PSYCHOPHARMACOLOGY IN THE MEDICALLY ILL

I. Interactions with General Properties of Illness

A. Vital Signs

1. Temperature

a. phenothiazines and butyrophenones can cause hyperpyrexia by poorly understood mechanisms.

b. phenothiazines suppress thermoregulation at the hypothalamic level and can mask fever.

c. singly or in combination MAOIs, tricyclics, and lithium can cause hyperpyrexia.

d. physostigmine (1-3 mg IM/IV) is antidote for hyperpyrexia due to tricyclics or anticholinergics.

2. Pulse: neuroleptics and tricyclics may cause tachycardia and arrhythmias due to a combination of central actions and as a reflex to peripheral adrenergic blockade.

3. Respiration

a. anticholinergic effects on secretions

b. neuroleptics can profoundly suppress respiration, especially in the critically ill (Post-cardiac surgery), presumably by general over-sedation.

4. Blood Pressure

a. postural hypotension: TCA and phenothiazines ($\geq$15 mm Hg)

b. phenothiazine induced hypotension is most marked in non-smokers, elderly, and elevated systolic ($\geq$140)

or diastolic (>100) pressures (Swett, C. Arch Gen Psych 34:661, 1977).

c. tricyclic induced postural hypotension can persist indefinitely.

II. Side Effects: Phenothiazines

A. General Properties

1. Central Effects

a. anticholinergic brain syndrome (see table)

b. "malignant neuroleptic syndrome" (Meltzer, H. Psychopharmacologia 29:337, 1973): hyperpyrexia, muscular rigidity, and coma.

c. temperature regulation: see above.

2. Peripheral Effects

a. cholinergic blockade: dry mouth, blurred vision, constipation or ileus, hypotension, uncoordination, vertigo, urinary retention, sweating, worsening of reflux esophagitis.

b. adrenergic blockade: vasodilatation; hypotension; inhibition of ejaculation (mostly with thioridazine). Anti-adrenergic activity parallels sedative properties: the more sedating agents are potent alpha antagonists.

B. Allergic or hypersensitivity reactions: Phenothiazines

1. Allergic hepatitis: fever, eosinophilia, obst. jaundice.

a. treatment is to switch to another class of antipsychotic agents.

b. incidence is 0.5%.

c. total bilirubin is 15 mg%, direct higher than indirect.

C. Idiosyncratic

1. Leucopenia, agranulocytosis

a. appears related to total dose of CPZ (or equivalent) of 5-10 g over 3 months.

b. incidence 1/1000.

c. elderly debilitated women may be at greatest risk.

III. Side Effects: Tricyclics

A. General Properties

1. Central Effects

a. anticholinergic brain syndrome (Granacher, R. Arch Gen Psych 32:375, 1975).

2. Peripheral Effects

a. cholinergic blockade: monomethylated TCA least: imipramine lowest of dimethylated TCAs.

b. all have about same degree of anti-adrenergic activity, with monomethylated TCA's least.

B. Allergic or hypersensitivity reactions

1. Cholestatic jaundice

C. Idiosyncratic

1. Hematologic

a. Leukopenia, agranulocytosis

b. leukocytosis, eosinophilia

c. thrombocytopenia

IV. Side Effects: Lithium (see Johnson, F.N. Lithium in Medical Practice, Baltimore, 1978)

A. Idiosyncratic

1. Hyper-hypothyroidism, cerebellar ataxia, thyromegaly
2. Interstitial nephritis (fibrous)
   a. decreased concentrating ability, decreased creatinine clearance.
   b. may be dose and time related, can occur with less than 6 mo's treatment.
   c. may persist after lithium withdrawn.

V. Specific Illnesses

A. Organic Heart Disease

1. Non-specific effects on the heart
   a. neuroleptics and tricyclics cause prolonged QT interval, lowering and inversion of T wave, and a bicuspid T or U wave: this may reflect efflux of cellular potassium
2. Tricyclics (Kantor, S.J. AJP 135:534, 1978)
   a. can produce ↑BP, ↓BP
   b. may have direct suppressing effects on myocardium (?CHF)
   c. at therapeutic levels: ↑HR, ↑PR, ↑QRS, ↑QT interval (intraventricular conduction delay), ↑bundle branch block

d. TCAs can be used in presence of atrial and ventricular arrhythmias: therapeutic imipramine concentrations suppress these arrhythmias.

e. may have additive effect with procaineamide and quinidine (because TCAs also prolong intraventricular depolarization and repolarization). Decrease dose of quinidine/procaineamide.

