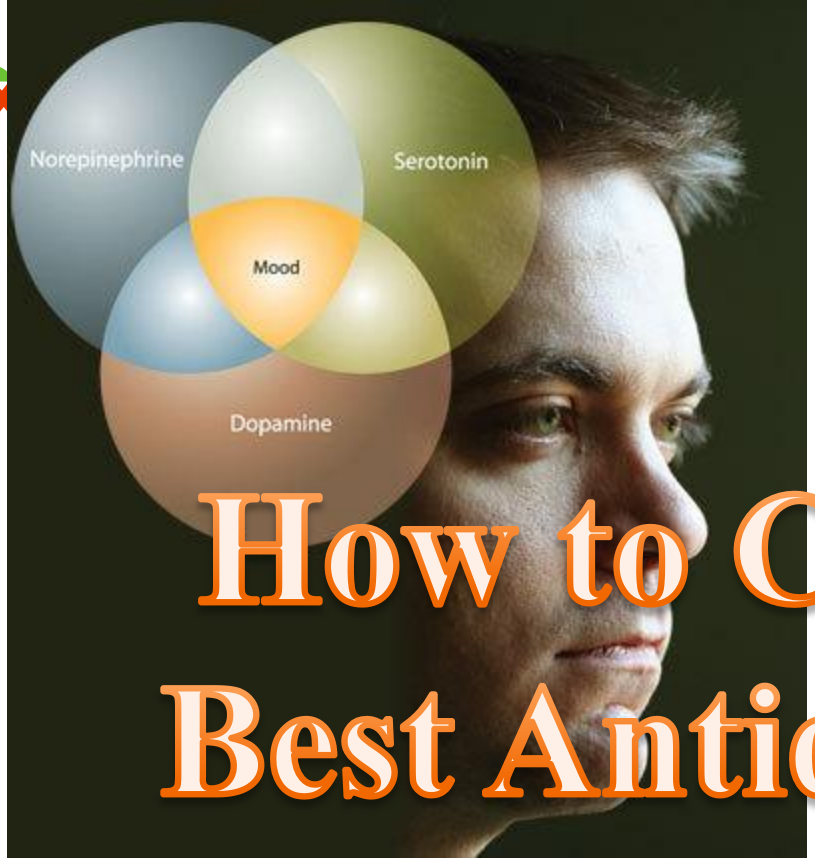


How to Choose the Best Antidepressant

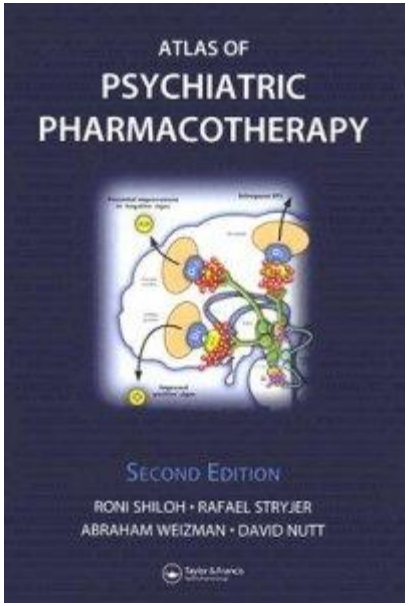
Legend

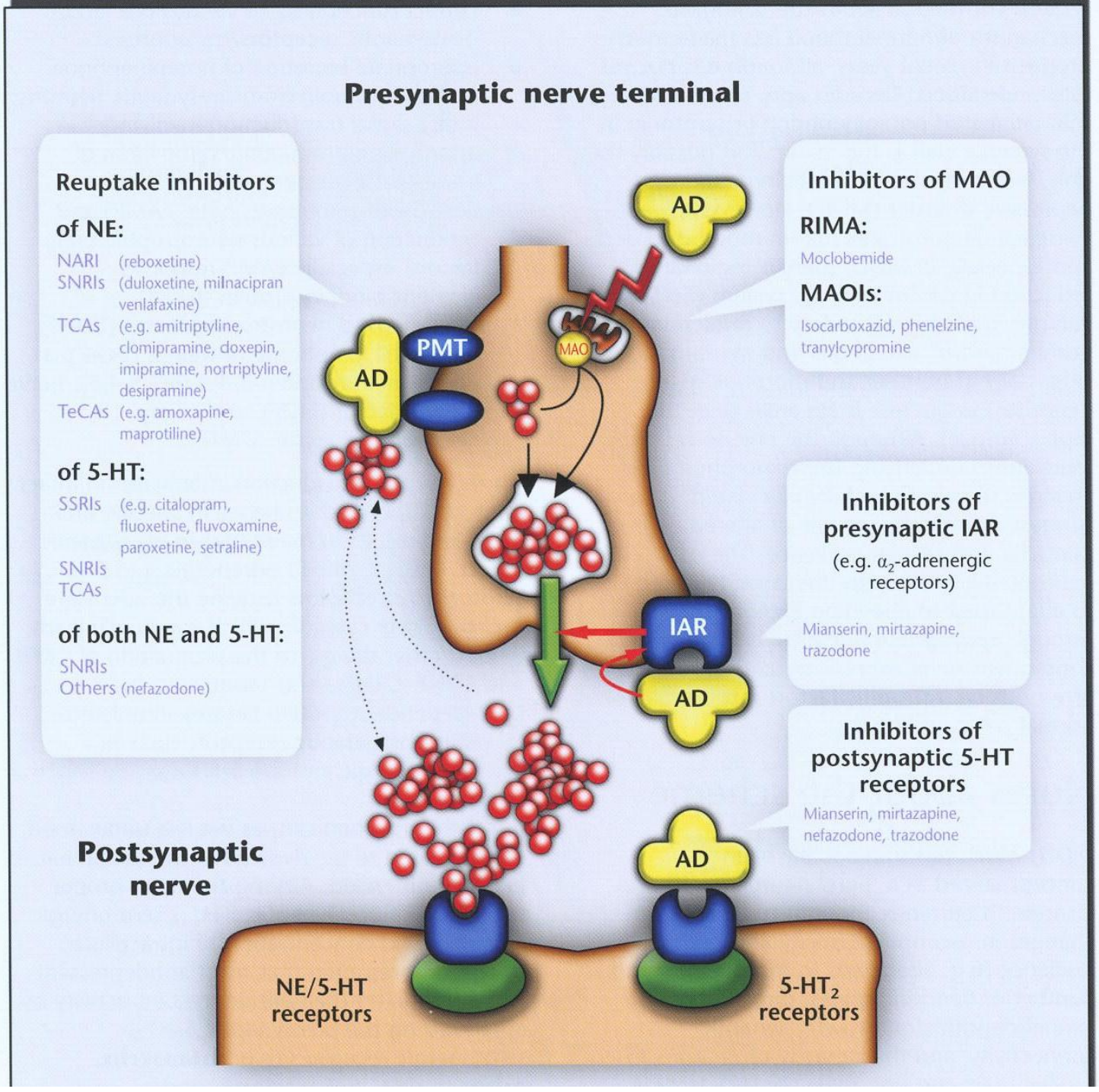
Inhibition

Inhibits

Enhanced secretion

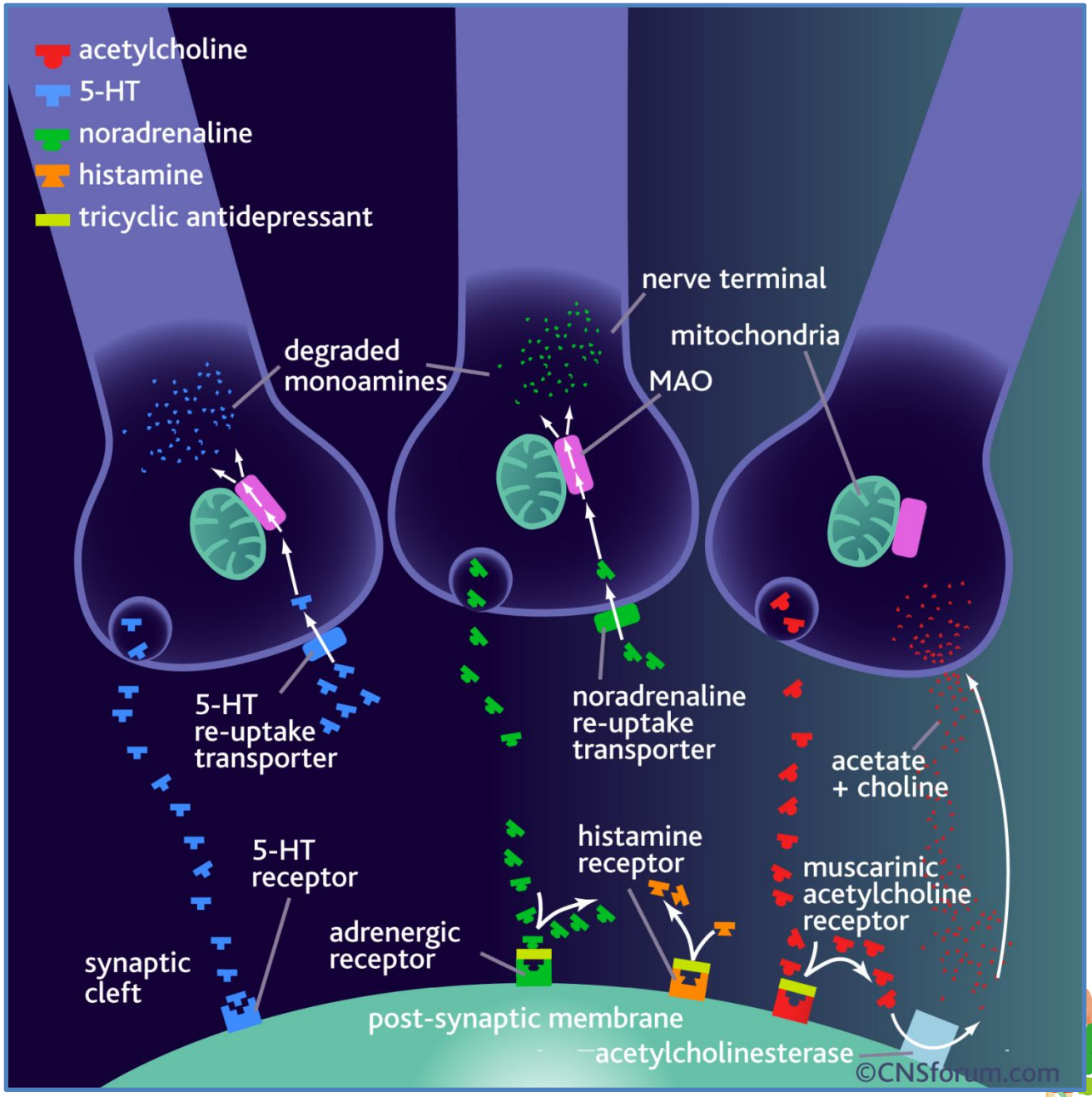
5-HT	Serotonin
AD	Antidepressant drug
IAR	Inhibitory autoreceptor
MAO	Monamine oxidase
MAOI	MAO inhibitor
NARI	Seletive noradrenaline (norepinephrine) inhibitor
NE	Norepinephrine
PMT	Plasma membrane transporter
RIMA	Reversible inhibitor of MAO type A
SNRI	Serotonin–norepinephrine reuptake inhibitor
SSRI	Selective serotonin reuptake inhibitor
T/TeCA	Tri/tetracyclic antidepressant




