

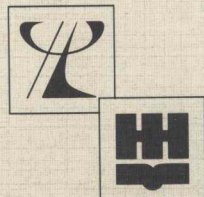


Clinical Handbook of Psychotropic Drugs

Editors

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Clarke Institute of Psychiatry, Toronto, Canada



Hogrefe & Huber Publishers

Toronto • Lewiston, N.Y. • Bern • Göttingen • Stuttgart

second revised edition

Clinical Handbook of Psychotropic Drugs

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Library of Congress Cataloging-in-Publication Data

The first edition of this book was published under:

Clinical handbook of psychotropic drugs / Kalyna Z. Bezchlibnyk-Butler,
principal editor, J. Joel Jeffries, co-editor ; Sandra B.
Bredin, Suvndram Naidoo, Carol E. Friesen, contributing editors.

p. cm

Bibliography: p.

ISBN 0-920887-38-4

1. Psychotropic drugs--Handbooks, manuals, etc. I. Bezchlibnyk-
Butler, Kalyna Z., 1947- II. Jeffries, J. Joel, 1929-

RM315.C547 1989

615'.788--dc19

88-21704

CIP

Canadian Cataloguing in Publication Data

Main entry under title:

Clinical handbook of psychotropic drugs

2nd rev. ed.

Includes bibliographical references

ISBN 0-920887-86-4

1. Psychotropic drugs - Handbooks, manuals, etc.

I. Bezchlibnyk-Butler, Kalyna Z., 1947- .

II. Jeffries, J. Joel, 1939-

RM315.C55

1990

615'.788

C89-095274-4

1st Edition

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2nd Edition, 1st Printing

Copyright © 1990 by Hogrefe & Huber Publishers

2nd Edition, 2nd Printing

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Printed in USA

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ISBN 0-920887-86-4

ISBN 3-456-81866-1

Hans Huber Publishers Toronto • Lewiston, NY

Hans Huber Publishers Bern • Stuttgart

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ANTIDEPRESSANTS

CLASSES

Cyclic Antidepressants: Tricyclic, Dibenzoxazepine, Tetracyclic, Triazolopyridine, Monocyclic, Bicyclic

Monoamine Oxidase Inhibitors (MAOIs)

INDICATIONS

- Treatment of major depressions; tricyclics and related groups are less effective for reactive or mild depressions
- Treatment and prophylaxis of recurrent depressions, as in unipolar affective disorder
- Panic disorder prophylaxis
- Phobic disorders
- Obsessive-compulsive disorder (clomipramine)
- Treatment of enuresis in children and adolescents (imipramine, other tricyclics)
- Others include: migraine headache, pain, ulcers

GENERAL COMMENTS

- Antidepressants reduce the degree of depression and usually increase psychomotor activity before affecting the depression; as energy increases, the risk of suicide may persist — this must be watched for at all times
- If tricyclics (or related drugs) and MAO inhibitors are to be used together, neither should be administered parenterally; both can be started together or the MAO inhibitor can be initiated *after* the tricyclic; patients should be carefully monitored for hypertension and other side effects
- Maximum antidepressant effects may not be apparent for 2 or more weeks

THERAPEUTIC EFFECTS

- Elevation of mood, improved appetite and sleep patterns, increased physical activity, improved mental functioning, decreased feelings of guilt, worthlessness, inadequacy and ambivalence, decrease in delusional preoccupation
- Combined therapy with lithium may increase antidepressant effect

DEXAMETHASONE SUPPRESSION TEST (DST)

- When a healthy person receives dexamethasone, cortisol levels in the blood are generally suppressed over 24 hours, while approximately 50-70% of patients with clinically diagnosed major depression fail to suppress cortisol following dexamethasone administration

DST Protocol

- 1) Administer 1 mg dexamethasone orally at 2300 hrs on Day 1
- 2) The following day, draw venous blood for a cortisol assay at 1530 and 2200 hrs