3. Phenothiazines (Fowler, N.O. Am J Card 37:223, 1976)

a. hypotension due to alpha adrenergic blockade, central effects, direct effect on vessels

b. depress myocardial contractility

c. effects on rhythm are controversial (? facilitate re-entrant excitation via decreasing conduction velocity)

d. thioridazine may be most cardio-toxic: fatal ventricular tachycardia at therapeutic doses.

B. Renal Disease: "Start low, go slow"

1. Tricyclics

a. hepatic metabolism. Metabolites?

b. dangers: volume depletion, vascular instability, compromised brain (susceptible to acute OMS with obtundation, asterixis, abnormal EEG)

2. Phenothiazines

a. hepatic metabolism

b. increased sensitivity to extrapyramidal sx

c. other dangers as above

3. Lithium: avoid

4. Benzodiazepines (Talcob, L. Lancet ii:704, 1976)

a. metabolic encephalopathy likely because of prolonged half-life.

C. Pregnancy, Labor, Delivery

1. Phenothiazines: second most commonly prescribed drug

a. can be safely administered without teratogenic effects, probably

b. excreted in breast milk in negligible amounts, except for HALDOL in significant amounts

c. behavioral teratogenicity possible

2. Tricyclics

a. apparently not teratogenic

b. not found in mother's milk: amitriptyline, nortriptyline metabolites, probably imipramine.

c. behavioral teratogenicity possible

3. Lithium

a. apparent increase in fetal cardiovascular anomalies: avoid use in first trimester, use only if strongly indicated afterwards.

b. mothers should not breast feed

4. Benzodiazepines
   a. teratogenic
   b. excreted in breast milk in significant amounts

D. Hepatic Disease
   1. Phenothiazines, tricyclics hepatic metabolism
   2. Benzodiazepines may or may not induce hepatic enzymes and their effect on metabolism of other psychotropics is controversial.

VI. Effects on Laboratory Tests (See Clinical Chemistry 21, April 1975)

A. Major Tranquilizers
   1. False Increases
      a. SGOT, SGPT
      b. alk phos
      c. bilirubin
      d. CSF protein
      e. fasting blood glucose
      f. porphyrins
      g. urobilinogen
      h. frog pregnancy test
   2. Inaccurate tests (inc. or dec.)
      a. uric acid
      b. PBI, I^{131} uptake
      c. urine 5H1AA, 17OHCS
      d. various tests of cortisol metabolism
      e. cholesterol

B. Tricyclics

1. False increases

a. SGOT, SGPT

b. alk phos

c. bilirubin

2. Inaccurate

a. FBS

b. cholesterol

C. Lithium

1. FT_4 decreased. Action of exogenous T_3, T_4 is unchanged.

2. Abnormal GTT

VII. Psychiatric Complications of Medical Drugs (Shader, R.I., Psych. Compl. of Med. Drugs, New York, 1972)

A. Digitalis

1. Neuropsychiatric disturbances

a. somnolence

b. apathy

c. depression

d. memory loss

e. confusion, disorientation ("CCU psychosis")

f. irritability

g. euphonia

h. excitement, combativeness

i. delusions

j. insomnia, nightmares

k. hallucinations (unformed)

B. L-DOPA (Moskovitz, C. AJP 135:669, 1978)

1. Psychiatric Side Effects (3%)

a. confusion, delirium

b. depression

c. agitation, anger

d. psychosis, delusions, paranoia in clear and confused sensorium

e. hypomania

f. hallucination: auditory, tactile, visual (formed, unformed)

2. Literature on depressive disorders is contradictory

C. See Chart for Mood Effects of

1. Anti-tuberculous agents

2. Anti-hypertensives

3. Anti-convulsants

VIII. Psychotropic Drug Withdrawal Syndromes

A. Antipsychotics (Gardos, G. AJP 135:1321, 1978)

1. Medical Effects: nausea, emesis, diarrhea, perspiration, restlessness, insomnia, rhinorrhea, headaches, increased appetite.

a. women at greater risk

b. not related to pre-withdrawal drug dose

c. possible "cholinergic rebound": more often after withdrawing strongly anticholinergic drugs (including imipramine)

d. time course: 1-2 wk.

