduced prolactin concentrations
         iii. Stimulation of D2 and D3 receptors may specifically mediate sexual behavior disorder
      b. Literature suggests adjunct dopamine agonists are a main contributor to ISB over levodopa/carbidopa
         i. Dopamine agonists – bromocriptine, pramipexole, ropinirole and pergolide
      c. Reported Case Series
         i. Klos K, et al 2005
            1. Hypersexuality reported in patients receiving dopamine agonists
               a. 13 patients with Parkinson’s Disease
               b. 2 patients with multiple system atrophy
2. 14 of 15 patients on therapeutic or high-dose dopamine agonist therapy
3. 4 patients on dopamine agonist monotherapy
4. 1 patient on levodopa monotherapy
5. Developed hypersexuality within 8 months of therapy in 14 of 15 cases
6. Discontinuation of dopamine agonist
   a. Complete resolution of symptoms in 3 patients with all other patients showing marked improvement
1. Hypersexuality reported in 13 patients with Parkinson’s Disease (11 males; 2 females)
2. Dopamine Therapy
   a. 4 patients on levodopa monotherapy
   b. 4 patients on direct-dopamine agonist monotherapy (bromocriptine, peroglide, amantadine)
   c. 3 patients on levodopa plus dopamine agonist
   d. 1 patient on carbidopa/levodopa monotherapy
   e. 1 patient on MAO-B inhibitor
3. Average age at onset of PD was much younger than general population (49.5 years)
4. Symptoms resolved upon discontinuation of offending drug
   a. Dose-dependent relationship to hypersexuality demonstrated in some patients

2. Alcohol and benzodiazepines
   a. Impair cognition and cause disinhibition
3. Stimulant drugs
   a. Increase libido

Behavioral Interventions

I. Family and Caregivers
   a. Supportive psychotherapy
      i. Useful for spouses of patients
      ii. To understand that behaviors are due to the illness and not a reflection of their relationship

II. Patients
   a. Types of interventions
      i. Redirection
      ii. Distraction
      iii. Sensory stimulation
         1. Keep resident busy with activities
      iv. Separate resident from social situations that exacerbate behaviors
         1. Change dinner table assignments
         2. Switch staffing to same gender
      v. Time with sexual partner (consenting)
1. Conduct a thorough assessment to determine if resident and partner are competent to make decision
2. Make privacy arrangements
   a. Secure a private room
   b. Find activity for roommate to participate in outside of room
vi. Privacy to fulfill sexual needs
vii. Clothing that fastens in the back or without zippers
   1. For patients with tendency to expose themselves or masturbate in public
b. Tune L, et al 2008\textsuperscript{20}
   i. Case report of 68 year old male with AD or frontotemporal dementia
      1. Inappropriately touched staff and female residents
      2. Failed multiple antipsychotics which “slowed him down”
      3. Provided stuffed toy, which he touched inappropriately but was less intrusive towards staff and other residents
c. Bird M, et al 2002\textsuperscript{21}
   i. Controlled Study
      1. Control group (n=22)
         a. Residents received usual care
      2. Intervention group (n=44)
         a. Included nurse and clinical psychologist
         b. Received individualized plan after extensive assessment
         c. Analyzed behaviors in detail and completed risk assessment
   3. Results
      a. Intervention group
         i. 77% received psychosocial interventions
         ii. 9% received pharmacological interventions
      b. Control group
         i. Only 9% received psychosocial interventions
         ii. Intervention group had a 44% reduction in difficult behaviors
d. Limitations
   i. Reduced ability to learn and remember redirection, education, and counseling even with repetition
   ii. Poor education and training of staff and caregivers on interventions