- The test is considered positive if either of the two plasma cortisol levels is 140 nmol/L or higher
- From a clinical standpoint, a negative DST does not rule out a valid diagnosis of depression

Cyclic Antidepressants

DOSES

- See page 10

PHARMACOLOGY

- Exact mechanism of action unknown; equilibrate the effects of biogenic amines through various mechanisms
- The action in the treatment of enuresis may involve inhibition of urination due to the anticholinergic effect and CNS stimulation, resulting in easier arousal by the stimulus of a full bladder

PHARMACOKINETICS

- Completely absorbed from the gastrointestinal tract; large percentage metabolized by firstpass effect
- Highly lipophilic; concentrated primarily in myocardial and cerebral tissue
- Highly bound to plasma protein
- Metabolized primarily by the liver
- Elimination half-life approximately 24 hrs (protriptyline = 78 hrs, trazodone = 8 hrs, fluoxetine = 96 hrs)

DOSING ROUTE

- Usual route of administration is oral - I. M. injection has no advantage except with patients unwilling or unable to receive drug orally
- There is a wide patient variation in dosage requirements (partly dependent on plasma levels)
- I. V. clomipramine up to 300 mg daily for treatment of obsessive compulsive disorder

ONSET AND DURATION OF ACTION

- Sedative effects are seen within a few hours of oral administration, with lessened sleep disturbances after a few days
- Therapeutic effect is seen after 7-28 days
- Tricyclics and related drugs are long-acting; they may be given in a single daily dose, usually at bedtime

ADVERSE EFFECTS

1. Anticholinergic Effects

- See accompanying charts (pp. 11 and 12) for incidence of adverse effects
- A result of antagonism at muscarinic receptors
- Occur frequently, especially in elderly patients
- Dry mucous membranes [Management: sugar-free gum and candy, oral lubricants (e.g., MoiStir, OraCare D, etc.), pilocarpine mouthwash (4 drops 4% solution to 12 drops water swished in mouth and spat out)]
- Blurred vision [Management: pilocarpine 1% eye drops]
- Dry eyes; may be of particular difficulty in the elderly or those wearing contact lenses [Management: artificial tears, but employ caution with patients wearing soft contact lenses; these patients should have their dry eyes managed with their usual wetting solutions or comfort drops]
- Constipation (frequent in children on therapy for enuresis) [Management: increase bulk and fluid intake, fecal softener, bulk laxative]
- Urinary retention, delayed micturition [Management: bethanechol]
- Sweating [Management: daily showering, talcum powder]

Continued

Cyclic Antidepressants (cont'd)

Adverse effects (cont'd)

2. CNS Effects

- A result of antagonism at histamine H_1 -receptors and α_1 -adrenoreceptors
- Occur frequently
- Drowsiness (most common adverse effect) [Management: prescribe bulk of dose at bedtime]
- Weakness, lethargy, fatigue
- Conversely, excitement, nightmares, agitation, restlessness and insomnia have occurred; vivid dreaming can occur, especially if all the medication is given at bedtime
- Confusion, disturbed concentration, disorientation, delusions and hallucinations (more common in elderly)
- Precipitation of hypomania or mania, panic reactions, anxiety or euphoria may occur
- Seizures (more common in children)
- Children being treated for enuresis may experience drowsiness, anxiety, emotional instability, nervousness and sleep disorders
- Weight gain

3. Neurological Effects

- Fine tremor
- Akathisia (rare)
- Tardive dyskinesia (reported primarily with amoxapine, but also seen on rare occasions with other antidepressants)

4. Cardiovascular Effects

- A result of antagonism at α_1 -adrenoreceptors and inhibition of 5-HT uptake
- More common in elderly
- Tachycardia
- Orthostatic hypotension [Management: sodium chloride tablets, caffeine]
- Arrhythmias, syncope, thrombosis, thrombophlebitis, stroke, and congestive heart failure have been reported on occasion

5. G.I. Effects

- A result of inhibition of 5-HT uptake
- Anorexia, nausea, vomiting, diarrhea
- Peculiar taste, "black tongue," glossitis