2. Parkinsonism

a. may persist for 4-18 mo.

b. if anti-Parkinsonian drugs stopped at same time as antipsychotics, symptoms may recur and peak at 4 days, then fade

3. Withdrawal dyskinesia

a. self-limited (4 wk to 4 mo)

b. signs resemble tardive dyskinesia

c. temporary hyperdopaminergic state

4. Covert dyskinesia

a. choreiform or orofacial dyskinesia appearing drug reduction/withdrawal lasts at least 6-12 wk.

b. may be permanent or transient

5. Tardive dyskinesia

a. choreiform or orofacial movements appear while patient is on antipsychotics and persist.

Drugs	Muscarinic Anticholinergic Potency per mg. compared to Chlopromatine	Common Daily Dose (mg)	Anticholinergic Potency of Daily Dose
Tricyclics			
Amitriptyline	100	200-300	25,000
Doxepin	25	200	5,000
Nortriptyline	17	150	2,500
Imipramine	13	200-300	3,000
Desipramine	6	200	1,200
Neuroleptics			
Clozapine	40		
Thioridazine	8	600	4,800
Chlorpromazine	1	600	600
Perphenazine	0.1	25	2.5
Haloperidol	0.05	20	1.6
Antiparkinsonian Drugs			
Trihexyphenidyl (Artane)	1,500	3	4,500
Benztropine (Cogentin)	600	6	3,600
MAO Inhibitors	<.01	75	0.75

Adverse Effects of Psychotropic Drugs on Specific Organ Systems

	CARDIAC	HEPATIC	RENAL	CNS
MAJOR TRANQUILIZERS				
1. Indications: Psychoses, acute severe agitation, OMS				
2. Problems	↓ BP, arrhythmia, Δ EKG	Metabolic rte., jaundice, sedation	Labile BP, metabolic rte, sedation	↓ seizure threshold, sedation
3. Recommendations:	Use with caution	↓ Dose	↓ Dose	↓ Dose
4. Drugs				
a. Thorazine	↓↓ BP	↑↑ Jaundice, sedation	↓ BP, ↑↑ sedation	↓↓ BP, ↑↑ sedation syncope, incontenence
b. Mellaril	↓ BP, arrhythmia - sudden death	↑ sedation	↓ BP, ↑ sedation	↓ BP, ↑ sedation syncope, incontinence
c. Stelazine	↓ BP	↑ sedation and ↑ sensitivity to EPS	↓ BP, ↑ sedation	↓ BP, ↑ sedation syncope, incontinence
d. Haldol	Safest			
MINOR TRANQUILIZERS				
1. Indications: Moderate self-limited anxiety, agitation without psychosis, not for chronic anxiety, Use for 2-4 weeks.				
2. Problems: Major caution is small amounts can give toxic OBS in severe renal diseases.	↓ BP	↑ Sedation	↑ Sedation, acute OBS	↑ Sedation, CNS depression, OBS
3. Recomdations:	O.K.	↓ Dose	↓ Dose by 2/3	O.K.→↓ Dose by 2/3
4. Drugs				
a. Librium	O.K.	↓ Dose, Active metabolites	Renally excreted ↓↓ dose	CNS depression, confusion
b. Valium	O.K.	↓ Dose, Active metabolites	↓ Dose, non-renally excreted	CNS depression, confusion
c. Serax	Preferred	No active metabolites	↓ Dose	↓ Dose

TRICYCLIC ANTIDEPRESSANTS

1. Indications: Established depression with a life of its own; chronic pain syndrome.

2. Problems:	CARDIAC	HEPATIC	RENAL	CNS
	↓ or ↓↓BP, tachycardia, ↑ IV conduction delay, myocardial depression. Use caution.	Hepatic metabolism. ↓ cerebral function, acute OMS	↓↓ BP, non-renal metabolism. Vascular instability, volume depletion.	Confusion
3. Drugs				
a. Amitryptilene: very anticholinergic Nortryptilene: weakly anticholinergic	All TCA's have some anti-adrenergic activity. Note differences in anticholinergic effects. Interact with antiarrhythmics, antihypertensives, anticoagulants.	Same as for Cardiac	Same as for Cardiac	Same as for cardiac
b. Imipramine and desimipramine: weakly anticholinergic				