Pharmacological Treatment

\textbf{I. Antidepressants}

a. Majority of case reports with selective-serotonin inhibitors (SSRIs)\textsuperscript{22-26}
   i. Majority of case reports with citalopram 20mg per day
b. Proposed Mechanism\textsuperscript{5,8,13}
   i. Increases serotonin leading to anti-libido and anti-obsessional effects
c. Side Effects\textsuperscript{27}
   i. Nausea, vomiting, diarrhea, fatigue, insomnia
   ii. QTc prolongation
II. Hormonal Agents
   a. Majority of case reports with anti-androgens\textsuperscript{28,29,31,35-38}
   b. Anti-androgens
      i. Medroxyprogesterone acetate (MPA) or cyproterone acetate (CPA)
         1. Most case reports with MPA
         2. Wide ranges of MPA and CPA doses reported
         3. CPA not available in the United States
      ii. Mechanism\textsuperscript{5,6,10,13}
         1. Inhibits levels of pituitary luteinizing hormone (LH) and follicle stimulating hormone (FSH)
            a. Blocks testosterone synthesis in the testes subsequently reducing serum testosterone
         2. MPA – No anti-androgen effects at receptor level
            a. More progestational than anti-androgen effects
            b. Less potent anti-androgen and progestogen than CPA
         3. CPA – Anti-androgen effects at receptor level
            a. Balanced progestational and anti-androgen effects
      iii. Testosterone levels
         1. Three case reports measured testosterone levels at initiation of therapy and after decrease of behaviors\textsuperscript{28,29,31}
         2. Serial testosterone levels may assist in dosing of MPA and CPA
            a. 90% decrease of testosterone levels\textsuperscript{30}
            b. Decrease testosterone to levels similar to females 25-90ng/mL\textsuperscript{32}

<table>
<thead>
<tr>
<th>Case Report</th>
<th>Previous Treatment</th>
<th>Patient</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>22Stewart J, et al 1997</td>
<td>Haloperidol, thioridazine, lorazepam, lithium, nortriptyline</td>
<td>69 y/o male; alcoholic dementia</td>
<td>Paroxetine 20mg/day</td>
<td>Reduction at 1 week; sustained at least 3 months</td>
</tr>
<tr>
<td>23Raji M, et al 2000</td>
<td>Paroxetine, risperidone, valproic acid, gabapentin</td>
<td>90 y/o female; dementia not otherwise specified (NOS)</td>
<td>Citalopram 20mg/day</td>
<td>Reduction at 1 week; remission remained at 9 months</td>
</tr>
<tr>
<td>24Mania I, et al 2006</td>
<td>Lamotrigine, clozapine, aripiprazole, ziprasidone, olanzapine, lithium, estrogen</td>
<td>54 y/o male; bipolar and Parkinson’s disease associated dementia</td>
<td>Citalopram 20mg/day</td>
<td>Reduction at 5 days; all ISB ended at 2 weeks</td>
</tr>
<tr>
<td>25Tosto G, et al 2008</td>
<td>Donepezil</td>
<td>55 y/o male; AD</td>
<td>Citalopram 40mg/day</td>
<td>Reduction at 60 days; remained at 12 month follow-up</td>
</tr>
<tr>
<td>26Chen S, et al 2010</td>
<td>Memantine, rivastigmine</td>
<td>85 y/o male; likely mixed AD and VaD</td>
<td>Citalopram 20mg/day</td>
<td>Reduction of ISB maintained at 7 months</td>
</tr>
</tbody>
</table>
iv. Side Effects

1. MPA\textsuperscript{10,33}
   a. Sedation, weight gain, mild depression, fatigue, hair loss, mild diabetes, dizziness, abdominal pain, thromboembolic disorders (DVT, PE), decreased bone mineral density, cardiovascular disorders

2. CPA\textsuperscript{34}
   a. Fatigue, gynecomastia, weight gain, hair loss, depressive mood, sedation, liver disease, hot flashes, cardiovascular effects, thromboembolism

