Is There a Place for Psychiatric Medication when Dealing with Prostate Cancer?

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Disclosures:

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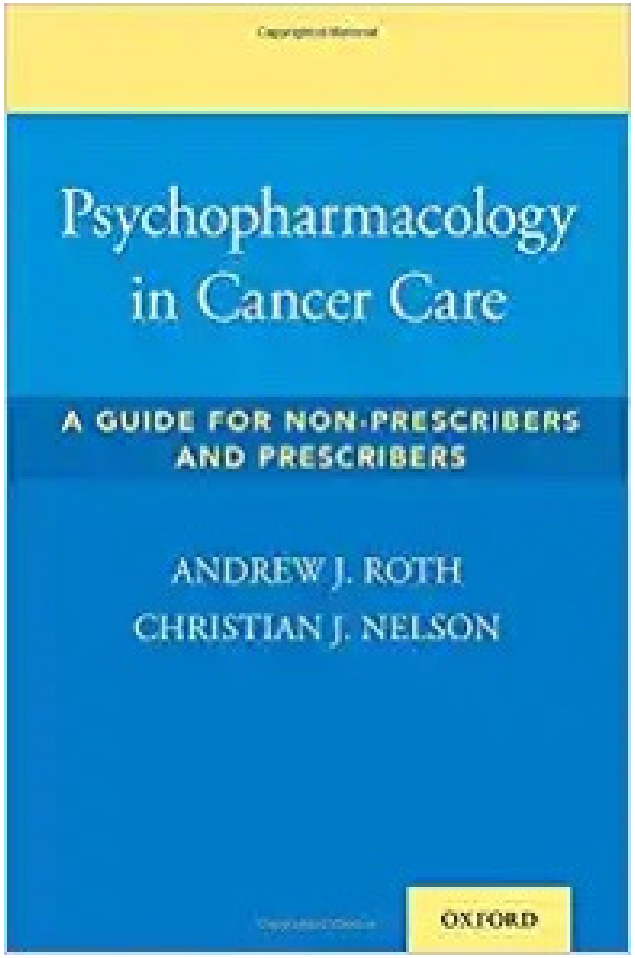
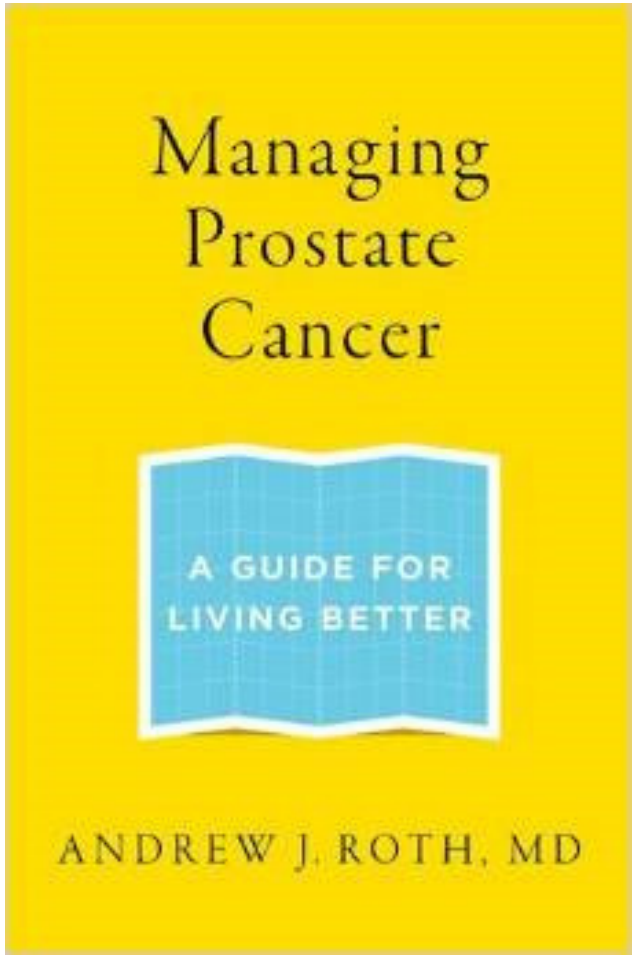
This talk and discussion on psychopharmacology in prostate cancer patients will include non-label uses ofFDA approved psychotropic medications.