QUADRACYCLIC ANTIDEPRESSANTS

	CARDIAC	HEPATIC	RENAL	CNS
SEDATIVES				
1. Barbiturates - short acting	Agitation	Hepatic coma	↓ Dose, acute OBS non-renally excreted	? May be idiosyncratic ? ↓REM, Δ SWS
2. Barbiturates - long acting	↓ Dose	↓ Frequency of dose	Contraindicated	Same as for short-action
3. Chloral Hydrate	O.K.	Metabolized in liver, ↓ dose	↓ Dose, Acute OBS	No effects on REM or SWS
4. Paraldehyde	O.K.	Hepatic coma	Non-renally excreted	O.K.
5. Dalmane	O.K.	↓ Dose	↓ Dose, acute OBS	Idiosyncratic
NARCOTICS				
1. Morphine	↓ BP	Contraindicated	O.K.	O.K.
2. Demerol	↓ BP, contra-indicated with atr. fibril.	O.K.	O.K.	O.K.
3. Codeine	↓ BP	?	O.K.	O.K.

	CARDIAC	HEPATIC	RENAL	CNS
STIMULANTS				
1. Indicators: Temporarily activate invalid, withdrawn medically ill; potentiate analgesics, counteract sedation of other drugs.				
2. Problems: Tolerance; tachyphylaxis; abuse possible, not invariable.				
3. Drugs				
a. D-amphetamine	↑ BP	Hepatic metabolism	Watch BP, HR	Perhaps ↑ toxicity agitation, confusion
b. Ritalin[R]	Few peripheral effects	Hepatic metabolism	Watch BP, HR	Same as D-amphetamine

SOME DRUGS CAUSING PROMINENT MOOD CHANGES

Depressive Mood Change	Reserpine	Aldomet	Propranolol	Clonidine	Steroids	INH SM ETH	Cycloserine	L-Dopa	BCP
Incidence	5-76%	4%	?	?	40-50%	Depression 1-10%	3-10%	4%	3-6%
Dose	>0.5 mg d	?	?	?	Variable >40 mg	Rx	0.5-1.0g	3.5g	Rx
Risk Factors	⊕Hx Dep	?	Current Dep ? ⊕ Hx	?	Psych Hist ? Not Risk	?	?	MDD Dep {1/3↑ 2/3↓	Past Hist No Risk
Onset	2W-2M	?	Sudden	MOS	3-4D	?	?	>3MOS	?
Course	1.Pseudo-Dep 2.Dep Gradual	Sudden	?	?	Euphoria ⩾ Depress Lability	?	Hostile Dep Paranoid	Mood 1.Improved 2.Dep 4% 3.Manic 2%	?
Rx	D/C→ TCA ECT	TCA	D/C	D/C	DDX 1.Mood 2. Cognition	D/C	D/C	D/C	D/C

From: American Psychiatric Association PKSAP-IV Syllabus (1979)

Interaction by Pharmacologic Category

Drug	Interacts with	Effect	Mechanism
1. Neuroleptics	psychomotor stimulants	↑ stimulation at low doses ↓ effect at higher doses	inhibition of metabolism receptor antagonism
	epinephrine	epinephrine reversal	α-blockade, permitting unopposed β-stimulation
	antihistamines	potentiation of antihistamine effect	additive at receptor site
	antihypertensives except guanethidine	potentiation of antihypertensive and orthostatic effect	additive blockade of dopamine
	anticholinergics	(a) ↑ anticholinergic effects (b) ↓ neuroleptic levels	(a) additive (b) enzyme induction
	oral hypoglycemics	↑ hypoglycemic effect	?
	L-dopa	↓ L-dopa effects	dopamine receptor blockade
	methyldopa	↑ extrapyramidal side effects	↓ dopamine effect-additive
2. Phenothiazines	guanethidine	↓ antihypertensive effect	blockade of neuronal uptake of guanethidine
	hydroxyzine	↓ phenothiazine effect	?
	CNS sedatives	sedative and hypotensive effects	additive
	barbiturates	↓ phenothiazine levels	enzyme induction
	MAOIs	(a) ↑ phenothiazine levels (b) ↑ hypotension	(a) enzyme inhibition (b) additive
	phenytoin	↑ phenytoin levels	enzyme inhibition
	oral anticoagulants	↑ anticoagulant effect	enzyme inhibition?
	halogenated anesthetics	profound hypotension	additive?
	succinylcholine	prolonged neuromuscular blockage	↓ anticholinesterase levels
	thiazides	hypotension	additive
	digoxin steroids	increased absorption	↓ GI motility
	estrogens	↑ phenothiazine levels	?
	cholestyramine activated charcoal	↓ phenothiazine levels	formation of non-absorbable complex
	fruit juice, milk, coffee, tea	↓ phenothiazine levels	non-absorbable complex
	chloroquine	↑ extrapyramidal side effects	?
	antacids	↓ phenothiazine levels	?
3. Thioridazine Mesoridazine	hydroxyzine	cardiotoxicity	potentiation of thioridazine and mesoridazine toxicity
	diuretics corticosteroids	enhancement of thioridazine and mesoridazine cardiotoxicity	hypokalemia
	quinidine	heart block	potentiation of quinidine effects
4. Chlorpromazine	piperazine	seizures	?
	acetaminophen	↑ chlorpromazine effects	inhibition of chlorpromazine metabolism
	cigarette smoking	↓ chlorpromazine effects	enzyme induction—may be true for other psychotropics as well
5. Haloperidol	oral anticoagulants	↓ anticoagulant effect	enzyme induction
	methyldopa	potentiation of haloperidol	synergism at receptor sites
6. Tricyclics	barbiturates	antidepressant effect	enzyme induction
	methyldopa clonidine	antihypertensive effect	?