Presynaptic nerve terminal
Reuptake inhibitors
of NE:
NARI (reboxetine)
SNRIs (duloxetine, milnacipran venlafaxine)
TCAs (e.g. amitriptyline, clomipramine, doxepin, imipramine, nortriptyline, desipramine)
TeCAs (e.g. amoxapine, maprotiline)
of 5-HT:
SSRIs (e.g. citalopram, fluoxetine, fluvoxamine, paroxetine, setraline)
SNRIs
TCAs
of both NE and 5-HT:
SNRIs
Others (nefazodone)
Inhibitors of MAO
RIMA:
Moclobemide
MAOIs:
Isocarboxazid, phenelzine, tranylcypromine
AD
PMT
MAO
IAR
Inhibitors of presynaptic IAR
(e.g. α_2-adrenergic receptors)
Mianserin, mirtazapine, trazodone
Inhibitors of postsynaptic 5-HT receptors
Mianserin, mirtazapine, nefazodone, trazodone
Postsynaptic nerve
NE/5-HT receptors
5-HT$_2$ receptors

Tricyclic Antidepressants & Related Compounds

Drug	Sexual Dysfunction	Reuptake Inhibition		Adverse Effects					
		N	S	ACH	Drowsiness	Orthostatic Hypotension	Conduction Abnormalities	GI Distress	Weight Gain
Amitriptyline	H	M	H	4+	4+	3+	3+	1+	4+
Amoxapine	H	M	L	2+	2+	2+	2+	0	2+
Clomipramine	Very H	M	Very H	4+	4+	2+	3+	1+	4+
Desipramine	H	H	M	1+	2+	2+	2+	0	1+
Doxepin	H	M	L	3+	4+	2+	2+	0	4+
Imipramine	H	M	H	3+	3+	4+	3+	1+	4+
Maprotiline	M	M	L	2+	3+	2+	2+	0	2+
Nortriptyline	H	M	L	2+	2+	1+	2+	0	1+
Protriptyline	H	H	L	2+	1+	2+	3+	1+	1+
Trimipramine	H	L	L	4+	4+	3+	3+	0	4+



http://www.cnsforum.com/imagebank/item/Drug_TCA_AE/default.aspx

Selective Serotonin Reuptake Inhibitors

Drug	Sexual Dysfunction	Reuptake Inhibition		Adverse Effects					
		N	S	ACH	Drowsiness	Orthostatic Hypotension	Conduction Abnormalities	GI Distress	Weight Gain
Citalopram	Very H	Very L	Very H	0	0	0	0	**3+**	1+
Escitalopram	Very H	Very L	Very H	0	0	0	0	**3+**	1+
Fluoxetine	Very H	L	Very H	0	0	0	0	**3+**	1+
Fluvoxamine	Very H	Very L	Very H	0	0	0	0	**3+**	1+
Paroxetine	Very H	M	Very H	1+	1+	0	0	**3+**	2+
Sertraline	Very H	L	Very H	0	0	0	0	**3+**	1+

