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A REVIEW OF PSYCHOPHARMACOLOGIC DRUGS

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Almost every week a new drug is marketed which is aimed at altering psychic behavior. This review is an attempt to group and to clarify the actions of this growing multitude. In many cases the actions of members of a group are essentially identical and the choice will be determined by which sales representative visited you or by a chance initial favorable response to one of them. There are however some advantages which may prove helpful in solving specific problems. The following is a general outline of current drugs, their indications, dosage, and side effects.

I. Psychic inhibitors

- A. Sedatives (in moderate doses) and Hypnotics (in larger doses) These reduce the activity of the cortex primarily although in large doses the functions of other portions of the nervous system may be reduced. No effect on delusions or other psychotic processes.
 - 1. Barbiturates Although this is a large group, many doctors do not take advantage of their varied durations of action. Short acting compounds given to older persons may produce delirium whereas the longer acting ones may not. A person having trouble falling asleep will benefit more from a short acting drug which will not impair his awareness upon arising while the person who can not remain asleep may require a longer acting compound. If given for pain without analgetics in addition, these may produce delirium. The prolonged administration of as little as 4 grains of sodium amytal daily may produce habituation with a withdrawal syndrome including convulsions.
 - 2. Bromides skin reactions and toxic psychoses may result.
 - Chloral hydrate usually well tolerated by even the aged. 0.5-1.0 gm. available in capsules and liquid.
 - Paraldehyde an ideal potent drug except for taste and odor. 5-10 cc.
 This objection can be reduced by taking in iced fruit juice. Paral (Fellows) 1.0 gm. capsules are also available.
 - 5. Doriden (Ciba) 250 mg t.i.d. for sedation, 500 mgm, h.s. for sleep.
 - 6. Noludar (Roche) 50 mg for sedation, 200 mg for sleep. Similar to pentobarbital.
 - 7. Carbital (Parke-Davis) 1 capsule for sleep.
 - 8. Valmid (Lilly) 500 mg; very rapid short action; for sleep.
 - 9. Lotusate (Winthrop-Stearns) 50 mg t.i.d.
 - 10. Placidyl (Abbott) 100 mg t.i.d. for sedation; 500 mg for sleep.
 - 11. Quiactin (Merrell) 400 mg q.i.d. for sedation.
 - 12. Softran (Stuart) 50 mgm t.i.d.
 - 13. Suvren (Ayerst) 100 mg t.i.d.; also spasmolytic.
 - 14. Scopolamine.

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- 15. Narcotics use only when severe pain is a factor.
- 16. Meprobamate 400 mg q.i.d. This is basically a sedative although it also has a definite effect upon the peripheral neuromuscular system producing muscle relaxation; actually this may be its primary action. Conditioned responses are blocked only at neurotoxic levels. Like barbiturates it is habituating and withdrawal syndromes may follow its discontinuance. Aplastic anemia and three deaths have been reported. It is a poor drug for producing sleep but is of special benefit in conditions where muscle relaxation as well as sedation is desired as in wry neck, tension headache, neuromyositis, etc.
- B. Neuroleptics these block conditioned and avoidance responses and are especially good for reducing aggressivity. In moderate doses cortical activity and peripheral actions are not impaired but persons working around moving machinery or driving should be cautioned and watched carefully initially as some persons are affected. Barbiturates and alcohol are potentiated. This must be considered in anaesthesia and in the patient who might have his usual few drinks and attempt to drive.
 - Rauwolfia compounds these act by liberating serotonin and biologically active catecholamines from various body cells whereupon they are destroyed by oxidases, especially monoamine oxidase. Adenosine triphosphate levels are also altered. These drugs act more slowly than phenothiazines and are more likely to produce parkinsonism, asthenia, depressions so are not widely used now.
 - 2. Phenothiazines these may act by interfering with the action of nor-epinephrine in the brain.