6. Endocrine

- Increased or decreased libido, impotence [Management: bethanechol]
- Testicular swelling, breast engorgement, and breast tissue enlargement in males and females
- Anorgasmia in females [Management: cyproheptadine]
- Increase or decrease in blood sugar levels

7. Allergic Reactions

- Rare
- Jaundice, hepatitis, rash, urticaria, pruritis, edema
- Photosensitivity

WITHDRAWAL SYMPTOMS

- Abrupt withdrawal from high doses may cause a syndrome consisting of akathisia, anxiety, chills, coryza, malaise, myalgia, headache, dizziness, nausea and/or vomiting



THEREFORE, THESE MEDICATIONS SHOULD BE WITHDRAWN GRADUALLY AFTER PROLONGED USE

PRECAUTIONS

- Use cautiously in patients in whom excess anticholinergic activity could be harmful, e.g., prostatic hypertrophy, urinary retention, narrow-angle glaucoma
- Use with caution in patients with respiratory difficulties, as antidepressants can dry up bronchial secretions and make breathing more difficult
- May lower the seizure threshold; therefore, administer cautiously to patients with a history of convulsive disorders, organic brain disease, or a predisposition to convulsions, e.g., alcohol withdrawal
- May impair the mental and physical ability to perform hazardous tasks (e.g., driving a car or operating machinery); will potentiate the effects of alcohol
- May induce manic reactions in up to 50% of patients with bipolar affective disorder
- May lead to increased cycling of bipolar affective disorder
- Combination of fluoxetine with other cyclic antidepressants can lead to increased plasma level of other antidepressant

TOXICITY

- The therapeutic margin is close to the toxic dose (lethal dose is about 3 times the maximum therapeutic dose)
- Symptoms of toxicity are extensions of the common adverse effects: anticholinergic, CNS stimulation followed by CNS depression
- Cardiac irregularities occur and are most hazardous; QRS duration on the electrocardiogram reflects the severity of the overdose; if it equals or exceeds 0.10 seconds, it should be considered to be a danger sign

Treatment

- Physical removal of drug from G.I. tract (emesis with Ipecac,* lavage)
- Activated charcoal (40-50 g initially, followed by 20-25 g) decreases tricyclic antidepressant absorption and lowers its blood level. (DO NOT GIVE CONCURRENTLY WITH IPECAC)
- Supportive treatment, with patient closely monitored in a hospital
- Physostigmine salicylate injection (Antilirium) 1 mg I.M. counteracts both the central and peripheral anticholinergic effects
- I.V. diazepam or I.V. lorazepam are the drugs of choice for convulsions

NURSING IMPLICATIONS

- Psychotherapy and education are also important in the treatment of depression
- Monitor therapy by watching for adverse side effects, mood and activity level changes; observe and chart all changes; keep physician informed
- Be aware that the medication reduces the degree of depression and may increase psychomotor activity; this may create concern about behaviour
- Expect a lag time of 7 to 28 days before antidepressant effects will be noticed
- Check for constipation; increase fluids and increase bulk in diet to lessen constipation
- Check for urinary retention; if required the physician may order bethanechol orally or by s.c. injection
- Warn patient to avoid driving a car or operating hazardous machinery until response to drug has been determined
- Reassure patient that drowsiness and dizziness usually subside after first few weeks; if dizzy, patient should get up from lying or sitting position slowly, and dangle legs over edge of bed before getting up
- Caution patient that alcohol or other CNS depressants will cause an increase in sleepiness, dizziness, and lightheadedness
- Excessive use of caffeinated foods, drugs, or beverages may increase anxiety and agitation and confuse the diagnosis
- Expect a dry mouth; suggest frequent mouth rinsing with water, and sour or sugarless hard candy or gum
- Warn patient to avoid extreme heat and humidity as these drugs may affect the body's ability to regulate temperature; photosensitivity reactions may occur on rare occasions so sunscreen agents may be indicated
- Artificial tears may be useful for patients who complain of dry eyes (or wetting solutions for those wearing contact lenses)

*Tincture of Ipecac: Emetic dose: 5-20 ml with plenty of water. Repeat if necessary in 1/2 hour.  DO NOT GIVE to patients in shock, coma, or those who have ingested corrosive substances.

