

**Psychotropic  
Medications**

**Antidepressants**

with Terry Broda

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**Spectrum of Depression and Anxiety Disorders**

Depression

Posttraumatic Stress Disorder

Social Anxiety Disorder

Panic Disorder

Obsessive-Compulsive Disorder

Generalized Anxiety Disorder

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**Other indications**

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- TCA, duloxetine/venlafaxine : chronic pain, fibromyalgia, migraine, premenstrual disorder
- SSRI : premenstrual disorder
- Bupropion : smoking cessation, ADHD
- Trazadone : bulimia, insomnia, challenging behaviors for those with dementia

## Antidepressants



- **Tricyclic Antidepressants**

Amitriptyline (Elavil), clomipramine (Anafranil), imipramine (Tofranil), doxepine (Sinequan)

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- **Monoamine Oxydase Inhibitors (reversible)**

Phenelzine (Nardil), tranylcypromine (Parnate), moclobemide (Manerix)

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- **Selective Serotonin reuptake Inhibitors (SSRI)**

Escitalopram (Cipralex), Citalopram (Celexa), fluoxetine (Prozac), Paroxetine (Paxil), fluvoxamine (Luvox), sertraline (Zoloft)

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## Antidepressants



- **Serotonin-2 antagonist/IRS:** Trazadone (Desyrel)

- **Other antidepressants:**

- norepinephrine(N), serotonin (S) & dopamine (D):

Duloxetine (Cymbalta), Desvenlafaxine (Pristiq), Venlafaxine (Effexor),

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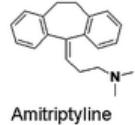
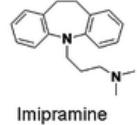
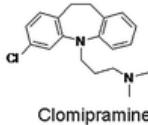
N & S: Mirtazapine (Remeron); N & D: Bupropion (Wellbutrin)

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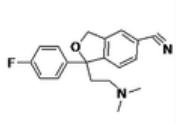
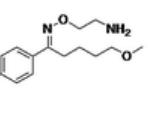
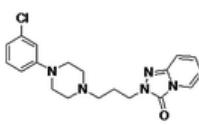
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## Structures



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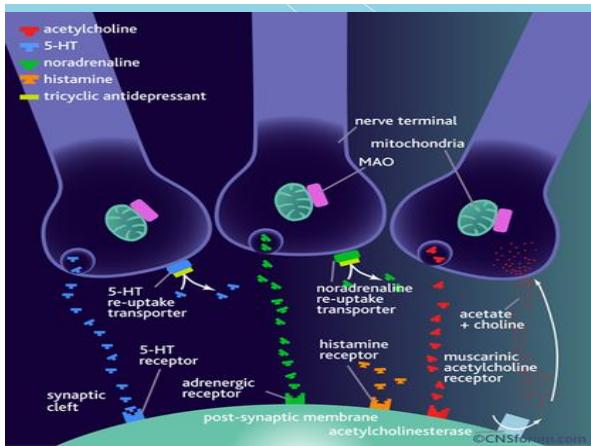
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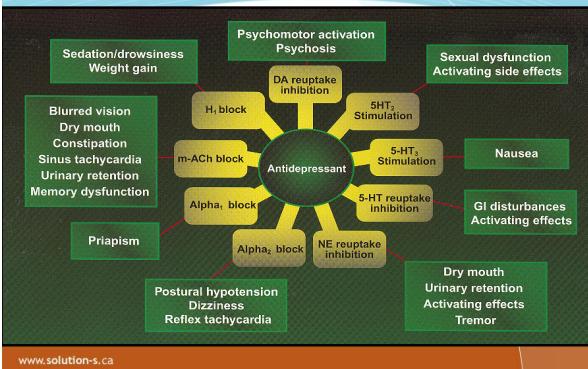
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## Adverse Effects of Neurotransmitter Activity and Receptor Binding

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## Side Effects

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Drug	Adverse Reactions <sup>a</sup>								
	Sedation	Orthostatic Hypotension	Constipation/ Dry Mouth	Cardio-toxicity	Insomnia	Weight Gain	Jitteriness	Seizures	
amitriptyline	+++	+++	+++	+++	+	+++	0	++	
amoxapine	+	++	+++	++	++	0/+	0/+	++	
clomipramine	+++	++	+++	+++	+	++	++	+++	
desipramine	+	+	+	+++	+	+	++	+	
doxepin	+++	++	+++	++	+	+++	+	+	
imipramine	++	+++	++	+++	++	+++	+++	++	
maprotiline	++	+	++	++	+	++	++	+++	
nortriptyline	+	+	++	++	+	+	++	+	
protriptyline	0/+	++	+++	++	+++	+	++	+	
trimipramine	+++	++	++	++	+	++	+	+	

Note. Adapted from Maxmen (1990) and Preskorn (1993).

a +++ = marked effects, ++ = moderate effects, + = weak effects, 0 = none

Reiss S., & Aman, M. (ed's). (1998).