Trade name	Manufacturer	Chemical name	Comparable Dose
Compazine	SKF	prochlorperazine	10 mg
Dartal	Searle	thiopropazate	10
Mellaril	Sandoz	thiodiazine	25
Pacatal	Warner	mepazine	50
Permitil	White	triflurmethyl phenazine	0.25
Prolixin	Squibb	fluphenazine	1
Sparine	Wyeth	promazine	50
Stelazine	SKF	trifluoperazine	2
Tentone	Lederle	methoxypromazine	25
Thorazine	SKF	chlorpromazine	25
Trilafon	Schering	perphenazine	4
Vesprin	Squibb	triflupromazine	10

Indications — Hyperactivity, panic, agitation, assaultiveness, destructiveness, obsessions and compulsions (but to a lesser degree), acting out especially when it is interfering with psychotherapy, and to reduce the awareness of pain when symptoms are physically painful. Schizophrenia may possibly be associated with excessive transamination in which case rauwolfia and phenothiazines would be chemically indicated. In the acute forms without paranoia or profound dissociation

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phenothiazines produce a cure of better quality and duration than does insulin coma. The paranoid type does better on phenothiazines than with either EST or insulin. The catatonic form does better with EST. The chronic form does as well on phenothiazines as any other therapy. Improvements seen with phenothiazines are of better quality than spontaneous cures. Initially some patients feel a void where the "voices" had counselled or governed them and experience difficulty at first in making their own decisions. Catatonic stupor and excitement are usually relieved. "Word salad" disappears and meaningful speech becomes possible.

The apperception of incoming stimuli both from within and from the environment is apparently reduced. Defenses and inhibitions may then be reduced as that against which they were defending is perceived as less threatening. Perhaps because the energies of instinctual drives is lessened the superego is not as rigid in denouncing them. Secondary delusions, obsessions, and compulsions become less imperative. The patient begins to feel less fearsome and less fearful both of himself and of others. Innate energies are released for further reorganization and reality testing and the personality undergoes progressive psychologic changes on the basis of more successful living. This may be hastened by psychotherapy. As the patient's behavior toward those about him improves, they will become more friendly toward him thus creating an improved and more gratifying environment.

In neurotics the dulling and stabilization of the autonomic system's functions reduces the physical complaints so that the patient can better see beyond them and concentrate on psychotherapy. The phenothiazines are often helpful in this without depressing cortical activity as much as the sedative group. Vague, generally uncomfortable, free-floating anxiety is not particularly relieved by any drug. The administration of any drug tends to increase the positive transference toward the doctor. This plus the attitude of the dispensing physician may produce powerful placebo effects of which you must be constantly cognizant. If the patient has no insight into the fact that psychologic factors are creating the symptoms and if you relieve the symptoms with drugs, it is possible that he may no longer desire to do anything about the cause but merely continue to demand the drugs. This is usually undesirable although in some individuals psychotherapy may not be feasible and also spontaneous cures under drugs alone are not unknown. Pathogenic drives are more readily affected than normal activities. However, if, as in character disorders, no such sharp distinction exists, an effective dose will likewise obtund normal functioning. In these only long term psychotherapy is indicated.

Complications with phenothiazines — The incidence of side effects is roughly proportional to the dosage but some individuals may react

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to even small doses. These reactions usually appear within the first two weeks so the patient should be observed carefully during that period. It is probably good practice to check the white blood count at the end of that period. The most common complication is the development of a Parkinson-like syndrome. Both this and akathisia respond well to a reduction in the dose plus one of the anti-Parkinson drugs (Artane, Cogentin, Kemadrin). Akathisia consists of motor restlessness, inner sensations of jitteriness, and restless feelings in the legs. This is difficult to distinguish from the symptom for which you may be giving the drug and, unles you are alert for its occurence, you may increase the dosage and only aggravate the situation. All of the phenothiazines may cause a toxic hepatitis with jaundice although this is less frequent in the newer compounds. Skin rashes may occur not only from consuming the drug but from handling it especially the injectionable solutions. Other side effects may be dry mouth, drowsiness, hypotension, dyskinetic spasms and movements, fibrillary twitchings, and agranulocytosis. Should any hypotension be prolonged intravenous nor-adrenalin is indicated.