3. Contraindications – thromboembolic disorder or liver disease

\begin{table}
\centering
\caption{Case Reports of Anti-androgens}
\label{table:case_reports}
\begin{tabular}{|c|c|c|p{0.5\linewidth}|}
\hline
Source & Failed Treatment & Patient & Treatment & Outcome \\
\hline
\textsuperscript{35}Light S, et al 2006 (n=5) & Donepezil, buspirone, haloperidol prior to MPA; haloperidol, olanzapine, quetiapine, buspirone, carbamazepine after MPA & 79 y/o male; mixed AD and VaD & 100mg IM monthly & Response in 2 weeks with no more ISB; MPA discontinued after 4 months due to “chemical castration” concerns by state; ISB returned \\
\textsuperscript{35}Light S, et al 2006 (n=5) & Received sertraline then venlafaxine for depression prior to MPA; thioridazine after MPA & 85 y/o male; VaD & 300mg IM monthly & Response in 2 weeks with no more ISB; MPA discontinued after 1 year due to “chemical castration” concerns by state; ISB returned \\
\textsuperscript{28}Stewart J, et al 2005 & Sertraline for depression; quetiapine for aggression & 81 y/o male; AD & 500mg IM weekly & ISB completely stopped; no ISB at 1 year \\
\textsuperscript{29}Cooper A, et al 1987 (n=4) & Quetiapine, trazodone, valproic acid, risperidone & 68 y/o male; VaD & 300mg IM weekly & ISB completely stopped; all psychotropics discontinued \\
\textsuperscript{28}Stewart J, et al 2005 & Donepezil, quetiapine for combativeness & 81 y/o male; dementia NOS & 500mg IM weekly & ISB completely stopped; quetiapine discontinued; no ISB at 1 year \\
\textsuperscript{28}Stewart J, et al 2005 & ISB controlled by paroxetine for 5 years & 76 y/o male; alcoholic dementia & 750mg IM weekly & Marked improvement in ISB; maintained at 2 months; testosterone levels decreased to 48.4ng/dL. \\
\textsuperscript{29}Cooper A, et al 1987 (n=4) & Behavioral management, thioridazine or chlorpromazine & 75-84 y/o males; dementia NOS & 100mg orally per day & ISB stopped within 2 weeks; maintained at 1 year \\
\hline
\end{tabular}
\end{table}
Table 3: Case Reports of Estrogens

<table>
<thead>
<tr>
<th>Source</th>
<th>Failed Treatment</th>
<th>Patient</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 Kyomen H, et al 1991</td>
<td>None reported</td>
<td>92 y/o male; AD</td>
<td>Diethylstilbestrol (DES) 1mg twice daily</td>
<td>ISB decreased within 1 week</td>
</tr>
<tr>
<td>41 Lothstein L, et al 1997</td>
<td>Enrolled if failed SSRI or were sexually acting out in dangerous ways</td>
<td>Avg age 70 y/o (range 61-81 y/o); males; dementia NOS</td>
<td>Estrogen 0.625mg PO daily or estrogen 0.5-0.1mg transdermal patches</td>
<td>Marked improvement in 38 of 39 patients</td>
</tr>
<tr>
<td>42 Kay P, et al 1995</td>
<td>Thioridazine</td>
<td>75 y/o male; dementia NOS</td>
<td>Transdermal estradiol 0.05mg daily</td>
<td>ISB stopped</td>
</tr>
<tr>
<td>43 Shelton P, et al 1999</td>
<td>Haloperidol, risperidone, lorazepam</td>
<td>78 y/o male; VaD</td>
<td>Conjugated estrogen 0.625mg daily</td>
<td>ISB decreased 50% at 5 months</td>
</tr>
</tbody>
</table>

31 Weiner M, et al 1992 (n=2)  
Thioridazine  
72 y/o male; organic mental disorder  
150mg IM every 2 weeks  
ISB completely eliminated after 2 weeks at this dose

Thioridazine  
84 y/o male; AD  
200mg IM every 2 weeks  
ISB stopped after two weeks

36 Haussermann P, et al 2003 (n=2)  
Valproate, olanzapine, lithium, lorazepam, levodopa  
79 y/o male; Parkinson’s disease associated dementia  
10mg daily  
Behaviors diminished within a few days; ISB eventually stopped completely

Valproate, mirtazapine, risperidone  
74 y/o male; VaD  
10mg daily  
Behaviors diminished within a few days; ISB eventually stopped completely

37 Nadal M, et al 1993  
Antidepressants and antipsychotics  
49 y/o female; Picks disease  
100mg daily  
At 1 month, ISB ceased; at 5 months CPA was withdrawn

38 Potocnik F, et al 1992  
Haloperidol, thioridazine, clozapine  
60 y/o male; AIDs dementia  
50mg twice daily  
No ISB by day 3; maintained at 5 months

c. Estrogens  
i. Most common – diethylstilbestrol (DES) and conjugated estrogens

ii. Mechanism  
1. Decreases testosterone production via reducing LH and FSH secretion

iii. Side Effects

1. Nausea, gynecomastia, fluid retention
2. Increased cardiovascular disorders and thromboembolism

iv. Contraindications: current or history of arterial thromboembolic disease or DVT/pulmonary embolism; hepatic disease
III. Antipsychotics
   a. Majority of case reports with atypical antipsychotics
   b. Mechanism
      i. Dopamine-blocking effects
      ii. Elevation of prolactin levels
   c. Side Effects
      i. Extrapyramidal symptoms, orthostatic hypotension, syncope, drowsiness, anticholinergic effects, blood dyscrasia, QTc prolongation, metabolic changes (diabetes, weight gain, increased cholesterol and triglycerides), neuroleptic malignant syndrome
   d. Black box warning – increased mortality in elderly patients with dementia-related psychosis