Disclosure:


Psychopharmacology
in Cancer Care
A GUIDE FOR NON-PRESCRIBERS
AND PRESCRIBERS
ANDREW J. ROTH
CHRISTIAN J. NELSON
OXFORD


Managing
Prostate
Cancer
A GUIDE FOR
LIVING BETTER
ANDREW J. ROTH, MD

Even Patients Need to Understand Some Pharmacodynamics

Education Before Starting a Psychotropic Medication:

- Discuss common adverse effects and therapeutic benefits
  - Gastrointestinal symptoms, anxiety, fatigue
- Duration of onset of action
- Likelihood of uncommon though well-known side effects (i.e., suicidal ideation; cardiac side effects)
- What to do about missed doses
- Compliance with dosage and titration

- *The body doesn't always read the textbook*

A BioPsychoSocial Approach

- Diagnosis: observe symptoms – try to fix the medical
- Education
- Psychotherapy
  - Supportive
    - Provide information, reassurance; validate emotions
  - Cognitive behaviorally oriented
    - Reframe automatic irrational, unhelpful cognitions
    - Relaxation exercises, rehearsal, hypnosis
  - Insight-oriented therapy
  - Meaning-centered psychotherapy
  - Dignity therapy
- Medication

Summary
4 Tips on Psychopharmacology in Cancer Care

- Don't assume all medicines are the same for all patients
- Understand what the body does to the drug
- Understand what the drug does to the body
- Understand essentials of taking psychotropic medications in cancer care.

Antidepressants

Risk Factors for Depression in Cancer Patients

- Poorly controlled symptoms such as:
  - Urinary incontinence
  - ED
  - Bowel incontinence
  - Fatigue
  - Poorly controlled pain
- Medications
- Metabolic or endocrine abnormalities
- Family or personal history of mental illness
- Absence of or poor social supports; other life stressors
- Substance issues
- Existential questions

What Are We Treating?

- Diagnoses?

- Symptoms?
  - Sad, demoralized, depressed mood
  - Loss of appetite, fatigue
  - Insomnia, anxiety, irritability, restlessness
  - Hopelessness, worthlessness, guilt
  - Suicidal ideation

In What Context?

- Are the symptoms ongoing or sporadic?
- Are they situation-specific or generalized?
- Are they a recurrence, or chronic, or new with the cancer?
- Are the symptoms due to physiological cause?
- Are they due to recent (lifestyle) changes?
  - Tobacco cessation
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Medications Can Cause of Depressive Symptoms in Cancer Patients

Glucocorticoids

Benzodiazepines

Some antibiotics

Opioids

Anticonvulsants

Beta blockers

Hormonal agents: ADT/Tamoxifen

Interferon

Major Depressive Episode

- Depressed mood
- Loss of interest or pleasure

  - Feelings of worthlessness or excessive guilt
  - Recurrent thoughts of death or suicide ideation
    - Poor concentration
    - Appetite changes
    - Sleep disturbance
    - Psychomotor agitation or retardation
    - Fatigue

Endicott J: 1984 Supp 2243-2248
Nelson CJ J Clin Oncol 2010 Jan 10; 28(2): 348–356.