Symptoms in psychiatry are the patient's deviant expressions of his inability to face himself and his inner impulses. The alteration or control of these symptoms by a drug may be experienced by the patient as either beneficial or undesirable. This is determined to a large degree by the attitudes of the doctors, nurses, and others around him. Some may see the doctor, hospital, and the medications as part and parcel of a threatening situation against which they must muster every defense. The administration of drugs may thus be followed by more disturbed paradoxical behavior sometimes similar to akathisia; this however is not relieved by anti-parkinson drugs.

- 3. Diphenyl methane derivatives.
 - a. Hydroxyzines
 - (1) Atarax (Roerig) 25 mg t.i.d.
 - (2) Vistaril (Pfizer) 25 mg t.i.d.
 - b. Benactyzine of Suavitil (Merck) 1 mg t.i.d.
 - c. Azacyclonol of Frenquel (Merrell) 100 mg t.i.d.

These compounds are closely related to antihistamines and perhaps act by blocking some of the actions of serotonin. They are considerably weaker than phenothiazines but have somewhat similar indications.

II. Psychic activators

- A. Stimulants enhance conditioned avoidance behavior and arousal. These may be helpful for moderate asthenia, tiredness, or depression but a tolerance tends to develop quickly.
 - 1. Amphetamines potent

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- 2. Meratran (pipradrol) Merrell 2.5 mg b.i.d. milder
- 3. Ritalin (phenidylate) Ciba 5 mg t.i.d. milder

B. Energizers

1. Hydrazines — The current theory is that these act by preventing the destruction of serotonin and catecholamines by mono-amine oxidase however there are some doubts now that this completely and accurately explains the action. Since depression is postulated to be related to excessive oxidative deamination, this group of drugs was tested for anti-depressive action and has proven to be helpful in many cases. The action however is not dramatic and may require as long as a month. If the depression is not severe or if EST is contraindicated in severe depressions, these drugs are useful. In severe depressions, however, the danger of suicide often makes the more rapid treatment by EST preferred. Hypotension, constipation, jitteriness, and jaundice may occur.

 Marsilid 	iproniazid	Roche	25-50 mg tid
b. Marplan	benzyl hydrazine	Roche	10 mg tid
c. Nardil	phenethyl hydrazine	Warner	15 mg tid
d. Niamid	a complex hydrazine	Pfizer	25 mg tid
e. Catron	phenylisoproply hydrazine	Lakeside	3 mg tid

- Tofranil dibenzephine Geigy 25-50 mg q.i.d.
 The action of this compound is not understood but empirically it has proven useful in combating depressions. Excessive sweating, dry mouth, and jitteriness may occur.
- Deaner diethylamino ethanol Riker 50 mg t.i.d.
 The action of this drug is much weaker than those above and is based upon the postulated conversion of the drug into acetyl choline which passes through the blood-brain barrier.

III. Psychomimetics or Dysleptics

This group consists of a number of compounds containing an indole nucleus such as lysergic acid diethylamide (LSD) and mescaline. Their effect may be through interfering with serotonin metabolism or other brain metabolic functions especially with carbohydrates. Their use thus far has been limited to experimental studies of the psychic and biochemical changes induced.

IV. Placebos

This group of "drugs" is probably the most neglected of all although repeated studies have shown that 25-35% of subjects reported definite improvement; some even developed remarkable "side effects". If the physician is able to afford his patient relief without introducing any potent and possibly harmful drug into his system, is he not to be more highly commended? This also helps prevent overenthusiastic claims for a drug when the favorable results are more closely related to the doctor's enthusiastic approach to the patient.