NDRI（norepinephrine dopamine reuptake inhibitor）

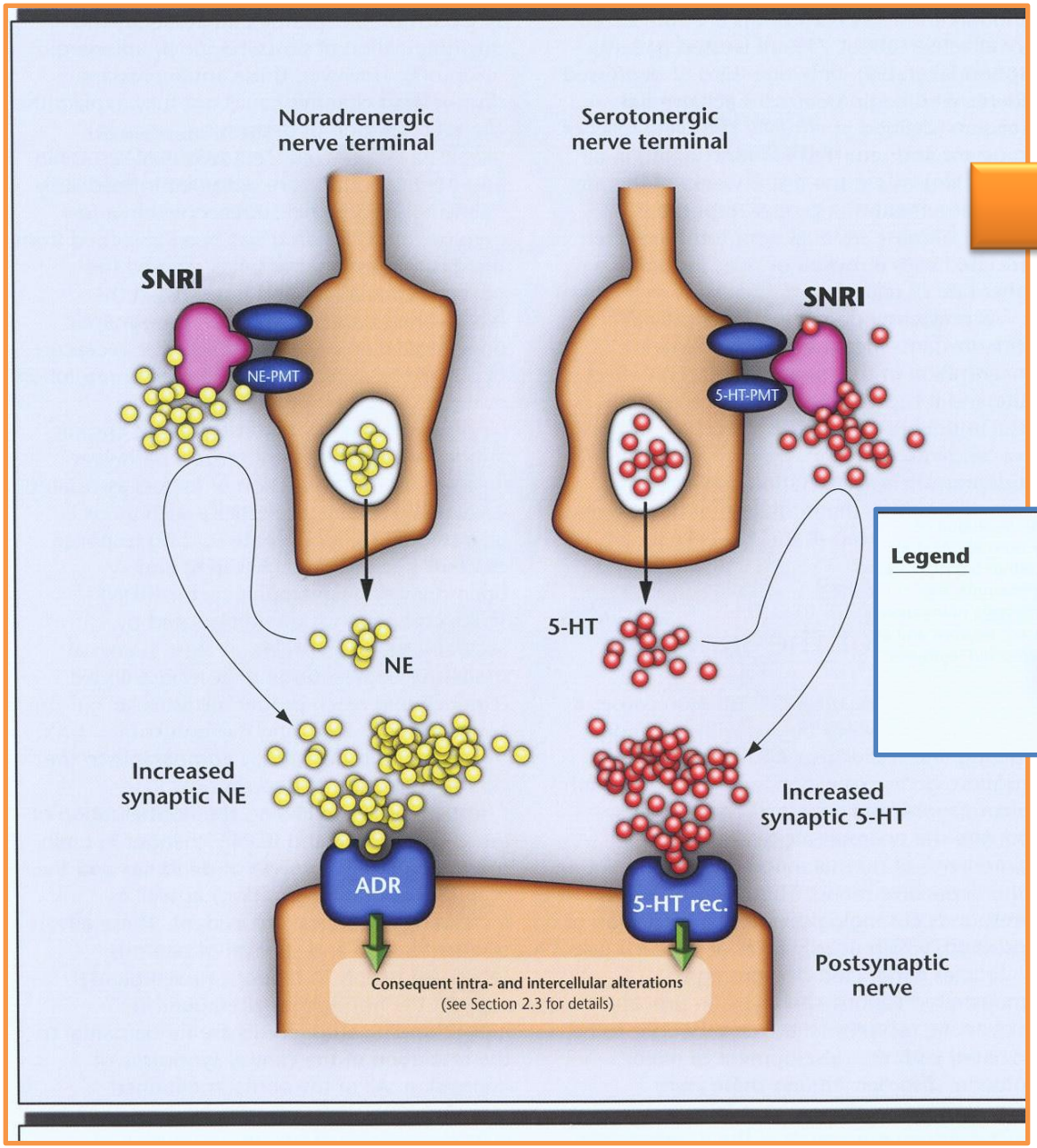
Dopamine-Reuptake Blocking Compounds

Drug	Sexual Dysfunction	Reuptake Inhibition		Adverse Effects					
		N	S	ACH	Drowsiness	Orthostatic Hypotension	Conduction Abnormalities	GI Distress	Weight Gain
Bupropion	**L**	Very L	Very L	0	0	0	1+/0	1+	0

Serotonin / Norepinephrine Reuptake Inhibitors

Drug	Sexual Dysfunction	Reuptake Inhibition		Adverse Effects					
		N	S	ACH	Drowsiness	Orthostatic Hypotension	Conduction Abnormalities	GI Distress	Weight Gain
Duloxetine	**H**	NA	NA	1+	1+	0	1+	3+	0
Desvenlafaxine	**H**	Yes	Yes	1+	1+	0	1+	3+	0
Venlafaxine	**H**	L-H dose dependent	H	1+	1+	0	1+	3+	0

SNRI



Legend

5-HT		**5-HT**	Serotonin
Induces		**ADR**	Adrenergic receptor
		NE	Norepinephrine
NE		**PMT**	Plasma membrane transporter
SNRI		**rec.**	Receptor
		SNRI	Serotonin–norepinephrine reuptake inhibitor

5-HT2 Receptor Antagonist Properties

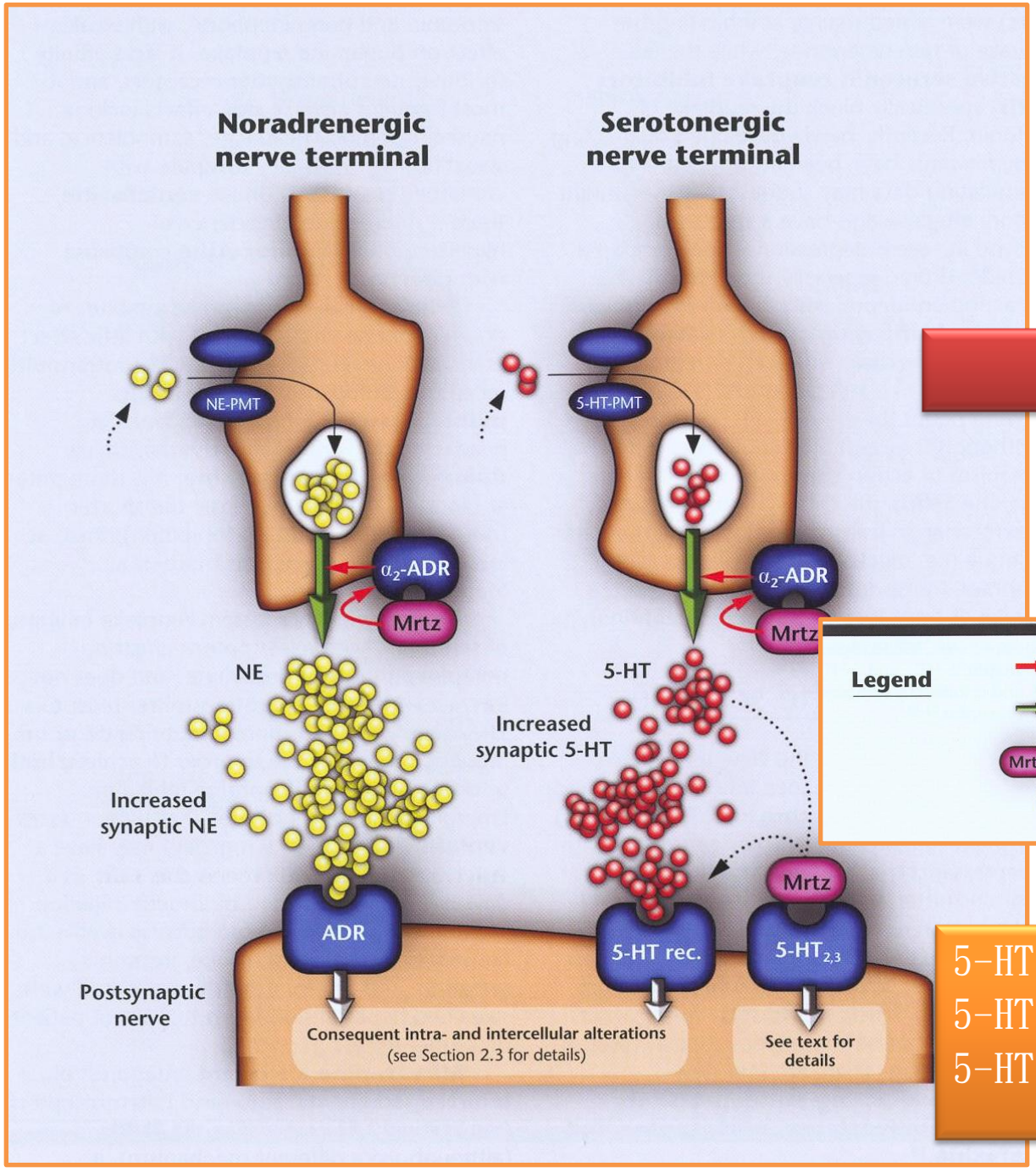
Drug	Sexual Dysfunction	Reuptake Inhibition		Adverse Effects					
		N	S	ACH	Drowsiness	Orthostatic Hypotension	Conduction Abnormalities	GI Distress	Weight Gain
Nefazodone	L	L	L	1+	1+	2+	1+	1+	0
Trazodone	**L**	Very L	L	0	4+	3+	1+	1+	2+