Depression: Antidepressant Treatment

- Psychopharmacology:
  - Serotonin, Norepinephrine, Dopamine
  - Neuroplasticity hypothesis
    - Glutamate
    - Intracellular signaling/mechanisms of gene expression
    - Neurotrophic mechanisms
    - Neurogenesis
    - Synaptic function/plasticity
    - Remodeling of neuronal cells/circuitry

Brain

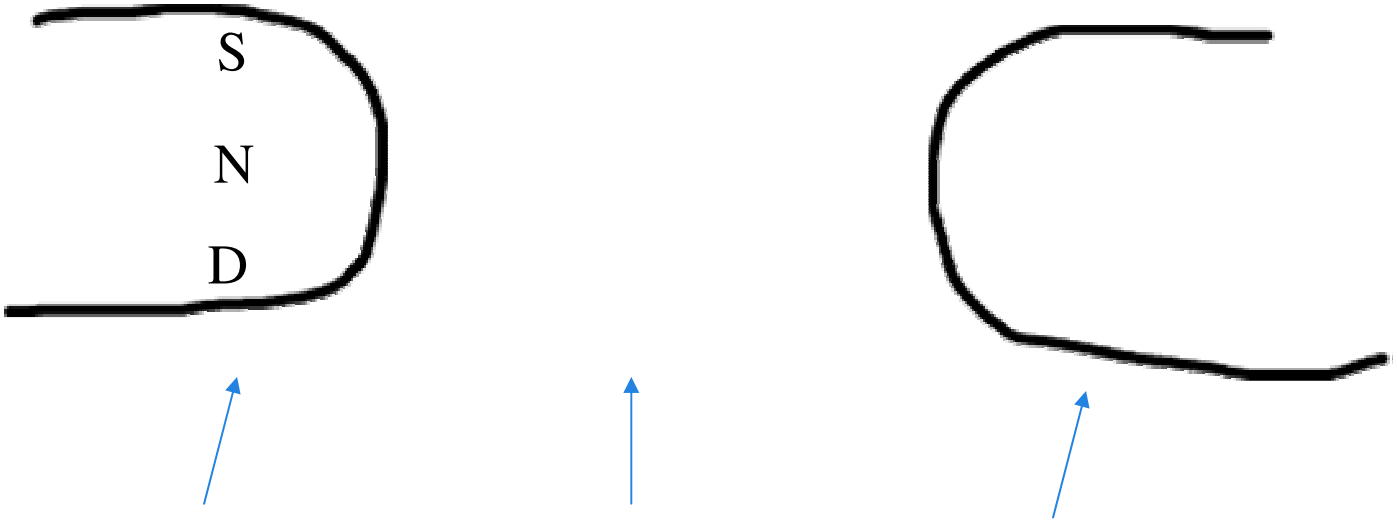
Pre-Synaptic Neuron

Synapse

Post-Synaptic Neuron

S = Serotonin
N = Norepinephrine