Interaction by Pharmacologic Category (*Continued*)

Drug	Interacts with	Effect	Mechanism
	guanethidine	↓ antihypertensive effect	blockade of uptake at target site—minimal with doxepin
	L-dopa	↓ L-dopa effect	↓ absorption
	sympathomimetic amines	↑ hypertensive effect	inhibition of re-uptake
	methylphenidate	↑ antidepressant effect	enzyme inhibition, synergism
	neuroleptics	↑ levels of both, ↑ side effects	enzyme inhibition
	MAOIs	(a) mutual potentiation of antidepressant effect (b) acute hypertensive response	(a) synergism at receptor site (b) uptake blockades
	CNS depressants, sedatives	potentiation of sedative and hypotensive effects	additive
	quinidine	heart block	additive
	ethchlorvynol	delirium	?
	chloral hydrate alcohol methaqualone glutethimide diphenhydramine cigarettes	↓ antidepressant effect	enzyme induction
	central anticholinergics	(a) ↓ tricyclic levels (b) anticholinergic toxicity	(a) enzyme induction (b) additive
	thyroid hormone	mutual enhancement of response	?
	diuretics	orthostatic hypotension	additive
	reserpine	reversal of sedative and hypotensive effect	?
	oral anticoagulants	↑ anticoagulant effect	enzyme inhibition
	phenylbutazone	↓ phenylbutazone absorption	↓ GI motility
	antihistamines	enhanced cardiotoxicity of tricyclic	mutual potentiation—additive
	methyltestosterone	paranoid psychosis	?
7. Imipramine	anticonvulsants	(a) ↓ tricyclic levels (b) ↑ anticonvulsant levels	(a) enzyme induction (b) enzyme inhibition?
	estrogen	lethargy, nausea, headache, tremor, hypotension	?
8. Amitriptyline	diazepam	↑ amitriptyline levels	?
	methyldopa	tachycardia, ↑ blood pressure	?
9. MAOIs	hypoglycemics	↑ hypoglycemia	?
	meperidine	hypotension and coma	?
	tyramine sympathomimetic amines, especially epinephrine, norepinephrine	hypertensive crisis	enzyme inhibition
	L-dopa	hypertensive crisis	enzyme inhibition
	phenothiazines	(a) ↑ phenothiazine levels (b) hypotension	(a) enzyme inhibition (b) additive effect
	barbiturates, other sedatives	prolonged barbiturate effect	enzyme inhibition
	central anticholinergics	(a) potentiation of anticholinergic effect (b) potentiation of antidepressant effect	(a) enzyme inhibition (b) ?

Interactions by Pharmacologic Category (*Continued*)