Cyclic Antidepressants (cont'd)

USE IN PREGNANCY

- Equivocal data indicate possible teratogenic effects, and therefore suggest avoiding antidepressants primarily in the first trimester

Breast Milk

- Antidepressants are excreted into breast milk and it is estimated that the baby will receive about 1% of the mother's dose; clinical significance in the newborn is unclear

DRUG INTERACTIONS

- Many interactions; only clinically significant ones listed below

Class	Example	Interaction Effects
Antiarrhythmics	Quinidine, procainamide	Cardiac conduction prolonged
Anticholinergic Drugs	Antiparkinsonian agents, antihistamines, neuroleptics	Increased anticholinergic effect; may increase risk of hyperthermia
Anticoagulants	Warfarin	Increased bleeding
Antidepressants (MAOIs)		If used together, do not add cyclic antidepressants to MAOI: start cyclic antidepressant first or simultaneously with MAOI. For patients already on MAOI, discontinue MAOI 10 to 14 days before starting combination therapy. Combined cyclic and MAOI therapy has increased antidepressant effects. Caution when fluoxetine given before or after MAOI; hypermetabolic syndrome (serotonergic) reported.
Antihypertensives	Bethanidine, clonidine, debrisoquin, guanethidine, reserpine Acetazolamide, thiazide diuretics	Decreased antihypertensive effect Hypotension augmented
CNS Depressants	Barbiturates, hypnotics, antihistamines, alcohol, neuroleptics	Increased sedation, CNS depression
Hypertensives	Epinephrine, norepinephrine (levarterenol), phenylephrine Isoproterenol	Enhanced pressor response May increase likelihood of arrhythmias
Lithium		Potentiates antidepressant effect, Caution with fluoxetine; report of increased lithium level
Thyroid Drugs	Triiodothyronine (T ₃ liothyronine), l-thyroxine (T ₄)	Potentiates antidepressant effect

Monoamine Oxidase Inhibitors (MAOIs)

INDICATIONS

- The management of anxiety disorders in which the predominant symptom is depression
- "Atypical" depression
- Panic disorder prophylaxis
- Obsessive-compulsive neurosis
- Possible anti-herpetic effect

PHARMACOLOGY

- Inhibits the action of monoamine oxidase, an enzyme that metabolizes the neurohormones responsible for stimulating physical and mental activity (serotonin, epinephrine, and norepinephrine)
- Combined therapy with cyclic antidepressants or lithium may increase antidepressant effect

DOSING

- Best response to MAOIs occurs at dosages that reduce MAO enzyme activity by at least 80%
May require up to 2 weeks to reach maximum MAO inhibition

SIDE EFFECTS

- The most common are: restlessness, insomnia, constipation, anorexia, nausea, vomiting, dry mouth, urinary retention, transient impotence, skin rash, drowsiness, headache, dizziness, weakness, orthostatic hypotension
- Occasionally, hypertensive patients may experience a rise in blood pressure

HYPERTENSIVE CRISIS

- Can occur due to ingestion of incompatible foods (containing elevated levels of tyramine) or drugs (see lists pp.9-10)
- Not related to dose of drug

Signs and Symptoms

- Occipital headache, neck stiffness or soreness, nausea, vomiting, sweating (sometimes with fever and sometimes with cold, clammy skin), dilated pupils and photophobia, sudden unexplained nose bleeds, tachycardia, bradycardia, and constricting chest pains

Treatment

- Withhold medication and notify physician immediately
- Phentolamine (Rogitine) can be ordered by the physician to counteract the hypertensive crisis
- Nifedipine 10 mg bitten and placed under the tongue may decrease blood pressure