突觸前 抑制 5-HT回收
突觸後 拮抗 5-HT2
代謝物 M- CPP 突觸後促進 5-HT
弱突觸前 α_2 Agonist
突觸後 α 1 antagonist

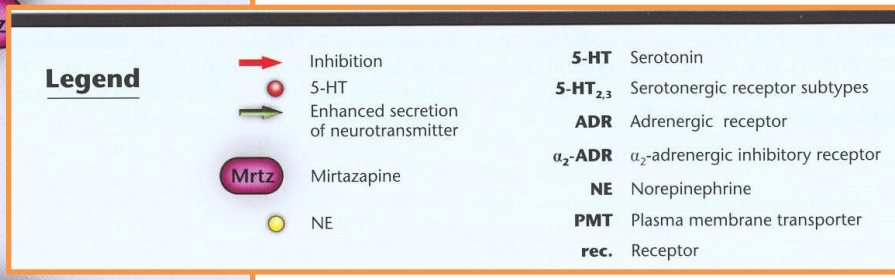
Noradrenergic Antagonist

Drug	Sexual Dysfunction	Reuptake Inhibition		Adverse Effects					
		N	S	ACH	Drowsiness	Orthostatic Hypotension	Conduction Abnormalities	GI Distress	Weight Gain
Mirtazapine	L	Very L	Very L	1+	3+	1+	1+	0	3+

NaSSA



Mirtazapine



5-HT2A 性功能
5-HT2C 食慾、 睡眠
5-HT3 噁心、嘔吐

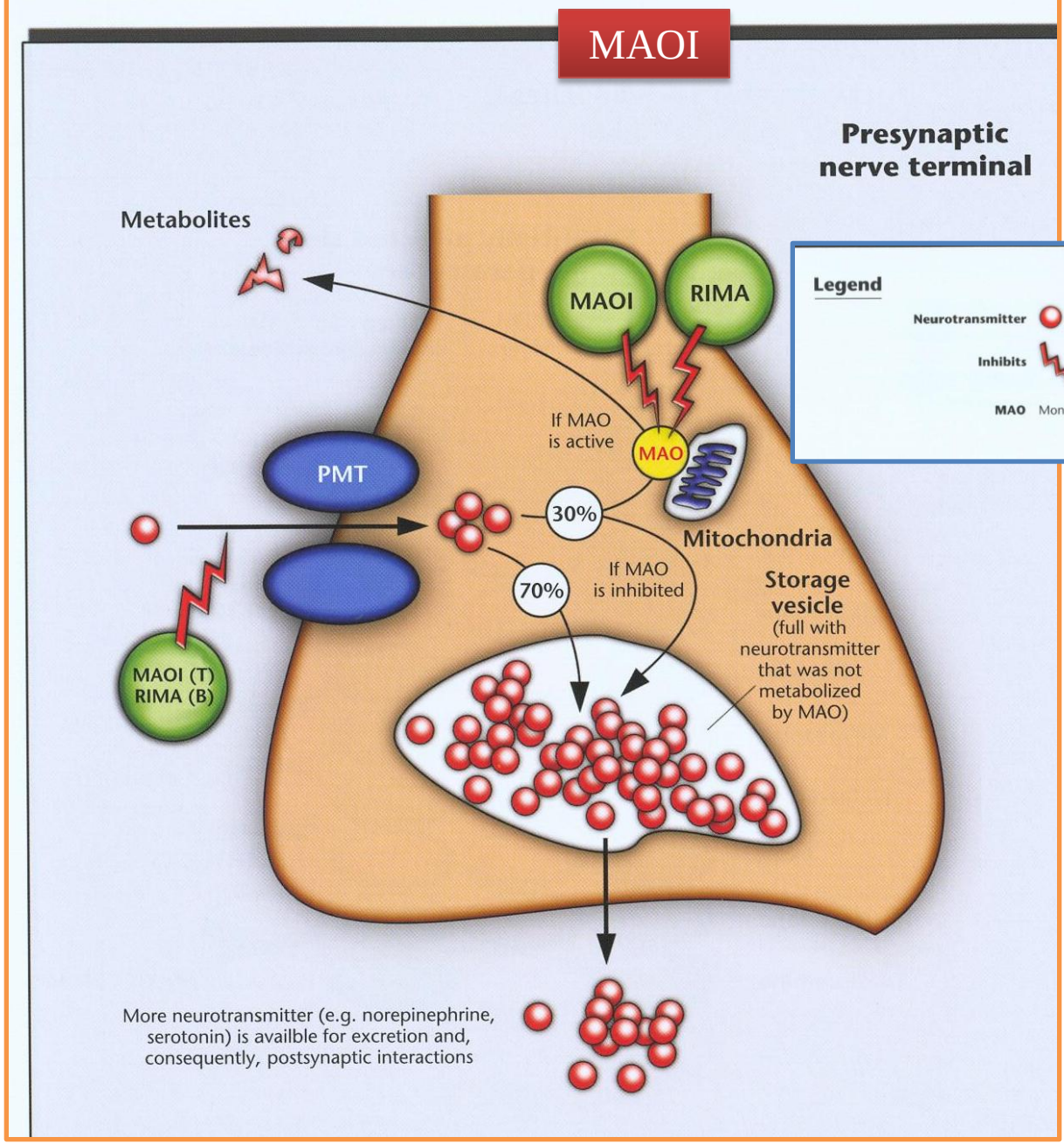
MAOI

Monoamine Oxidase Inhibitors

Drug	Sexual Dysfunction	Reuptake Inhibition		Adverse Effects					
		N	S	ACH	Drowsiness	Orthostatic Hypotension	Conduction Abnormalities	GI Distress	Weight Gain
Isocarboxazid	Very H	—	—	2+	2+	2+	1+	1+	2+
Phenelzine	Very H	—	—	2+	2+	2+	0	1+	3+
Tranylcypromine	H	—	—	2+	1+	2+	1+	1+	2+