Drug	Interacts with	Effect	Mechanism
	anesthetics	(a) ↑ anesthetic dose requirement	(a) ↑ levels of presser amines
		(b) hypotension	(b) additive
	prazosin hydralazine	potentiation of hypotensive effects	(a) enzyme inhibition (b) additive effect
	thiazides	hypotension	additive
	reserpine	hypertension	inhibition of metabolism of released norepinephrine
	guanethidine	hypotension	additive
	hypoglycemics	hypoglycemia	additive
	thyroid hormone	↓ antidepressant effect	?
	doxapram	CNS stimulation, hypertension	synergism
	succinylcholine	prolonged muscle relaxation	enzyme inhibition
10. Lithium	thiazides	↑ lithium levels, toxicity	↑ Na reabsorption in proximal tubule
	xanthine derivatives	↓ lithium levels	↑ lithium excretion
	tricyclics	↓ tricyclic levels	?
	neuroleptics	(a) ↑ hyperglycemic effect (b) ↑ extrapyramidal side effects	(a) additive (b) synergism
	methyldopa	↑ extrapyramidal side effects	synergism
	succinylcholine	prolonged neuromuscular blockade	?
	hydroxyzine	cardiotoxicity	↑ lithium effects on cardiac repolarization
	nephrotoxic antibiotics	lithium toxicity	↓ lithium excretion
	indomethacin phenylbutazone	lithium retention and toxicity	enhancement of ADH → lithium retention
	digoxin	enhanced digoxin toxicity	intracellular hypokalemia induced by lithium
	antidepressants	potentiation of antidepressant effect	?
	alcohol	lithium toxicity	lithium retention
	succinylcholine	prolongation of relaxation	?
11. Benzodiazepines	antacids	diazepam, chlordiazepoxide: reduces rate of absorption prazepam, chlorazepate: prevents transformation to active form	↑ gastric pH
	CNS sedatives	enhanced CNS depression	additive
	MAOIs	enhanced benzodiazepine effect	enzyme inhibition
12. Diazepam	amitriptyline	↑ amitriptyline levels	enzyme inhibition
	succinylcholine	prolongation of neuromuscular blockade	additive?
13. Chlordiazepoxide	disulfiram	↑ chlordiazepoxide levels	enzyme inhibition
14. Disulfiram	isoniazid	psychosis, ataxia	alteration in catecholamine metabolism
	oral anticoagulants	↑ anticoagulant effect	enzyme inhibition
	phenytoin	↑ phenytoin effect	inhibition of enzymes
	long-acting benzodiazepines	prolongation of benzodiazepines	enzyme inhibition

Interactions by Pharmacologic Category (*Continued*)

Drug	Interacts with	Effect	Mechanism
15. Chloral hydrate	oral anticoagulants	↑ anticoagulant effect	displacement from protein binding sites
	CNS depressants	prolonged sedation	synergism
	furosemide	vasomotor instability	?
	tricyclics	↓ tricyclic levels	enzyme induction?
16. Barbiturates	(a) chronic alcoholism	(a) ↓ sedative effect	(a) enzyme induction by alcohol
	(b) acute alcohol intoxication	(b) ↑ CNS depression	(b) additive, ↓ metabolism
	anticoagulants, antidepressants, steroids, digitoxin, neuroleptics, quinidine	↓ effects	induction of microsomal enzymes
	rifampin	↓ barbiturate effect	enzyme induction
	tetracycline	↓ tetracycline levels	enzyme induction

I ANTIPSYCHOTICS

A Phenothiazines

1. Aliphatic Subgroup

   Chlopromazine (Thorazine)

2. Piperidine Subgroup

   Thioridazine (Mellaril)

   Mesoridazine (Serentil)

3. Piperazine Subgroup

   Acetophenazine (Tindal)

   Prochlorperazine (Compazine)

   Perphenazine (Trilafon)

   Trifluoperazine (Stelazine)

   Fluphenazine (Prolixin)

B Thioxanthenes

   Thiothixene (Navane)

   Chlorprothixene (Taractan)

C Butyrophenone

   Haloperidol (Haldol)

D Dibenzoxazepine

   Loxapine succinate (Loxitane)

E Dihydroindolone

   Molindone (Moban)

II STIMULANTS

1. Dextroamphetamine (Dexadrine)
2. Pemoline (Cylert, Cylert Chewable Tablets)

3. Methylphenidate (Ritalin)

III ANTIDEPRESSANTS

A MAO Inhibitors

1. Hydrazines

Phenelzine (Nardil)

Isocarboxazid (Marplan)

2. Nonhydrazines

Tranylcypromine (Parnate)

B Tricyclics

Imipramine (Tofranil, Presamine)

Desipramine (pertofrane, Norpramin)

Amitriptyline (Elavil, Endep)

Nortriptyline (Aventyl)

Protriptyline (Vivactil)

Doxepin (Sinequan, Adapin)

IV ANTIANXIETY AGENTS

A Benzodiazepines

Diazepam (Valium)

Chlordiazepoxide Hydrochloride (Librium)

Oxazepam (Serax)

Lorazepam (Ativan)

B Barbiturates

Phenobarbital

C Glycerol Derivatives

Meprobamate (Miltown, Equanil)

Tybamate

D Diphenylmethane Antihistaminics

Hydroxyzine Pamoate (Vistaril)