PRECAUTIONS

- Should not be administered to patients with cerebrovascular difficulty, cardiovascular disease, or a history of hypertension
- Should not be used alone in patients with marked psychomotor agitation
- When changing from one MAOI to another, or to a tricyclic antidepressant, allow a minimum of ten medication-free days
- Need 10-14 days to be excreted from the system before an incompatible drug or food is given, or before surgery
- Hypertensive crisis can occur if given concurrently with certain drugs or foods (see lists pp. 8-9)

**ANTI-
DEPRESSANTS**

Monoamine Oxidase Inhibitors (MAOIs) (cont'd)

TOXICITY

- Symptoms same as side effects but intensified
- Severe cases progress to extreme dizziness and shock
- Overdose, whether accidental or intentional, can be fatal: patient may be symptom-free up to 6 hours, then progress to restlessness - coma - death — therefore, close medical supervision is indicated for 48 hours following an overdose
- Education of patient regarding foods and drugs to avoid is important; a diet sheet should be provided for each patient
- The incidence of orthostatic hypotension is high, especially in the elderly and at the start of treatment: tell patient to get out of bed slowly

FOOD AND DRUG INTERACTIONS

There are many serious food and drug interactions that may precipitate a hypertensive crisis:

Foods to avoid

- All matured or aged cheeses (Cheddar, Brick, Mozzarella, Parmesan, Blue, Gruyere, Stilton, Brie, Swiss, Camembert, etc.)
- Broad bean pods
- Meat extract (e.g., "Marmite," "Bovril," "Oxo"), concentrated yeast extracts
- Pickled herring, dried salted fish

Reactions have also been reported with

- Sour cream, yoghurt
- Soya sauce, meat tenderizers
- Caviar, snails, tinned fish
- Homemade red wine, beer, sherry
- Tea, coffee, cola
- Tinned and packet soup
- Sausage: bologna, salami, pepperoni, summer sausage, or other unrefrigerated fermented meats, game meat that has been hung
- Chocolate
- Overripe fruit, avocados, canned figs, raisins

It is **SAFE** to use cottage cheese, cream cheese, farmer's cheese, processed cheese, and liver (as long as they are fresh), white wine and spirits.
MAKE SURE ALL FOOD IS FRESH, STORED PROPERLY AND EATEN SOON AFTER BEING PURCHASED.
 Never touch food that is fermented or possibly "off."

Over-the-counter drugs to avoid

- Cold remedies, decongestants (including nasal sprays and drops), most antihistamines and cough medicines
- Narcotic pain killers (e.g., 222s)
- All stimulants including "Pep-pills" ("Wake-ups")
- All appetite suppressants
- Anti-asthma drugs
- Sleep aids and sedatives ("Sominex")

DRUG INTERACTIONS

Class	Example	Interaction Effects
Anaesthetics		May enhance CNS depression
Analgesics	Narcotics	Excitation, sweating, hypotension; if a narcotic is required, meperidine should not be used Other narcotics should be instituted cautiously
Anticholinergic agents	Antiparkinsonian agents, neuroleptics	Increased atropine-like effects
Anticonvulsants	Carbamazepine	Due to the structural similarity between carbamazepine and cyclic antidepressants, there is a theoretical possibility that there will be an interaction between these drugs
Antidepressants (cyclic)		If used together, do not add cyclic antidepressants to MAOI. Start cyclic antidepressant first or simultaneously with MAOI. For patients already on MAOI, discontinue the MAOI for 10 to 14 days before starting combination therapy. Combined cyclic and therapy MAOI has increased antidepressant effects
CNS depressants	Barbiturates, sedatives, alcohol	May enhance CNS depression
Levodopa		Increased blood pressure
L-tryptophan		Reports of "serotonin syndrome," with hyperreflexia, tremor, myoclonic jerks, and ocular oscillations
Muscle relaxants	Succinylcholine	May prolong apnea
Sympathomimetic amines	1. Indirect acting: amphetamine, methylphenidate, ephedrine, pseudo-ephedrine, phenylpropanolamine, dopamine, tyramine 2. Direct acting: epinephrine, isoproterenol, norepinephrine (levarterenol), methoxamine 3. Phenylephrine	Release of large amounts of norepinephrine with hypertensive reaction. AVOID No interaction Increased pressor response