2.14 Antidepressant drugs

Monoamine oxidase inhibitors

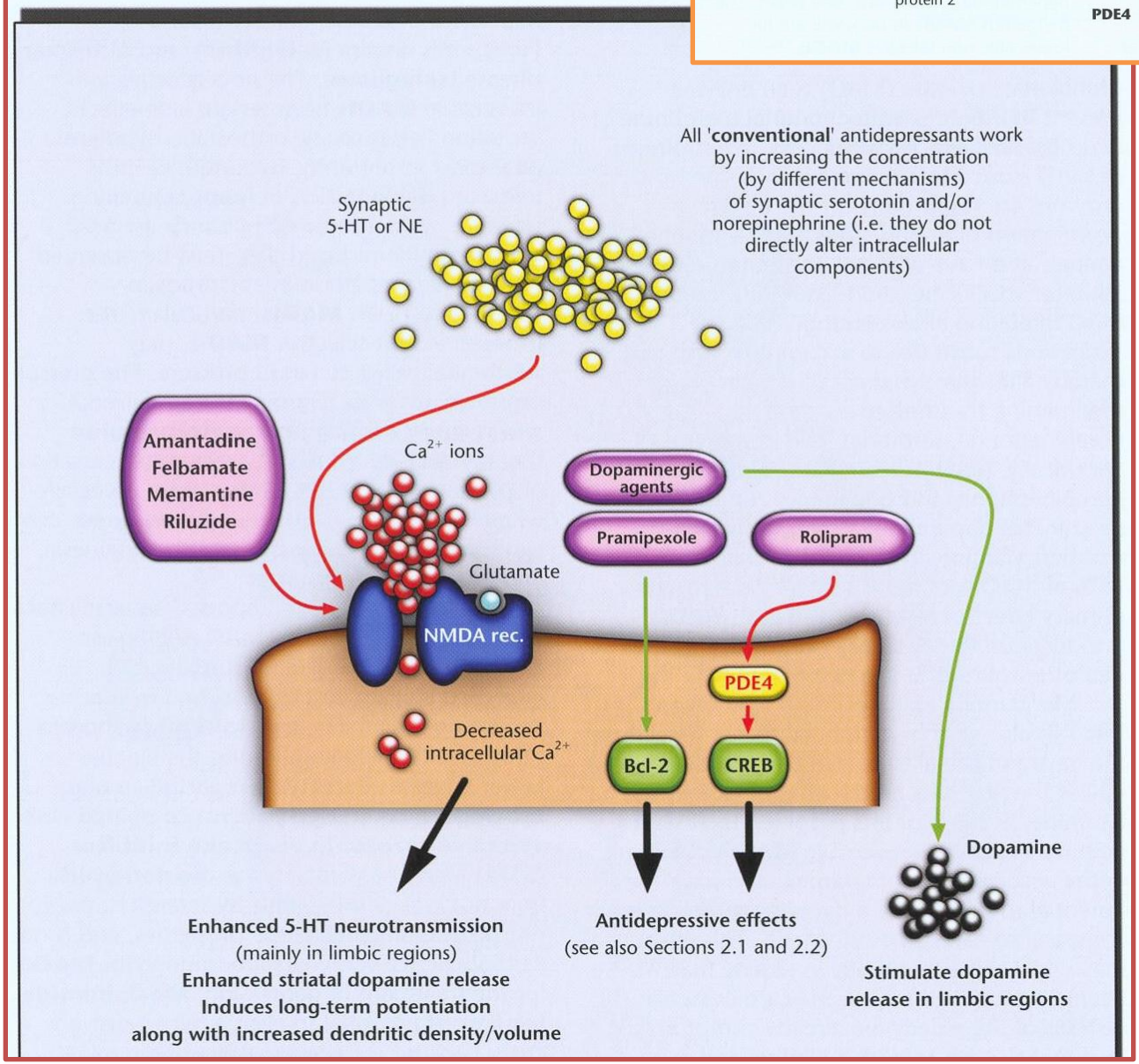


2.15 Antidepressant drugs

Potential future developments

Legend

- Stimulates
- Inhibits
- **5-HT** Serotonin
- **Bcl-2** B-cell lymphoma protein 2
- **CREB** Cyclic adenosine monophosphate (cAMP)-response element-binding protein
- **NE** Norepinephrine
- **NMDA rec.** *N*-Methyl-D-aspartate recepto r (subtype of glutamatergic receptor)
- **PDE4** Phosphodiesterase-4 (metabolizes CREB)