Table 4: Case Reports with Antipsychotics

<table>
<thead>
<tr>
<th>Case Reports</th>
<th>Previous Treatment</th>
<th>Patient</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>45MacKnight C, et al 2000</td>
<td>Cyproterone acetate, paroxetine</td>
<td>85 y/o male; dementia NOS</td>
<td>Quetiapine 25mg daily</td>
<td>ISB stopped at 2 days; sustained at 2 month follow-up</td>
</tr>
<tr>
<td>46Prakash R, et al 2009</td>
<td>Memantine, olanzapine; carbidopa/levodopa for parkinsonism</td>
<td>61 y/o female; DLB</td>
<td>Quetiapine 75mg daily</td>
<td>ISB stopped at 7 days; sustained at 1 month follow-up</td>
</tr>
<tr>
<td>47Dhikav V, et al 2007</td>
<td>None reported</td>
<td>70 y/o male; AD</td>
<td>Olanzapine 5mg daily</td>
<td>Reduced ISB</td>
</tr>
<tr>
<td>48Rosenthal M, et al 2003</td>
<td>None reported</td>
<td>90 y/o male; AD</td>
<td>Haloperidol 1.5mg daily</td>
<td>Reduced ISB</td>
</tr>
</tbody>
</table>

IV. Anticonvulsants
   a. Majority of case reports with gabapentin 900-2700mg daily
   b. Proposed Mechanism
      i. Gabapentin
         1. May increase GABA synthesis in the brain, while decreasing the release of monoamine transmitters
   c. Side Effects
      i. Drowsiness, fatigue, dizziness, ataxia, gastrointestinal effects
   d. Dose adjustment for renal impairment
Table 5: Case Reports with Anticonvulsants

<table>
<thead>
<tr>
<th>Case Reports</th>
<th>Previous Treatment</th>
<th>Patient</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 Alkhalil C, et al 2004 (n=3)</td>
<td>Behavioral interventions</td>
<td>Average age 73 y/o; genders not reported; AD (n=2), VaD (n=1)</td>
<td>Gabapentin 1800-2700mg daily</td>
<td>Reduction of ISB in 2 of 3 patients; complete resolution in 1 of 3 patients at 6 months</td>
</tr>
<tr>
<td>49 Alkhalil C, et al 2003</td>
<td>Quetiapine, firm nursing redirection and behavioral interventions</td>
<td>76 y/o male; AD</td>
<td>Gabapentin 300mg TID</td>
<td>ISB resolved; stable at 6 month follow-up</td>
</tr>
<tr>
<td>50 Miller L, et al 2001</td>
<td>Valproic acid, mesoridazine</td>
<td>62 y/o male; VaD +/- delirium</td>
<td>Gabapentin 300mg TID</td>
<td>Reduction in ISB</td>
</tr>
<tr>
<td>52 Freyman N, et al 2005</td>
<td>Pipamperone and galantamine</td>
<td>78 y/o male; AD</td>
<td>Carbamazepine 200mg daily</td>
<td>Reduction at 3 weeks; stable at 6 month follow-up</td>
</tr>
</tbody>
</table>