Antidepressant Doses

Drug	Therapeutic Dose Range (mg)	Maximum Therapeutic Dose in Literature (mg)	Equivalent Dose (mg)	Suggested Plasma Level (nmol/L **)	Neurotransmitter Affected
TRICYCLIC					
Amitriptyline (Elavil)	75 - 300	500	50	* 400 - 800	NE (++) 5-HT (++++) DA (+)
Clomipramine (Anafranil)	75 - 225	500	50	300 - 1000	NE (+) 5-HT (++)
Desipramine (Norpramin)	75 - 300	400	50	500 - 1000	NE (+++++) 5-HT (++++)
Doxepin (Sinequan)	75 - 300	350	50	* 500 - 950	NE (+) 5-HT (++)
Imipramine (Tofranil)	75 - 300	750	50	* 150 - 500	NE (++++) 5-HT (++++)
Nortriptyline (Aventyl)	40 - 200	400	25	150 - 500	NE (++++) 5-HT (+)
Protriptyline (Triptil)	30 - 60	150	15		NE (+++++) 5-HT (++)
Trimipramine (Surmontil)	75 - 300	800	50		NE (++) 5-HT (+) DA (+)
DIBENZOXAZEPINE					
Amoxapine (Asendin)	100 - 400	900	100		NE (++++) 5-HT (++) DA (++)
TETRACYCLIC					
Maprotiline (Ludiomil)	100 - 225	400	50	650 - 950	NE (++++) 5-HT (+)
TRIAZOLOPYRIDINE					
Trazodone (Desyrel)	150 - 400	600	100	2000 - 5000	5-HT (++)
MONOCYCLIC					
Bupropion (Wellbutrin)***	225 - 450	900			NE (u) DA (u)
BICYCLIC					
Fluoxetine (Prozac)	20 - 80	80			5-HT (++++)
MAO INHIBITORS					
Isocarboxazid (Marplan)	30 - 50	80	10		NE (u) 5-HT (u) DA (u)
Phenelzine (Nardil)	45 - 90	150	15		NE (u) 5-HT (u) DA (u)
Tranylcypromine (Parnate)	20 - 60	300	10		NE (u) 5-HT (u) DA (u)

Doses used at the Clarke Institute often fall in the range between monograph doses and maximum doses used in the literature. Monograph doses are just a guideline, and each patient's medication must be individualized.