Comparison of Selected Antidepressants

American family physician 2003;67(3);548

Drug	*Availability*	*Cost (generic)**	*Indications†*
SSRIs			
Fluoxetine (Prozac)	Capsules, 10, 20, 40 mg Tablets, 10 mg‡ Oral solution, 20 mg/5 mL	$ 91 (78 to 80) (26 to 78)§ 138 per 120 mL	Depression; OCD; bulimia nervosa
(Prozac Weekly)	Capsules, 90 mg	76	Depression; OCD; bulimia nervosa
(Sarafem)	Capsules, 10, 20 mg	91	PMDD
Sertraline (Zoloft)	Tablets, 25,‡ 50,‡ 100 mg‡ Oral concentrate, 20 mg/mL	75 60 per 60 mL	Depression; OCD; panic disorder; PTSD; PMDD
Paroxetine (Paxil)	Tablets, 10,‡ 20,‡ 30, 40 mg Oral suspension, 10 mg/5 mL	81 131 per 250 mL	Depression; OCD; panic disorder; social phobia; GAD; PTSD
(Paxil CR)	Tablets, 12.5, 25, 37.5 mg	83	Depression; panic disorder
Fluvoxamine (Luvox)	Tablets, 25, 50, 100 mg Tablets, 25, 50,‡ 100 mg‡	88 70 to 81	OCD
Citalopram (Celexa)	Tablets, 10, 20,‡ 40 mg‡ Oral solution, 10 mg/5 mL	65 106 per 240 mL	Depression
Escitalopram (Lexapro)	Tablets, 5, 10,‡ 20 mg‡	63	Depression
Venlafaxine (Effexor)	Tablets, 25,‡ 37.5,‡ 75,‡ 100 mg‡	41	Depression; GAD
(Effexor XR)	Capsules, 37.5, 75, 150 mg	78	Depression; GAD
Mirtazapine (Remeron)	Tablets, 15,‡ 30,‡ 45 mg	83	Depression

SSRIs = selective serotonin reuptake inhibitors; OCD = obsessive-compulsive disorder; PMDD = premenstrual dysphoric disorder; PTSD = post-traumatic stress disorder; GAD = generalized anxiety disorder.

Factors to Consider in Selecting an Antidepressant

- History of prior response (personal or family member)
- Safety in overdose
- Adverse effect profiles
- Patient age
- Concurrent medical/psychiatric conditions
- Concurrent medications (e.g., potential for drug interactions)
- Convenience (e.g., minimal titration, once-daily dosing)
- Cost
- Patient preference

Applied Therapeutics: The Clinical Use Of Drugs, 9th Edition

Seven Things That Everyone Should Know About Depression

- **Depression is NOT a personality flaw or a weakness of character.**
  Depression has been associated with a chemical imbalance in the nervous system, which can be easily corrected with antidepressant medications and associated counseling.
- **All antidepressants are equally effective.**
  Approximately 65% of patients receiving a therapeutic trial of any antidepressant medication will have a beneficial response.
- **Most patients receiving antidepressants will experience some side effect(s) initially.**
  Identify an accessible health professional who can answer your questions.
- **Antidepressants should be taken at the same time daily.**
  This will make it easier for you to remember to take the medication and may also minimize side effects.

Seven Things That Everyone Should Know About Depression

- **The response to antidepressants is delayed.**
  Several weeks may pass before you begin to feel better, and it may take 4 to 6 weeks before maximal benefits are evident.

- **Antidepressants must be taken for at least 6 to 9 months.**
  Even if you are feeling completely better, studies have shown that people who stop their medication during the first 6 months are much more likely to become depressed again.

- **Antidepressants are NOT addictive substances.**
  Antidepressants may elevate the moods of depressed individuals, but they do not act as stimulants and are not associated with craving or other abuse patterns. However, if certain antidepressants are discontinued abruptly, mild withdrawal reactions may occur.

Discontinuation of Antidepressants

Withdrawal syndrome

- Worse with paroxetine, venlafaxine
- Symptoms: dizziness, nausea, paresthesias, anxiety/insomnia, flulike symptoms
- Onset: 36–72 hr
- Duration: 3–7 days

Taper schedule (for patients receiving long-term treatment)

- Fluoxetine: generally unnecessary
- Sertraline: decrease by 25–50 mg every 1–2 wk
- Paroxetine: decrease by 5–10 mg every 1–2 wk
- Citalopram: decrease by 5–10 mg every 1–2 wk
- Escitalopram: decrease by 5 mg every 1–2 wk
- Venlafaxine: decrease by 25–50 mg every 1–2 wk
- Nefazodone: decrease by 50–100 mg every 1–2 wk
- Bupropion: generally unnecessary
- Tricyclics: decrease by 10%–25% every 1–2 wk

Note: Risk of relapse greatest 1 to 6 months after discontinuation.

憂鬱症治療指引

隨時監測：

- 自傷與傷人之險程度
- 症狀變化
- 功能變化
- 治療反應
- 副作用
- 服藥順從度
- 其他精神疾患
- 內外科狀況

治療步驟1

單一治療：
bupropion, mirtazapine, moclobemide, nefazodone(trazodone), SNRIs, SSRIs, TCAs,
或心理治療。

治療步驟2

單一治療：
bupropion, mirtazapine, moclobemide, nefazodone(trazodone), SNRIs, SSRIs, TCAs,
或心理治療。
換藥原則為：不同種類的TCAs不建議互換，但可接受不同SSRIs互換，SNRIs互換是否有效，目前尚無資料。

治療步驟3

合併治療：
兩種抗憂鬱藥 + 心理治療
Bupropion+Nefazodone; Bupropion+SSRIs; Nefazodone+SSRIs; SSRIs+TCAs

治療步驟4

電痙攣治療

治療步驟5

其他藥物 或 特殊/實驗性治療

（台灣憂鬱症防治協會）

Management of SSRI-Induced Sexual Dysfunction

- Patience (may improve after 2-4 weeks)
- Reduced dosage (if possible)
- Drug holidays (sertraline, paroxetine, citalopram, escitalopram *only*)
- Antidotes
  - Bupropion SR 150 mg QD–BID
  - Sildenafil 50–100 mg QD PRN
  - Mirtazapine 7.5–15 mg HS
  - Cyproheptadine 4–12 mg PRN (1 hour prior)
  - Methylphenidate 2.5–5.0 mg QD
  - Others: yohimbine, amantadine, buspirone, gingko
- Change of antidepressants (e.g., bupropion, mirtazapine)