V. Retrospective Chart Review

Table 6: Bardell A, et al. Intern Psychogeriatrics 2011; 23(7): 1182-1188

<table>
<thead>
<tr>
<th>Purpose</th>
<th>To provide descriptions of the phenomenology of inappropriate sexual behavior (ISB) in the geriatric population, to identify potential contributing factors, and to review the efficacy of interventions</th>
</tr>
</thead>
</table>
| Design           | • Retrospective chart review of inpatients admitted to the Geriatric Inpatient Unit of the Royal Ottawa Mental Health Center  
|                  | • Two groups  
|                  |   ○ Study group – various pharmacologic interventions for ISB  
|                  |   ○ Matched control group – matched on gender, age and marital status                                                                                                                                 |
| Patients         | • Inclusion Criteria  
|                  |   ○ Admitted in the previous 3 years  
|                  |   ○ Identified reason for admission documented as ISB in medical chart  
|                  | • Exclusion Criteria  
|                  |   ○ None                                                                                                                                                                                        |
| Outcomes         | • Study and matched control group  
|                  |   ○ Demographics, remote and current medical and psychiatric history, length of stay in hospital, criminal history, medications prior to admission and at discharge, cardiovascular risk factors, cognitive testing, substance use history, presence and type of dementia, history and location of stroke  
|                  | • Study group  
|                  |   ○ Effectiveness of intervention for ISB, discontinuation of interventions due to adverse effects  
|                  |   ○ Effectiveness of interventions categorized into three groups  
|                  |     ○ No effect on ISB  
|                  |     ○ Some reduction but not complete extinction of ISB  
|                  |     ○ Extinction of ISB  
|                  | • Statistics  
|                  |   ○ Fisher's Exact Test and Mann-Whitney U tests for non-parametric variables  
|                  |   ○ T-test for parametric variables  
|                  |   ○ Two-tailed significance levels for all analysis |
### Table 7: Demographics and Cognitive Impairment History

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study Group (n=10)</th>
<th>Matched Control Group (n=10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Age, years (range)</td>
<td>76.4 (69-85)</td>
<td>NA</td>
<td>---</td>
</tr>
<tr>
<td>Gender ratio (male:female)</td>
<td>9:1</td>
<td>NA</td>
<td>---</td>
</tr>
<tr>
<td>Diagnosis of Dementia, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vascular Dementia</td>
<td>100 (10)</td>
<td>50 (5)</td>
<td>0.037</td>
</tr>
<tr>
<td>Alzheimer's Disease</td>
<td>50 (5)</td>
<td>10 (1)</td>
<td>0.1</td>
</tr>
<tr>
<td>Mixed</td>
<td>30 (3)</td>
<td>NR</td>
<td>---</td>
</tr>
<tr>
<td></td>
<td>10 (1)</td>
<td>NR</td>
<td>---</td>
</tr>
<tr>
<td>History of Stroke, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right frontal stroke</td>
<td>80 (8)</td>
<td>40 (4)</td>
<td>0.17</td>
</tr>
<tr>
<td></td>
<td>60 (6)</td>
<td>0 (0)</td>
<td>0.011</td>
</tr>
<tr>
<td>MMSE Score, mean (SD)</td>
<td>15.44 (6.88)</td>
<td>22.1 (5.9)</td>
<td>0.036</td>
</tr>
<tr>
<td>NR=not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- No statistically significant difference between
  - Length of stay, current or remote psychiatric history, criminal history, history of legal charges, substance abuse, current or remote medical diagnoses, quantity and class of medications at admission and discharge, cardiovascular risk factors

### Table 8: Interventions Aimed at Reducing ISB

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Study Group, n(%)</th>
<th>Dose Range</th>
<th>Duration</th>
<th>Reduction of ISB, n</th>
<th>AEs, n</th>
<th>AEs Reported</th>
<th>D/C due to AEs, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>7(70)</td>
<td>10-50mg/d</td>
<td>2 – 10 wk</td>
<td>None, Some, Complete</td>
<td>1</td>
<td>1</td>
<td>Worsening of ISB</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>1(10)</td>
<td>30mg/d</td>
<td>6 wk</td>
<td>---</td>
<td>1</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Lithium</td>
<td>1(10)</td>
<td>600mg/d</td>
<td>6 wk</td>
<td>---</td>
<td>1</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>6(60)</td>
<td>2.5-12.5mg/d</td>
<td>5 d – 8 wk</td>
<td>---</td>
<td>2</td>
<td>NMS; sedation</td>
<td>2</td>
</tr>
<tr>
<td>Risperidone</td>
<td>3(30)</td>
<td>0.5-2mg/d</td>
<td>5 d – 8 wk</td>
<td>---</td>
<td>3</td>
<td>EPS, worsening of ISB</td>
<td>2</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>1(10)</td>
<td>150mg/d</td>
<td>2 wk</td>
<td>1</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>MPA</td>
<td>5(50)</td>
<td>100-300mg/d</td>
<td>2 – 11 wk</td>
<td>5</td>
<td>1</td>
<td>Fatigue</td>
<td>---</td>
</tr>
<tr>
<td>Leuprolide</td>
<td>1(10)</td>
<td>7.5mg/mo</td>
<td>8 wk</td>
<td>1</td>
<td>1</td>
<td>Depressed mood</td>
<td>---</td>
</tr>
</tbody>
</table>