D = Dopamine

Brain



Pre-Synaptic Neuron

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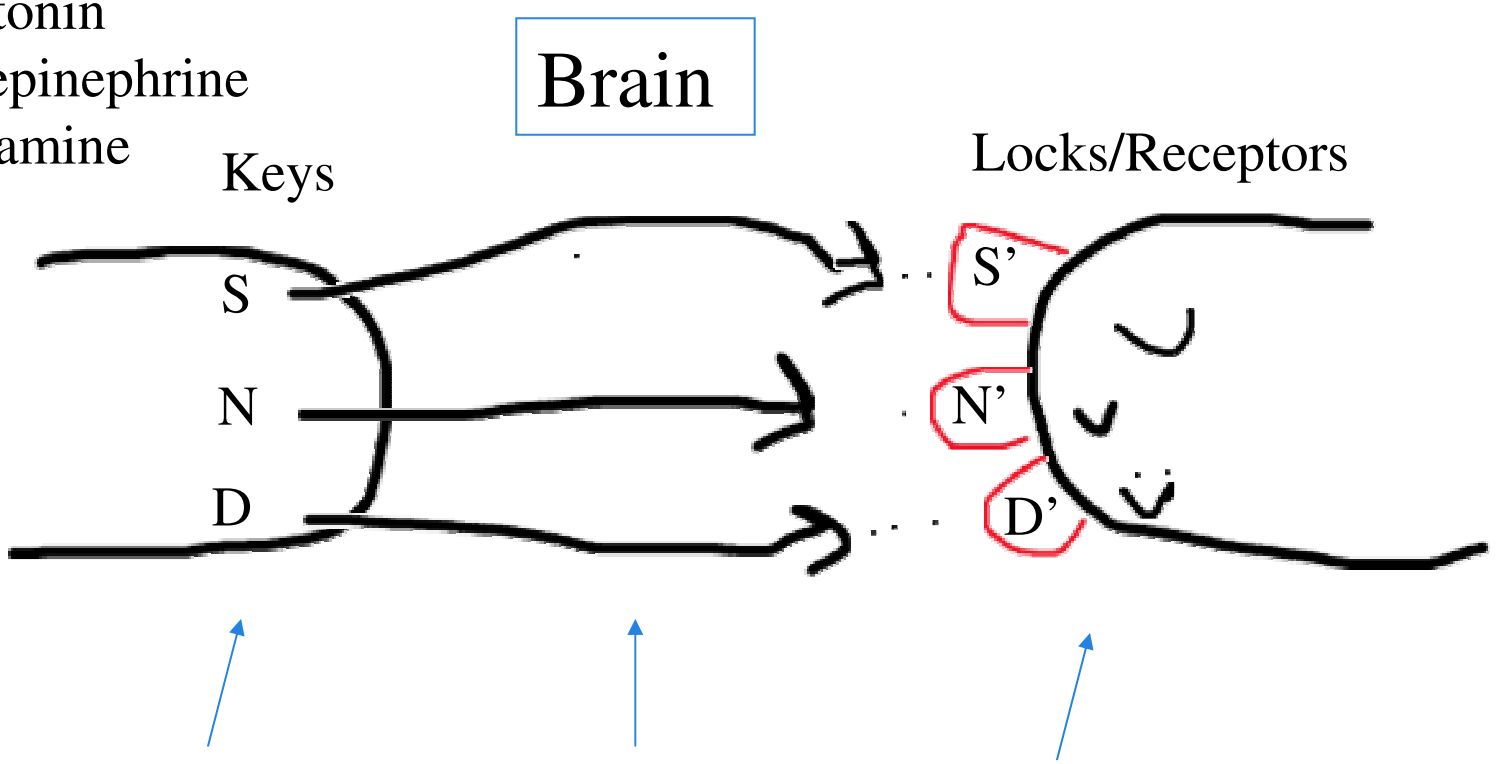
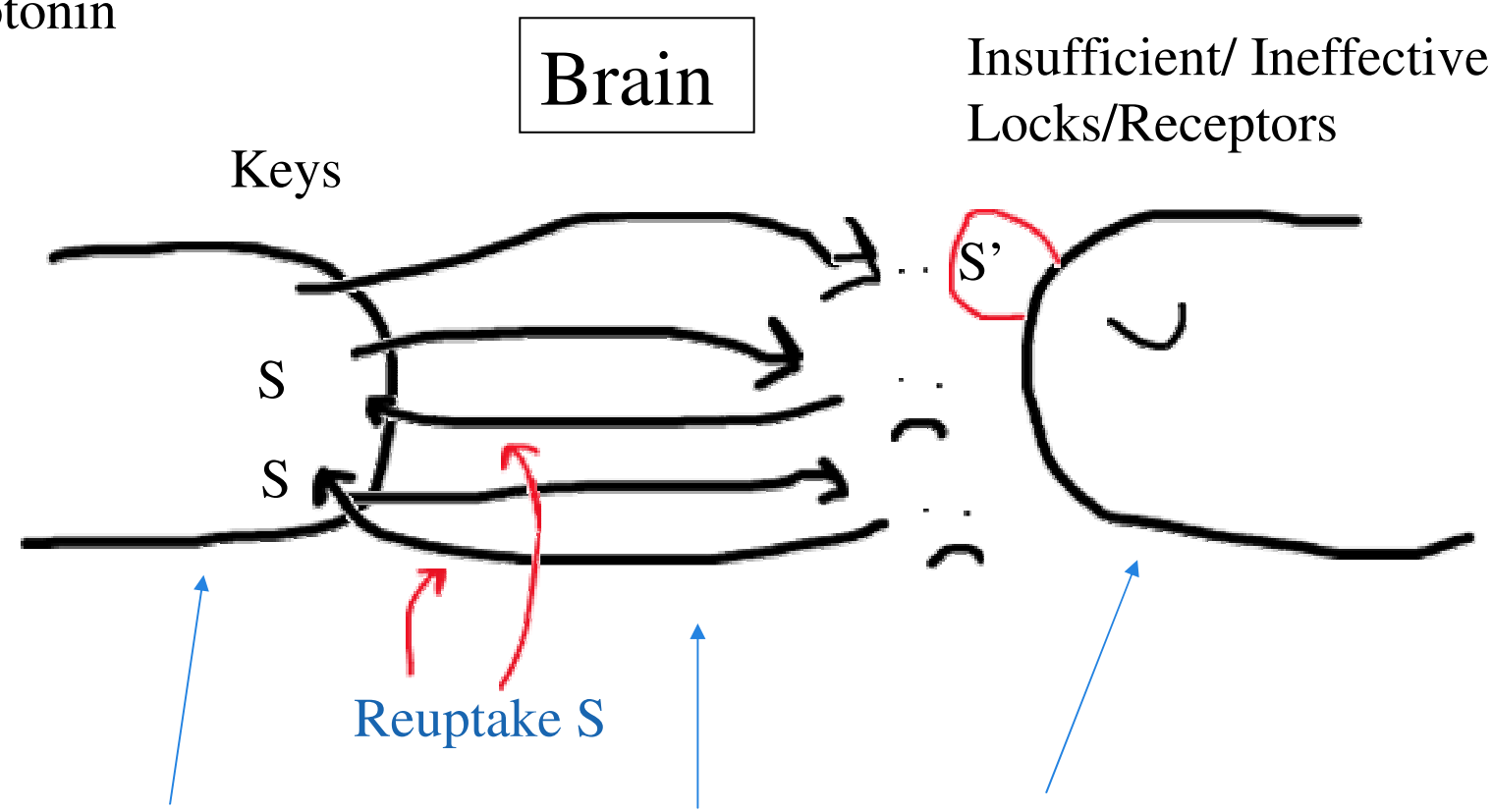
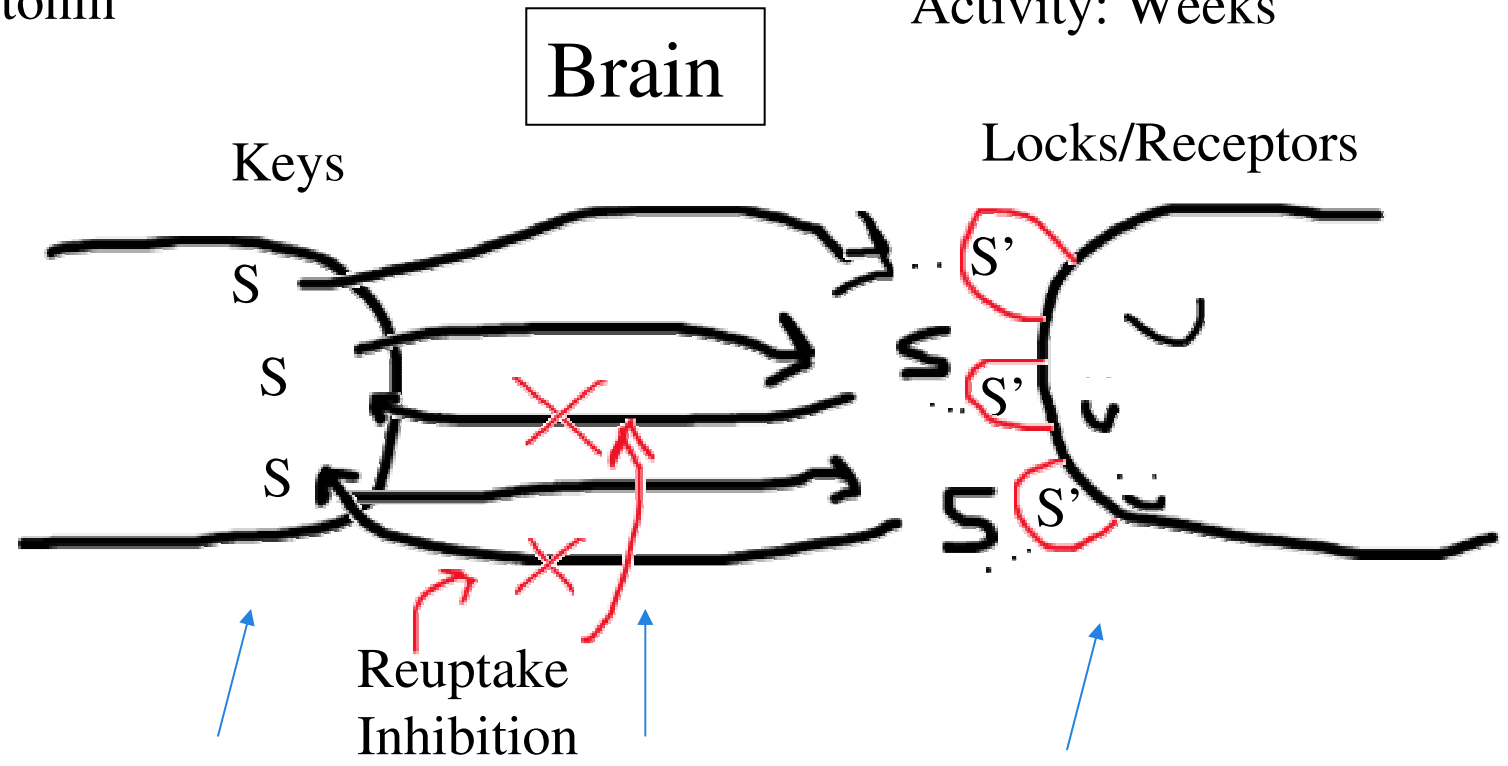