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Frequency of Adverse Reactions to Cyclic Antidepressants at Therapeutic Doses										
Reaction	Amitriptyline	Clomipramine	Desipramine	Doxepin	Imipramine	Norimipramine	Protriptyline	Trimipramine	Amoxapine	Maprotiline
<b>CNS Effects</b>										
Drowsiness, sedation	> 30%	> 2%	> 2%	> 30%	> 2%	< 2%	> 30%	> 10%	> 30%	> 30%
Insomnia	> 2%	> 10%	> 2%	> 2%	< 2%	< 2%	> 10%	> 10%	> 2%	> 2%
Excitement, hypomania*	< 2%	< 2%	> 2%	< 2%	> 2%	> 2%	> 10%	< 2%	> 2%	> 2%
Disorientation/confusion	> 30%	> 2%	> 2%	< 2%	> 2%	> 30%	> 30%	> 2%	> 2%	> 2%
Headache	> 2%	> 2%	< 2%	< 2%	> 30%	< 2%	—	> 2%	> 2%	< 2%
Orthostatic fatigue	< 2%	> 2%	> 2%	> 30%	> 10%	> 10%	> 10%	> 2%	> 2%	> 2%
<b>Anticholinergic Effects</b>										
Dry mouth	> 30%	> 30%	> 30%	> 30%	> 10%	> 10%	> 10%	> 30%	> 30%	> 30%
Blurred vision	> 10%	> 10%	> 2%	> 10%	> 10%	> 2%	> 10%	> 2%	> 2%	> 30%
Constipation	> 10%	> 30%	> 2%	> 30%	> 10%	> 10%	> 10%	> 30%	> 30%	> 30%
Sweating	> 10%	> 30%	> 2%	> 2%	> 10%	< 2%	> 30%	> 2%	> 2%	> 2%
Delayed micturition**	> 2%	> 2%	—	< 2%	> 30%	< 2%	< 2%	< 2%	> 30%	> 2%
<b>Extrapyramidal Effects</b>										
Unspecified	> 2%	< 2%	< 2%	> 2%	< 2%	—	—	< 2%	> 2%	> 2%
Tremors	> 10%	> 30%	> 2%	> 2%	> 10%	> 10%	> 2%	> 30%	> 2%	> 30%
<b>Cardiovascular Effects</b>										
Orthostatic hypotension/dizziness	> 30%	> 30%	> 2%	> 30%	> 30%	> 2%	> 10%	> 30%	> 30%	> 2%
Tachycardia, palpitations	> 10%	> 30%	> 2%	> 30%	> 10%	> 2%	> 2%	> 2%	> 30%	> 2%
ECG changes***	> 10%	> 30%	> 2%	> 2%	> 30%	> 2%	> 10%	> 10%	> 2%	> 2%
Cardiac arrhythmia	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
GI distress	> 2%	> 30%	> 2%	< 2%	> 30%	< 2%	< 2%	< 2%	< 2%	< 2%
Dermatitis, rash	> 2%	> 2%	> 2%	> 2%	> 2%	< 2%	< 2%	< 2%	< 2%	< 2%
Weight gain (over 6 kg)	> 30%	> 30%	> 2%	> 30%	> 30%	> 2%	> 2%	> 2%	> 2%	> 30%
Sexual disturbances	> 2%	> 2%	< 2%	< 2%	> 30%	< 2%	< 2%	< 2%	< 2%	< 2%
Sedation*	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%

Note: reported in literature present. \*More likely in elderly patients. \*\*Primarily in the elderly. \*\*\*ECG abnormalities usually without cardiac injury  
= Under 65 years old. \*\*No effect on ECG sleep. \*\*\*In non-epileptic patients. ^Higher incidence if dose about 250 mg daily clomipramine, 225 mg daily maprotiline, or 300 mg daily amoxapine. ^Conduction delays increased PR, QRS, or QTc intervals.