* includes sum of drug and its metabolites

** approximate conversion: nmol/L = 3.5 x ng/mL

*** Approved but not marketed in U.S.

5-HT = Serotonin
NE = Norepinephrine
DA = Dopamine

High ++++
Moderate +++
Low ++
Very Low +
Potency unknown u

Frequency of Adverse Reactions of Tricyclic Antidepressants at Therapeutic Doses

Reaction	Amitriptyline	Clomipramine	Desipramine	Doxepin	Imipramine	Nortriptyline	Protriptyline	Trimipramine
ANTICHOLINERGIC EFFECTS								
Dry mouth	> 30%	> 30%	10-30%	> 30%	> 30%	10-30%	10-30%	10-30%
Blurred vision	10-30%	10-30%	2-10%	10-30%	10-30%	2-10%	10-30%	2-10%
Constipation	10-30%	10-30%	2-10%	10-30%	10-30%	10-30%	10-30%	10-30%
Sweating	10-30%	10-30%	2-10%	2-10%	10-30%	< 2%	10-30%	2-10%
Delayed micturition *	2-10%	10-30%	-	< 2%	10-30%	< 2%	< 2%	< 2%
CNS EFFECTS								
Drowsiness, sedation	> 30%	2-10%	2-10%	> 30%	10-30%	2-10%	< 2%	> 30%
Insomnia	2-10%	10-30%	2-10%	2-10%	10-30%	< 2%	10-30%	2-10% ^(b)
Excitement/Hypomania***	< 2%	< 2%	2-10%	< 2%	10-30%	2-10%	10-30%	< 2%
Disorientation/Confusion	10-30%	2-10%	-	< 2%	2-10%	10-30%	-	10-30%
Headache	2-10%	2-10%	< 2%	< 2%	10-30%	< 2%	-	2-10%
EXTRAPYRAMIDAL EFFECTS								
Unspecified	2-10% ^(a)	< 2% ^(a)	< 2%	2-10% ^(a)	< 2%	-	-	< 2%
Tremor (fine)	10-30%	10-30%	2-10%	2-10%	10-30%	10-30%	2-10%	10-30%
CARDIOVASCULAR EFFECTS								
Orthostatic hypotension/ dizziness	10-30%	10-30%	2-10%	10-30%	> 30%	2-10%	10-30%	10-30%
Tachycardia	10-30%	10-30%	10-30%	2-10%	10-30%	2-10%	2-10%	2-10%
ECG changes **	10-30%	10-30%	2-10%	2-10%	10-30%	2-10%	10-30%	10-30%
Cardiac arrhythmia	2-10%	2-10%	2-10%	2-10%	2-10%	2-10%	2-10%	2-10%
G.I. distress (nausea)	2-10%	2-10%	2-10%	< 2%	10-30%	< 2%	-	< 2%
Dermatitis, rash	2-10%	2-10%	2-10%	< 2%	2-10%	< 2%	< 2%	< 2%
Weakness, fatigue	10-30%	2-10%	2-10%	2-10%	10-30%	10-30%	10-30%	2-10%
Weight gain (over 6 kg)	> 30%	10-30%	2-10%	2-10%	10-30%	2-10%	-	10-30%
Sexual disturbances	2-10%	10-30%	2-10%	2-10%	2-10%	< 2%	< 2%	-
Epileptic seizures ^(c)	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%	< 2%

* Primarily in the elderly ** ECG abnormalities usually without cardiac injury (a) Tardive dyskinesia reported (rarely) (b) No effect on REM sleep (c) In non-epileptic patients
 *** More likely in bipolar patients - None reported in literature perused

Frequency of Adverse Reactions of Other Classes of Antidepressants at Therapeutic Doses