Diphenhydramine Hydrochloride (Benadryl)

V SIDE EFFECTS OF ANTIANXIETY AGENTS

Drowsiness, Sedation

Ataxia

Paradoxical agitation reaction

Depression-like syndrome

Organic brain syndrome

VI SIDE EFFECTS OF LITHIUM

Dose Related

Lethargy, Sluggishness, patient dazed, muscle twitchings, hand tremor (fine or coarse)

Extrapyramidal signs (predominantly parkinsonism)

EEG abnormalities

Seizures

Increased muscle tone

Nausea, vomiting, abdominal pain

Polyuria

Excessive thirst

Coma

Nondose Related (Idiosyncratic)

Organic brain syndrome, usually reversible off lithium.

Hashimoto's disease-like syndrome with diffuse thyroid enlargement; usually without disturbance of thyroid function, but there are some reports of hypothyroidism.

Diabetes-insipidus-like syndrome with polyuria and excessive thirst.

Leukocytosis (as high as 20,000 cells per cubic milliliter or slightly greater)

Teratogenic effects

Skin eruptions; begin as acneiform papules that may erupt, coalesce, and/or spread.

Flattening or inversion of T-wave on EKG

VII SIDE EFFECTS OF ANTIPSYCHOTICS

A Vital Signs

1. Blood pressure. Orthostatic hypotension (hypotension resulting from change from lying to sitting or standing or sitting to standing positions) in most cases; severe cases heavy hypotension in supine (lying flat on back) position.
2. Pulse rate. Tachycardia (increased heart rate)
3. Respiratory rate. Tachypnea (increased breathing)

4. Temperature
5. Weight Increase

B Central Nervous System

1. Sedation. Usually self-limited, ending approximately two to three weeks after final increase of medication.
2. Organic Brain Syndrome.
3. Worsening of Psychosis
4. Lowering of seizure threshold
5. Extrapyramidal disorders: Parkinsonism, hypokinesia, mask-like faces, drooling, stooped posture, loss of associated arm movements on walking, shuffling gait, cog-wheel rigidity: usually has its onset 5 - 20 days after onset of major tranquilizer treatment

   Acute dystonia and dyskinesia:

   Dystonia: Irregular, nonrhythmical, involuntary movements or postures of the trunk, limbs, face, tongue or neck; including retrocollis (fixed posterior movement of head) tortocollis (fixed lateral movement of head), opisthotonus (fixed arching of the back), and oculogyric crisis (head and eyes turned superiorly): usually has its onset one hour to five days after onset of major tranquilizer treatment.

Dyskinesia: Rhythmical, involuntary movements of the trunk and limbs: usually has its onset one hour to five days after onset of major tranquilizer treatment.

Akathesia: Motor restlessness; the individual cannot sit still for longer than a few seconds: onset usually five to 40 days from onset of major tranquilizer treatment.

Tardive Dyskinesia: Lip smacking, darting tongue (like a frog catching flies), inconsistent lateral jaw movements, all of which may be accompanied by axial hyperkinesis (anterior-posterior rocking of trunk), tonic contractions of neck, choreoathetoid movements of fingers and toes, and foot tapping: onset usually after 100 days of major tranquilizer therapy.

C Eyes:

1. Retina. Retinitis pigmentosa-like syndrome
2. Anterior compartment:

Anterior Lens and Posterior Cornea: Disposition of pigment.

Blurring of vision and potential intraocular pressure increase.

D Nose: Dryness, stuffiness

E Mouth: Dryness with occasional thirst. Few reported cases of oral moniliasis.

F Neck: Increased PBI and I_{131} uptake.

G Thorax:

Bronchopulmonary axis. Tachypnea

Heart. Prolonged Q-R interval and depressed or inverted T-wave on EKG, ventricular arrhythmias.

Breasts (female). Galactorrhea

H Abdomen: Gastrointestinal tract. Constipation, dysphagia

Liver: Various degrees of an acute hepatitis-like syndrome, including malaise, lassitude, nausea, vomiting, abdominal pain, hepatomegaly, jaundice, pruritis, and abnormalities in one or more liver-function tests (SGOT, SGPT, total/direct bilirubin, alkaline phosphatase)

I Reproductive Tract:

Female: Hypomenorrhea or amenorrhea

Male: Impotence, inhibition of ejaculation, retrograde ejaculation.