Applied Therapeutics: The Clinical Use Of Drugs, 9th Edition

Partial Response to Antidepressant Treatment Augmentation Strategies (With SSRIs)

- Ensure completion of full therapeutic trial (4–6 wk).
- Ensure optimal dose of antidepressant.
- Consider augmentation therapies:
  - Bupropion
  - Lithium
  - Thyroid supplements
  - Buspirone
  - Atypical antipsychotics
  - Modafinil
  - Lamotrigine

Applied Therapeutics: The Clinical Use Of Drugs, 9th Edition

Q & A in Depression treatment

painful neuropathy

Anxiety disorders

Treatment options for painful neuropathy

Antidepressants
Duloxetine 60 mg once a day
Amitriptyline 50 to 150 mg at night
Nortriptyline 50 to 150 mg at night
Imipramine 100 mg once a day
Desipramine 100 mg once a day
Paroxetine 40 mg o
Trazodone 50 to 15

Anticonvulsants
Pregabalin 50 to 10
Gabapentin 600 to 1
Carbamazepine 200

Others
Capsaicin topical cream 0.075%
Mexiletine 150 to 450 mg once a day
Alpha-lipoic acid 600 mg once a day
Controlled release (CR) oxycodone 10 to 30 mg twice a day
Tramadol 50 to 100 mg twice a day
Transcutaneous electrical nerve stimulation (TENS)
Acupuncture

Treatment of diabetic neuropathy- ***UpToDate***

Treatment Options for Anxiety Disorders

Disorder	First-Line Treatments	Second-Line Treatments
Generalized anxiety disorder	Venlafaxine XR **Buspirone** **Benzodiazepines** Paroxetine Escitalopram Duloxetine	Sertraline Citalopram
Panic disorder	Paroxetine Sertraline Fluoxetine **Alprazolam** **Clonazepam**	Fluvoxamine Citalopram Clomipramine **Lorazepam** Escitalopram
Social anxiety disorder	Paroxetine Sertraline Venlafaxine XR Fluvoxamine CR	Citalopram **Clonazepam** **Alprazolam** Escitalopram
Posttraumatic stress disorder	Sertraline Paroxetine	Fluoxetine Fluvoxamine Venlafaxine Nefazodone Citalopram Escitalopram
Obsessive-compulsive	Paroxetine Fluoxetine Sertraline Fluvoxamine CR Fluvoxamine	Clomipramine[b] Venlafaxine Citalopram Escitalopram

Applied Therapeutics: The Clinical Use Of Drugs, 9th Edition

Generalized anxiety disorder

- **Benzodiazepines** provide a **rapid** symptomatic relief from acute anxiety states
- Due to potential for abuse, dependence, and resultant withdrawal symptoms, benzodiazepines should be used at the minimum effective dose and for the shortest time period possible (maximum of **4** weeks)
- Use is applicable in emergency treatment of **acute anxiety**

Duloxetine

- A **S**erotonin- **N**orepinephrine-**R**euptake **I**nhibitor
- FDA-Labeled Indications
  - Diabetic peripheral neuropathy - **Pain**
  - Fibromyalgia
  - **G**eneralized **A**nxiety **D**isorder
  - **Major depressive disorder**
- Non-FDA Labeled Indications
  - Urinary incontinence

Late-life depression

Risk factors

- Female sex
- Social isolation
- Widowed, divorced, or separated marital status
- Lower socioeconomic status
- Comorbid medical conditions
- Uncontrolled pain
- Insomnia
- Functional impairment
- Cognitive impairment

UpToDate

Late-life depression

The risk of depression in physically ill elderly increases with:

- Recent onset of physical illness
- Greater severity of physical illness
- Functional disability and limited mobility
- Poorly treated pain
- Multiple illnesses

UpToDate

Late-life depression

- Medications typically take up to four to six weeks to show efficacy. In elderly patients a full antidepressant response may not occur until **8 to 12 or even 16 weeks** of therapy
- **Monotherapy is preferr**ed in the elderly in order to minimize drug side effects and drug-drug interactions
- **Initial medication dosage should be adjusted** for the older adult, typically cutting the usual starting dose for younger patients in half.
- Patients should be contacted or seen **within two weeks** of initiating medication to discuss tolerance, address concerns, and adjust dose as indicated.

UpToDate

Late-life depression

- SSRI medications are considered **first line** treatment because of safety and tolerability.
- **Mirtazapine** may be useful for patients with insomnia, agitation, restlessness, or anorexia and weight loss.
- **Venlafaxine** and **duloxetin**e are frequently used as **second line** agents and may be particularly helpful in patients with depression and **neuropathic pain**
- Tricyclic antidepressants are third- or fourth-line therapy in the elderly due to significant **arrhythmic side effects**, as well as **anticholinergic effects** causing urinary retention, orthostasis, and possible exacerbation of dementia.

UpToDate

Late-life depression

- **MAO inhibitors** can be used for depression that is resistant to other agents. This class of drugs has not been well studied in the elderly.
- ECT is used **more frequently** in the elderly than in younger patients, and may be effective for the older patient who is intolerant of medications or not responding to adequate medication trials.
  - ECT is generally well **tolerated in the older** patient, although it causes transient memory loss.

UpToDate

Conclusion

- 了解antidepressants之差異
- 了解antidepressants在臨床使用之多樣化
- 回答患者問題時，需了解患者所有診斷，否則概括回答
  - 治療精神不適狀態、症狀
  - 治療神經性疼痛、慢性疼痛

藥事照護

- 了解疾病與藥物
- 是否有藥物問題
- 如何與醫師溝通
- 還需要什麼病患資料
- 需追蹤什麼(治療目標)
- 藥物衛教
  - 注意事項、藥囑執行正確性
- 其他衛教(預防疾病、確保治療)

察言觀色
因才施教
爾虞我詐

謝謝聆聽 請發問