Reaction	Amoxapine	Maprotiline	Trazodone	Isocarboxazid	Phenelzine	Tranlycypromine	Bupropion ^(l)	Fluoxetine
ANTICHOLINERGIC EFFECTS								
Dry mouth	> 30%	> 30%	2-10%	10-30%	> 30%	10-30%	10-30%	2-10%
Blurred vision	2-10%	10-30%	2-10% ^(m)	2-10%	10-30%	2-10%	2-10%	2-10%
Constipation	> 30%	10-30%	2-10%	2-10%	10-30%	2-10%	2-10%	2-10%
Sweating	2-10%	2-10%	-	< 2%	2-10%	-	2-10%	2-10%
Delayed micturition*	10-30%	2-10%	< 2%	2-10%	2-10%	2-10%	2-10%	< 2%
CNS EFFECTS								
Drowsiness, sedation	10-30%	10-30%	10-30%	2-10%	10-30%	10-30%	2-10%	10-30%
Insomnia	10-30%	< 2%	< 2%	2-10%	10-30% ^(f)	10-30% ^(f)	2-10%	10-30%
Excitement/Hypomania***	2-10%	2-10%	- ^(d)	2-10%	10-30%	10-30%	2-10%	10-30%
Disorientation/Confusion	2-10%	2-10%	< 2%	2-10%	2-10%	2-10%	2-10%	10-30%
Headache	2-10%	< 2%	2-10%	10-30%	2-10%	-	2-10%	10-30%
EXTRAPYRAMIDAL EFFECTS								
Unspecified	2-10% ^(a)	2-10%	2-10% ^(a)	2-10%	2-10%	< 2%	2-10%	2-10%
Tremor (Fine)	2-10%	10-30%	2-10%	2-10%	10-30%	2-10%	2-10%	10-30%
CARDIOVASCULAR EFFECTS								
Orthostatic hypotension/ dizziness	10-30%	2-10%	10-30% ^(g)	10-30%	10-30%	10-30%	2-10%	10-30%
Tachycardia	10-30%	2-10%	2-10%	-	10-30%	10-30%	< 2%	- ^(k)
ECG changes**	< 2%	< 2%	< 2%	-	-	-	< 2%	< 2%
Cardiac arrhythmia	< 2%	< 2%	< 2% ^(e)	2-10%	-	< 2%	< 2%	< 2%
G.I. distress (nausea)	2-10%	2-10%	10-30%	10-30%	10-30%	2-10%	2-10%	10-30%
Dermatitis, rash	10-30%	10-30%	< 2%	2-10%	< 2%	2-10%	2-10%	2-10%
Weakness, fatigue	2-10%	-	< 2%	2-10%	< 2%	< 2%	2-10%	-
Weight gain (over 6 kg)	< 2%	10-30%	2-10%	10-30%	10-30%	2-10%	< 2% ^(j)	- ^(j)
Sexual disturbances	2-10%	< 2%	< 2% ^(h)	2-10%	10-30%	2-10%	< 2%	2-10%
Epileptic seizures ^(c)	< 2%	2-10% ⁽ⁱ⁾	< 2%	-	< 2%	- ^(b)	< 2% ⁽ⁱ⁾	< 2%

- not reported in literature perused

* primarily in the elderly

** ECG abnormalities usually without cardiac injury

*** more likely in bipolar patients

(a) tardive dyskinesia reported (rarely)

(b) may have anticonvulsant activity

(c) in non-epileptic patients

(d) less likely to precipitate mania; agitation may occur

(e) patients with pre-existing cardiac disease have a 10% incidence of premature ventricular contractions

(f) especially if given in the evening

(g) less frequent if drugs given after meals

(h) priapism reported

(i) higher incidence if doses above 225 mg/day (maprotiline) and 450 mg/day (bupropion)

(j) weight loss reported

(k) decreases heart rate

(l) approved but not marketed in U.S.

(m) found to lower intraocular pressure

NEUROLEPTICS (ANTIPSYCHOTICS)

CLASSES

Phenothiazines: Aliphatic, Piperidine, Piperazine

Thioxanthenes

Butyrophenone

Diphenylbutylpiperidine

Dibenzoxazepine

Dihydroindolone

INDICATIONS

- Treat symptoms of acute and chronic psychoses (i.e. schizophrenia, manic phase of manic-depressive psychosis, delusional disorder)

OTHER USES

- Anti-emetic
- An adjunct to anaesthesia, refractory hiccups
- Antipruritic, especially in neurodermatitis and pruriginous eczema
- Gilles de la Tourette syndrome (especially haloperidol and pimozide)
- Porphyria
- Possibly in the prophylaxis of cyclic mood disorders
- Agitation in depression
- Agitated dementia
- Impulsivity (pericyazine)
- Obsessive compulsive disorder (pericyazine)

GENERAL COMMENTS

- Significant pharmacological characteristics:
 - 1) Antipsychotic activity
 - 2) Production of extrapyramidal side effects (both reversible and tardive dyskinesia)
 - 3) Absence of deep coma or anaesthesia with administration of large (not toxic) doses
 - 4) Absence of physical or psychic dependence
- The term "tranquillizer" was introduced to describe the psychic effects of reserpine (which is rarely used for this indication now); the term is outmoded
- Neuroleptics must be distinguished from both anxiolytics and sedatives as neither of these possesses antipsychotic properties in usual doses
- Appear to control symptoms of schizophrenia such as thought disorders, hallucinations, delusions, alterations in affect, and autism