*Multiple patients on concurrent treatments
D/C=discontinued; d=day; mo=month; wk=weeks; NMS=neuroleptic malignant syndrome; EPS= extrapyramidal effects

- Treatment
  - No intervention resulted in complete extinction of ISB behaviors
**Conclusion**

- Interventions
  - Citalopram is well tolerated but not effective
  - Atypical antipsychotics are helpful but adverse effects are concerning
  - Hormonal agents are well tolerated and effective
- Observations
  - Higher association of ISB with a diagnosis of vascular dementia, right frontal lobe stroke, and more severe dementia
- ISB under reported as a treatable problem due to the low prevalence of ISB reported in medical records

**Strengths**

- Provides more strength over previous literature on ISB consisting mainly of case reports

**Limits**

- Small sample size
- Retrospective study design
- Did not correct statistically for multiple comparisons because exploratory study
- Difficult to differentiate effective treatment as most patients were on concurrent treatments

---

**VI. Additional Agents for ISB**

a. See Appendix A for case reports with additional agents including
   i. Tricyclic antidepressants (TCAs), trazodone, and buspirone (*Table 9*)
   ii. Non-hormonal anti-androgens (*Table 10*)
   iii. Pindolol (*Table 11*)
   iv. Finasteride (*Table 12*)

**VII. Analysis of Evidence**

a. Majority of evidence is case reports
   i. Usually only positive results are reported through case reports
   ii. Most residents on multiple psychoactive drugs
b. Behavioral interventions not often described in detail
   i. Only one case report and one controlled trial published
c. No randomized controlled trials to demonstrate medication efficacy, safety, and appropriate dosing
d. No trials comparing effectiveness of different agents

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**Ethics**

**I. Ethical Dilemmas**

a. *Question: Should a resident be allowed to have sexual relations?*
   i. Elderly have sexual needs too\(^8\)
      1. 50-80% of >60 years old reported to be sexually active once per month
      2. Sexual activity continues through the seventh and eighth decade
b. *Question: Should 2 demented persons or 1 demented and 1 non-demented person be allowed to participate in a sexual relationship?*
   i. Capacity to Consent\(^53\)
      1. Conditions of informed consent for sexual relationships
         a. Voluntary participation – not physically or psychologically coerced
         b. Mental competence – more difficult to assess
         c. Awareness of risks and benefits – major risk most likely psychologically (ex. partner transferred to another ward, discharged home)
ii. Guidelines to determine capacity for sexual relationship\textsuperscript{53}

2. Awareness of the relationship
   a. Cognizant of the other’s identity and intent
   b. Understands what level of sexual intimacy is comfortable

3. Ability to avoid exploitation
   a. Behavior is consistent with previous beliefs
   b. Able to say no to an uninvited sexual contact

4. Awareness of potential risks
   a. Understands relationship is time limited
   b. Patient can describe reaction when relationship ends

c. \textit{Question: Does restricting a resident’s sexual expression follow federal regulations which mandate as least restrictive as possible institutional care?} \textsuperscript{54}

   i. U.S. Resident Bill of Rights
   ii. Conflict – resident’s autonomy and right to sexual expression versus risk for physical or mental harm of the individual or other residents

d. \textit{Question: Does “chemical castration” with hormonal agents violate the human rights of the patient?} \textsuperscript{54}

   i. Balance the rights of all parties including facility staff and other residents
   ii. Inability of patient to give informed consent for therapy