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Virani, Bechlibnyk-Butler & Jeffries, 2009

## Anticholinergic Side Effects




- Blurry vision
- Nasal congestion
- Dry mouth
- Urinary retention
- Constipation

Rx : tricyclic antidepressants

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### THE BRISTOL STOOL FORM SCALE



Type 1      Separate hard lumps, like nuts

Type 2      Sausage-like but lumpy

Type 3      Like a sausage but with cracks in the surface

Type 4      Like a sausage or snake, smooth and soft

Type 5      Soft blobs with clear-cut edges

Type 6      Fluffy pieces with ragged edges, a mushy stool

Type 7      Watery, no solid pieces

**IDEAL:** Type 4,  
(Type 3 also OK)

« they glide out easily  
with no fuss  
whatsoever »

Source: Heaton KW, et al. Gut. 1992;33:818-824

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Adapted from CANMAT (1999)

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### Side Effects

**Adverse Reactions<sup>a</sup>**

Drug	Sedation	Orthostatic Hypotension	Constipation/Dry Mouth	Cardiovascular Toxicity	Insomnia	Nausea/Vomiting	Diarrhea	Irritability	Headaches	Seizures
fluoxetine	+	0	+	0/+	++	++	+	++	++	+
fluvoxamine	+	0	+	0/+	+	++	++	+	++	+
nefazodone	++	+	+	0/+	+	++	++	+	+	+
paroxetine	+	+	+	0/+	+	++	++	+	++	+
sertraline	++	0	+	0/+	+	++	++	+	++	+
trazodone	+++	++	+	0/+	0	++	++	+	+	+
venlafaxine	+	0	+	0/+	+	++	+	+	++	+
bupropion	++	0	+	0/+	++	+	+	++	++	+/-

Note. Adapted from Drug Facts and Comparisons (1995).  
Reiss S., & Aman, M. (ed's). (1998).

a +++ = marked effects, ++ = moderate effects, + = weak effects, 0 = none

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### Frequency of Adverse Reactions to Cyclic Antidepressants at Therapeutic Doses (cont.)

Reaction	SARI			NDR			SNRI			SSRI			MAOAs		
	Trazodone	Nefazodone	Buproprion	Venlafaxine	Doxepin	Desvenlafaxine	Citalopram	Escitalopram	Fluoxetine	Fluvoxamine	Paroxetine	Sertraline	Fluvoxamine		
<b>CNS Effects</b>															
Drowsiness, sedation	> 30%	> 30%	> 2%	> 30%	> 30%	> 30%	> 2%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 2%	> 2%
Insomnia	> 2%	> 2%	> 10%	> 30%	> 30%	> 30%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
Exacerbated, hyperactive <sup>b</sup>	< 2%	< 2%	> 30%	> 30%	> 30%	> 30%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
Disorientation/confusion	< 2%	> 10%	> 2%	> 2%	?	—	< 2%	< 2%	< 2%	> 2%	> 2%	> 2%	< 2%	< 2%	< 2%
Headache	> 2%	> 30%	> 30%	> 30%	> 30%	> 30%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
Aheadache, fatigue	> 30%	> 30%	> 2%	> 30%	> 30%	> 30%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
Delayed micturition <sup>c</sup>	< 2%	< 2%	< 2%	< 2%	?	< 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
<b>Anticholinergic Effects</b>															
Dry mouth	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%
Blurred vision	> 2%	> 30%	> 30%	> 30%	> 30%	> 30%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
Constipation	> 2%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%
Sweating	> 2%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%
Delayed micturition <sup>c</sup>	< 2%	< 2%	< 2%	< 2%	?	< 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
<b>Endocrinologic Effects</b>															
Hypertension	> 2%	< 2%	> 2%	> 2%	?	< 2%	> 2%	< 2%	< 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
Tremor	> 2%	< 2%	> 2%	> 2%	?	> 2%	> 2%	< 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
<b>Cardiovascular Effects</b>															
Orthostatic hypotension/dizziness	> 30%	> 30%	> 2%	> 30%	> 30%	> 30%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
Tachycardia, palpitations	> 2%	< 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
ECG changes <sup>d</sup>	> 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%
Cardiac arrhythmias	> 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%
<b>GI Adverse Effects</b>															
Constipation	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%
Diarrhea, rash	< 2%	< 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
Weight gain (over 6 kg) <sup>e</sup>	> 2%	> 2%	< 2%	< 2%	> 2%	?	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%	> 2%
Sexual disorders <sup>f</sup>	< 2%	> 2%	> 2%	< 2%	< 2%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%	> 30%
Seizures <sup>g</sup>	< 2%	< 2%	< 2%	< 2%	< 2%	?	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%