S = Serotonin

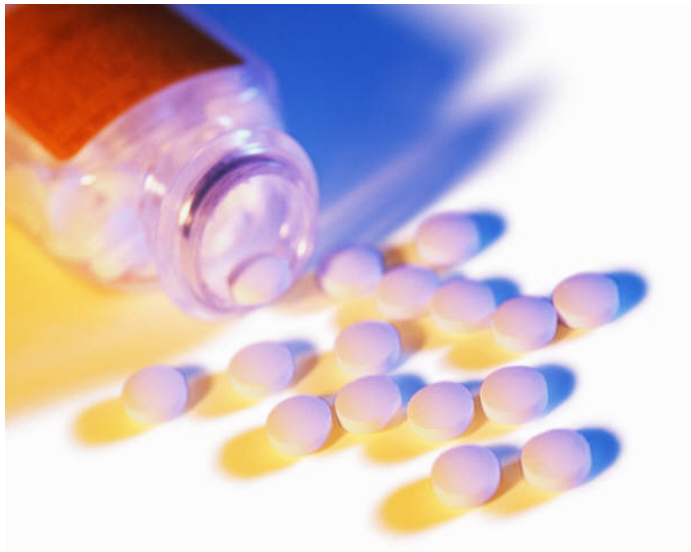


S = Serotonin

Time to Enhance Receptor Activity: Weeks



Do Antidepressants Work?