J Urinary Tract Function: Urinary hesitancy and retention

PSYCHOPHARMACOLOGY IN THE MEDICALLY ILL

I. Interactions with General Properties of Illness

A. Vital Signs

1. Temperature

a. phenothiazines and butyrophenones can cause hyperpyrexia by poorly understood mechanisms.

b. phenothiazines suppress thermoregulation at the hypothalamic level and can mask fever.

c. singly or in combination MAOIs, tricyclics, and lithium can cause hyperpyrexia.

d. physostigmine (1-3 mg IM/IV) is antidote for hyperpyrexia due to tricyclics or anticholinergics.

2. Pulse: neuroleptics and tricyclics may cause tachycardia and arrhythmias due to a combination of central actions and as a reflex to peripheral adrenergic blockade.

3. Respiration

a. anticholinergic effects on secretions

b. neuroleptics can profoundly suppress respiration, especially in the critically ill (Post-cardiac surgery), presumably by general over-sedation.

4. Blood Pressure

a. postural hypotension: TCA and phenothiazines (>15 mm Hg)

b. phenothiazine induced hypotension is most marked in non-smokers, elderly, and elevated systolic (>140)

K Skin:

Diffuse maculopapular urticaria.

Localized contact dermatitis-like picture.

Photosensitivity reaction, Sun-exposed areas demonstrate sunburn-like picture, which, without treatment, may progress to brown to purplish to bluish areas of pigmentation (slate-blue skin)

L Hematopoietic System:

Pancytopenia.

Agranulocytosis. Manifested by elevated temperature and sore throat, pharyngeal inspection usually reveals erythema and ulcerations, and the c.b.c. shows a decline and/or significant reduction to only a few white cells, specifically neutorphils; may occur at any time after major tranquilizer treatment initiation, but is usually seen between six and eleventh week of therapy; any evidence of sore throat and/or elevated temperature requires immediate c.b.c. with differential and serial c.b.c.s with differential, as indicated, regardless of the duration of major tranquilizer treatment.

VIII SIDE EFFECTS OF TRICYCLIC ANTIDEPRESSANTS

A Vital Signs

1. Blood Pressure. Orthostatic hypotension in most cases; severe cases have hypotension in supine position
2. Pulse Rate
3. Temperature
4. Weight

B Central Nervous System

1. Sedation. Usually self-limited, ending approximately two to three weeks after final increase of medication.
2. Organic Brain Syndrome
3. Worsening of existing delusions, hallucinations, incipient of manifest schizophrenia, or making incipient delusions manifest.
4. Lowering Seizure Threshold
5. Extrapyramidal Disorders. Can make latent tardive dyskinesia manifest.
6. Fine tremor of upper extremities.
7. Sweating of head and neck.

C Eyes

1. Blurring of Vision
2. Decreased accommodation
3. Elevation of intraocular pressure

D Nose Nasal dryness, stuffiness

E Mouth Dryness with occasional thirst; occasional reports of moniliasis.

F Heart T-Wave flattening and inversion; lengthwise of P-R interval; tachycardia; lengthening of QRS complex; lengthening of Q-T interval; second degree or complete A-V block; ventricular arrhythmias (ventricular premature depolarization, ventricular tachycardia, ventricular fibrillation); atrial arrhythmias (atrial tachycardia, atrial flutter, atrial fibrillation).

G Abdomen

1. Gastrointestinal tract. Constipation
2. Liver. Various degrees of an acute hepatitic-like syndrome, including malaise, lassitude, nausea, vomiting abdominal pain, hepatomegaly, jaundice, pruritis, and abnormalities in one or more liver function tests (SGOT, SGPT, total/direct bilirubin, alkaline phosphate).

H Genitourinary Tract

1. Urinary Tract. Urinary hesitancy or retention
2. Reproductive Tract.

   Female: Amenorrhea and irregular menses

   Male: Orgasmic or ejaculatory dysfunction (absent or delayed).

I Skin Systemic reaction.

MEDICALLY ILL (CONT.)

J Hematopoietic System

Agranulocytosis, manifested by elevated temperature and sore throat; pharyngeal inspection usually reveals erythema and ulcerations, and the c.b.c. shows a decline and/or significant reduction to only a few white cells, specifically neutrophils; may occur at any time in treatment, but usually occurs between sixth and eighth week of therapy; any evidence of sore throat and/or elevated temperature requires immediate c.b.c. with differential and serial c.b.c.s with differential, as indicated, regardless of the duration of tricyclic antidepressant treatment.