Conclusion

<table>
<thead>
<tr>
<th>I. Weigh Risks versus Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. No agent with significant evidence based on literature</td>
</tr>
<tr>
<td>b. Safety most prominent factor in decision</td>
</tr>
<tr>
<td>c. Prefer oral agents over IM agents if possible</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>II. First Line – Behavioral interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Limits adverse effects</td>
</tr>
<tr>
<td>b. Need for education and training of staff</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>III. Second Line – Pharmacologic Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Antidepressants – SSRIs</td>
</tr>
<tr>
<td>i. Overall best side effect profile</td>
</tr>
<tr>
<td>b. Gabapentin or atypical antipsychotics</td>
</tr>
<tr>
<td>i. Atypical antipsychotics if additional symptoms of aggression</td>
</tr>
<tr>
<td>ii. Gabapentin has safer side effect profile in elderly</td>
</tr>
<tr>
<td>c. Hormonal Agents</td>
</tr>
<tr>
<td>i. Anti-androgens over estrogen</td>
</tr>
<tr>
<td>1. More case reports with MPA</td>
</tr>
<tr>
<td>2. Controversial – must obtain consent from family/guardian</td>
</tr>
<tr>
<td>ii. Estrogen</td>
</tr>
<tr>
<td>1. Less evidence</td>
</tr>
<tr>
<td>2. Greater thromboembolic and cardiovascular risks</td>
</tr>
</tbody>
</table>
References:


47. Dhikav V, Anand K, and Aggarwal N. Grossly Disinhibited Sexual Behavior in Dementia of Alzheimer’s Type. Arch Sex Behav. 2007;36:133–134
### Appendix A

**Table 9: Case Reports of Antidepressants**

<table>
<thead>
<tr>
<th>Source</th>
<th>Previous Treatment</th>
<th>Patient</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>55 Leo R, et al 1995 (n=2)</strong></td>
<td>Thioridazine, MPA</td>
<td>65 y/o male; dementia NOS</td>
<td>Clomipramine 150mg daily</td>
<td>At 4 weeks significant decrease in ISB</td>
</tr>
<tr>
<td></td>
<td>Thioridazine and buspirone</td>
<td>75 y/o male; dementia NOS</td>
<td>Clomipramine 175mg daily</td>
<td>ISB ceased</td>
</tr>
<tr>
<td><strong>56 Simpson D, et al 1986</strong></td>
<td>Mesoridazine, haloperidol, diazepam</td>
<td>72 y/o male; alcohol/TBI</td>
<td>Addition of trazodone 100mg QID</td>
<td>ISB disappeared</td>
</tr>
<tr>
<td><strong>57 Tiller J, et al 1988</strong></td>
<td>None reported</td>
<td>80 y/o male; VaD</td>
<td>Buspirone 5mg TID</td>
<td>ISB ceased after 5 days; treatment stopped after 6 weeks with no relapse</td>
</tr>
</tbody>
</table>

**Table 10: Retrospective Chart Review of Non-hormonal Anti-androgen Therapy**

<table>
<thead>
<tr>
<th>Source</th>
<th>Previous Treatment</th>
<th>Patient</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>58 Wisemen S, et al 2000 (n=20)</strong></td>
<td>Some also administered clozapine, carbamazepine, perphenazine, venlafaxine, and loxapine for delusions/hallucinations and irritability</td>
<td>n=17 male, n=3 female; Avg age 73yrs; dementia NOS</td>
<td>Cimetidine 600-1600mg daily +/- spironolactone 75mg daily or ketoconazole 100-200mg daily</td>
<td>Decreased ISB in 14 of 20 with cimetidine alone; Decreased ISB in 6 with combination therapy; Response seen within 1-8 weeks</td>
</tr>
</tbody>
</table>

**Table 11: Case Report of Pindolol**

<table>
<thead>
<tr>
<th>Source</th>
<th>Previous Treatment</th>
<th>Patient</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>59 Jensen C, et al 1989</strong></td>
<td>Haloperidol, hydroxyzine</td>
<td>75 y/o male; AD</td>
<td>Pindolol 20mg daily</td>
<td>Reduced ISB; stopped within 2 weeks</td>
</tr>
</tbody>
</table>

**Table 12: Case Series with Finasteride**

<table>
<thead>
<tr>
<th>Source</th>
<th>Previous Treatment</th>
<th>Patient</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Na H, et al 2009 (n=11)</strong></td>
<td>None</td>
<td>Average age 77 y/o; males; VaD</td>
<td>Finasteride 5mg daily</td>
<td>N=6: ISB stopped within 8 weeks N=5: required additional agents for ISB including propranolol, quetiapine, oxycarbamazepine, Gonadotropin-releasing hormone agonist analogue</td>
</tr>
</tbody>
</table>