Yes.
Holland et al 1998

Depression: Antidepressant Treatment

- Antidepressants need to be taken daily
- Antidepressants can take 2-5 weeks to work at any dose
- Ask about all other medications and supplements
- Rule of thumb: 9 months to 1 year of therapy
- When it is time to stop the medication, TAPER

Drugs Don't Work if Not Taken

- One-third of patients in the real world never fill prescription for antidepressants (AD)
- Less than half who take an AD for one month will take it for a second month
- One fourth get 3 month trial

Simon GE Psychiatr Serv 2014 65(7) 944-946

Depression

IMPACT (Improving Mood-Promoting Access to Collaborative Treatment) Program *(Fann 2009)*:

- 215 older cancer patients with a depressive disorder
- Education
- Care management
- Antidepressant
- Brief, structured psychosocial intervention

Fann JR, Fan MY, Unützer J.
J Gen Intern Med. 2009 Nov;24 Suppl 2(Suppl 2):S417-24.

Choosing An Antidepressant

- History of past response (or family response)
- Consideration of Drug-Drug interactions
- Onset of action required
- Multiple target symptoms

Method

- Start one antidepressant
- Evaluate dose over 4-8 weeks.
- If no response or insufficient response, increase dose if safe, add drug or change drug
- Focus is to minimize side effects, maximize benefit

The Not-So-Good Side Effects

- GI distress
- Headache
- Sedation, anxiety or insomnia
- Weight gain or loss
- Sexual dysfunction
- High or low blood pressure
- Dry mouth

Jacobsen P et al J Sex Med 2019; 16:1638–1649.

Reuptake Inhibitors: Dopamine

Pros	Cons
Improves mood	May cause uncomfortable anxiety, agitation, and insomnia
Smoking cessation	May aggravate psychotic symptoms
Stimulating or activating effect (counter fatigue)	May lower seizure threshold
Does NOT cause any sexual side effects	

Serious Adverse Reactions

- Suicidal thoughts or behaviors
- Antidepressant-induced mania
- Restlessness or agitation/akathisia
- Serotonin syndrome

Choosing an Antidepressant: The Good and the Bad Side Effects

(Passik, Roth: Amtrak <2000)

- Medication can be based on additional actions or on side effect profile to maximize benefits:
  - Mirtazapine to help anxiety, sleep and appetite or if gastric upset is present
  - Venlafaxine or Paxil for hot flashes
  - Tricyclics, Duloxetine to help with neuropathic pain
  - Bupropion, Psychostimulants to help fatigue
- Start at lower doses for elderly patients, titrate slowly
- Minimize potential discomfort based on the patient's review of symptoms

Discontinuation Syndrome: Antidepressants Should be Tapered

- Malaise or flu-like symptoms
- Dizziness
- Electric-shock like pains in head or extremities

Psychostimulants

• Depression	• Mood, apathy, psychomotor slowing
• Cognitive deficits	• Attention, concentration, neuropsychiatric test performance
• Adjuvant analgesia • Counteract sedation • Fatigue	• Potentiate opioid effects • Secondary to opioids • Weakness, hypoactivity, quality of life, mood
• Appetite	• Increase appetite, sense of wellbeing

Breitbart W et al:
Arch Intern Med. 2001 Feb 12;161(3):411-20.
Roth AJ et al: Cancer 2010 116(21):5102-10.

Antianxiety Medications

Anxiety

- Prevalence in cancer 24%
- Estimates range from 7-44%
- Adjustment disorder with anxiety most common
- Serotonergic antidepressants first line for chronic anxiety disorders
- Benzodiazepines for short-term use in adjustment disorder or procedure anxiety

Brintzenhofe-Szoc KM ete al Psychosomatics. 2009 50(4):383-91.
Thekdi S: Psychopharmacology in Cancer, Current Psychiatry Reports, 2014
Nelson AM et al Anxiety Disorders in Psycho-Oncology, 2021

What Are We Treating?