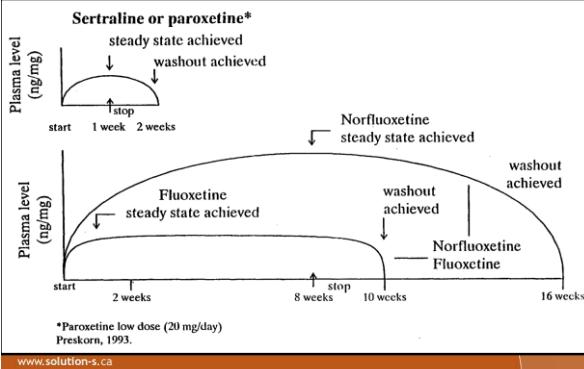
<sup>a</sup> None reported in literature protocol. <sup>b</sup> Most likely in bipolar patients. <sup>c</sup> Possibly in elderly. <sup>d</sup> ECG abnormalities, usually without cardiac rhythm. <sup>e</sup> In susceptible patients, risk increased with elevated plasma levels. <sup>f</sup> Increased risk of sexual dysfunction in patients with preexisting cardiovascular disease have a 30% incidence of premature ventricular contractions. <sup>g</sup> Report reported. <sup>h</sup> Typically if given in the morning. <sup>i</sup> Delays in onset of action. <sup>j</sup> Increased risk of seizures in patients with preexisting hypertension. <sup>k</sup> Increased risk of seizures in patients with preexisting hypertension.

<sup>a</sup> Weight loss reported initially. <sup>b</sup> Hypertension reported, may be more common in patients with preexisting hypertension. <sup>c</sup> Insulin resistance in patients with preexisting hypertension. <sup>d</sup> Increased incidence of sexual dysfunction. <sup>e</sup> Increased risk of sexual dysfunction. <sup>f</sup> Increased risk of sexual dysfunction. <sup>g</sup> Increased risk of seizures. <sup>h</sup> Increased risk of seizures. <sup>i</sup> Increased risk of seizures. <sup>j</sup> Increased risk of seizures. <sup>k</sup> Increased risk of seizures.

Virani, Bezchlibnyk-Butler & Jeffries, 2009.

## Time to Steady State and Time to 95% Washout

The logo consists of a stylized orange and blue swoosh above the word "solutions".



# SSRI Side Effects

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- N & V
  - Diarrhea
  - Headaches
  - Irritability
  - Sedation / insomnia
  - Dry mouth
  - Seizures

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SE	Non-pharmacological	Pharmacological
Dry mouth	Gum, pastilles/cough drops 6-8 glasses H2O/day Special tooth paste	
N & V	Rx with food Crackers, toast	
Weight gain	Diet Exercise	Change Rx
Urinary retention	6-8 glasses H2O/day	
Constipation	6-8 glasses H2O/day Exercise Diet rich in fruits, vegetables & fibre	Laxative
Orthostatic Hypotension	Increase hydration Get up/change position slowly	
Fatigue/sedation	Planned exercise & rest Avoid alcohol Caffeinated beverages (1/day)	Change Rx Change time of dose Decrease the dose
Blurry vision	Magnifying glasses temporarily	Eye drops
Diaphoresis	Light clothing Showers/baths frequently	Decrease the dose Change Rx
Tremor	May decrease w/ dose decrease	Decrease the dose

## Serotonin Syndrome



Accumulation of serotonin : **Symptoms :**

- Agitation, confusion
- Nausea, Diarrhea
- Dizziness
- Diaphoresis
- Ataxia, Tremor
- Myoclonus, Convulsions
- Hyperreflexia
- ↑ BP, Palpitations, tachycardia
- Hyperthermia/fever
- Rhabdomyolysis
- Severe respiratory depression & coma

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## Withdrawal of SSRIs



**Symptoms :**

- Dizziness , lethargy, N & V, diarrhea, headache, fever, diaphoresis, malaise, insomnia, intense dreams, myalgia, paresthesia, sensations of 'electric shock', anxiety agitation, irritability, confusion, disorientation, aggression rarely
- 1-7 days after decrease or discontinuation of Rx
- Duration: 3 weeks

**Tx :**

- Decrease the dose by 25% per week

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## Considerations



- Trazadone at bedtime: on empty stomach
- Active Metabolites : TCAs, fluoxetine
- Dosing : TCAs, SSRIs : die; others : BID
- Interactions with CYP450 enzymes
- Special diet with MAOIs tyramine)

**\*\* Verify the risk of suicide regularly**

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