- Diagnoses?
- Symptoms?
  - Worry, restlessness or pacing
  - Panic symptoms:
    - Palpitations, diaphoresis, shortness of breath
  - Phobias
  - Irritability
  - Suicidality

In What Context?

- Are the symptoms ongoing or sporadic?
- Are they situation-specific or generalized?
- Are they a recurrence, or chronic, or new with the cancer?
- Are the symptoms due to physiological cause?
- Are they due to recent (lifestyle) changes?
  - Tobacco cessation
  - Alcohol cessation or decrease
- Are the symptoms interfering with ability to carry on and enjoy life

Special Stressors in Cancer Care

- Fear of recurrence or dying--'awareness' of mortality
- Less confidence about future
  - "Damocles Syndrome"
  - Anniversaries
- Anticipation of tests, results
- Paradoxical increase at END of treatment:
  - Not being seen as often by oncology team
  - Loss of protection from treatment
  - "On my own"
- Post Traumatic Stress Something

Medical Causes of Anxiety in Cancer Care

- Poor pain control
- Metabolic disturbances:
  - hypoxia
  - delirium
  - sepsis
  - bleeding
  - pulmonary embolus
  - endocrine
- Drug induced:
  - Corticosteroids
    - Dexamethasone
    - Prednisone
    - Antiemetics
    - Bronchodilators
- Substances:
  - Intoxication or withdrawal

Medications for Anxiety

- Benzodiazepines
- Antidepressants
- Buspirone
- Beta blockers
- Atypical antipsychotics
- Antihistamines

Benzodiazepines

Generic Name

Shorter Acting

Alprazolam

Oxazepam

Intermediate Acting

Lorazepam

Longer Acting

Diazepam

Clonazepam

Benzodiazepines: Pros

- Fast acting anxiolytics
  - Relieve panic attacks
  - Treat phobic symptoms
    (i.e., MRI scans, awaiting test results)
  - Relieve akathisia caused by other medications such as antiemetics
  - Control agitation during acute manic and psychotic episodes in medical settings
  - Treat alcohol withdrawal

Benzodiazepines: Cons

- Drowsiness
- Respiratory depression
- Impaired coordination
- Memory loss/Amnesia
- Toxicity in vulnerable, frail patients like the elderly which can lead to falls
- Paradoxical anxiety and agitation
- Dependence, Tolerance and Addiction

Education about the Distinctions Between

- Normal ***physical dependence*** (after about a month of daily use)
- ***Physical tolerance*** (which may lead some patients to need a higher dose after a few months of daily treatment to obtain the same amount of relief they got with lower doses earlier on)
- ***Addiction***: compulsive psychological and biochemical drug-seeking behaviors

Benzodiazepine Withdrawal

- Anxiety
- Insomnia
- Restless
- Irritable
- Tremors/hyperreflexia
- Headache
- Sweats
- Tachycardia
- Hypertension
- Panic symptoms
- Skin-crawling
- Depression
- Visual disturbances
- Hallucinations
  - Tactile
  - Auditory
  - Visual
- ❖ Seizures

Nonbenzodiazepine Anxiolytics

Antidepressants: Panic D/O; OCD; GAD

SSRI's

Paroxetine (CR)

Citalopram/escitalopram

Mirtazapine Sertraline

SNRI's

Venlafaxine

Duloxetine

Buspirone (Buspar) GAD; no abuse potential

Lyrica/Neurontin GAD/pain/mood stabilizers

Antipsychotics: Olanzapine (Zyprexa); Quetiapine (Seroquel)

Risperdal (risperidone)

Summary

- Depression and Anxiety are not easily diagnosed in men with prostate cancer
- Psychotherapy can treat many depressive and anxiety syndromes
- Medications can also be helpful
  - Need to be aware of other medications/supplements
  - Other medical issues that can cause depressive or anxiety syndromes
  - Follow up is important