Psychopharmaceuticals: Effects and Side Effects

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Drugs which affect psychological behaviour are being used in vast amounts nowadays, with, in all too many cases, but scant regard for their exact uses or possible side effects. This article contains a clinical classification of these drugs, followed by an account of their principal side effects and the means of obviating them.

CLINICAL CLASSIFICATION OF PHARMACEUTICALS INFLUENCING PSYCHOLOGICAL STATES

Even the full-time worker in the field becomes confused at times by the plethora of names and descriptive terms used for drugs influencing psychological states. The classifications of the drugs proposed by various authorities during the past four years are actually in quite close agreement; difficulty arises because a variety of terms are employed to describe a single principle of drug action, and because at other times one and the same name is used to indicate quite different groups of pharmaceuticals. I list the common alternatives, with an indication of those which appear to me most suitable, and the reasons for such a choice.

The entire group of drugs

The most concise term designating all drugs which affect psychological function is PSYCHOPHARMACEUTICALS. "Tranquillizers" is obviously unsuitable, since stimulants are included in this group. The alternative, "psychochemicals," should be reserved for the even broader category of chemical substances, whether exogenous or endogenous, that are involved in psychological functioning. Psychopharmaceuticals are limited to substances of exogenous origin. As for the frequently used term "phrenotropic", this literally means mind-influencing, and is perfectly acceptable. The alternative "neurotropic" (influencing the nerves), although not particularly objectionable, introduces a theoretical assumption which may or may not be warranted. We should seek out words that make clear the actions of pharmaceuticals in terms of their effect on psychological behaviour; whether a drug does or does not alter brain function is irrelevant to this purpose. A term such as "neurotropic" also prejudgethes the case, by presuming that the sole or major site of action is the brain, whereas there is certainly a real possibility that the endocrine glands, the liver, or other organs of the body may be of equal importance.

There are three major categories of psychopharmaceuticals: (1) drugs which restrict, limit, restrain or depress either normal or abnormal psychological functioning, (2) drugs which increase, elevate, arouse or stimulate either normal or abnormal psychological functioning, and (3) compounds which produce abnormal psychological states of one kind or another.

1. The psycho-inhibitors. This term, which means that they restrict or restrain psychological activity, is selected because it describes the outstanding characteristic of the entire group and is itself a neutral word. The term "tranquillizers," originally used to designate a particular sub-category, is sometimes assumed to refer to all the psycho-inhibitors. Another alternative, "depressants," has a specific physiological meaning which implies a particular mode of action. It is also too closely associated with "depression", as used in reference to the emotional state. Professor Delay has proposed the term "psycholeptic", which is perfectly acceptable. It is only that the suffix "inhibitor" is a more familiar one to English readers.

The psycho-inhibitors may be divided into the following sub-categories:

(a) Hypnotics: drugs which induce sleep (whatever other action they have).

(b) Sedatives: compounds which reduce excitement, agitation and overactivity, whether physical or psychological. The ideal sedative would be one
which, regardless of the magnitude of the dose, would not produce hypnosis.

(c) Muscle relaxants: pharmaceuticals which have as their primary action the relaxation of muscular tension. They apparently thereby break the feedback chain of anxiety ⇔ tension. The effects are not dissimilar to hydrotherapy. They may be said to constitute “a Turkish bath in a tablet”.

(d) Ataraxics (noun: ataractic; adjective: ataractic): This term means freeing from turmoil and confusion. A great deal of stress has been laid on the capacity of these drugs to reduce, restrain and restrict hypermotility and emotional excitement. If the drugs did only this there would be no reason to classify them as other than super-sedatives. The one really unique property which they possess is their capacity to remove, reverse, restrict or inhibit psychopathological states, including hallucinations and delusions—a property not possessed by the sedatives or the hypnotics. A new term was needed to designate this action; but since the *modus operandi* was unknown it seemed sensible to avoid any implication as to whether it was biochemical, neurological, or something else.

Although the term neuroleptic, as proposed by Professor Delay, has had quite widespread acceptance on the Continent of Europe, it implies a more or less specified mode of action, which may be quite correct, but for which sufficient evidence is not yet available to be certain. Although the ataraxics are the sub-category (of the psycho-inhibiting drugs) to which the term “tranquillizer” was originally applied, this word has been so abused that it has lost its original identity. To this might be added one other legitimate objection—that the drugs do more than merely tranquilize.

Some objection to the term has been raised since one drug firm unfortunately patented the word Atarax as a trade name (and for a drug which is not an ataractic). This pharmaceutical house has recently introduced the same compound under a different name, with what they consider more adequate recommendations on dosage, so perhaps the problem will solve itself if the new trade name supplants the older one.

(e) Undetermined: pharmaceuticals with which sufficient experience has not yet been accumulated to make a clear assignment as to where they belong. Rather than that they should be forced into a Procrustean bed, they are tentatively placed here until evidence is available on which of the above categories they belong to or on whether new sub-categories must be created.

2. *Psycho-activators*. Professor Delay’s term for this group of drugs is psycho-analeptics, to which we would take no exception, merely preferring the suffix “activator”, which is more familiar to some of us than “analptic.”

(a) Psychomotor stimulants: compounds which stimulate both psychological and motor reactions. They tend to speed up mental activity, but also introduce distractibility and hyper-responsiveness to external stimuli. As a rule they will elevate the mood, often to the point of euphoria (i.e., a feeling of more than normal elation). Blood pressure and heart rate are usually increased, although appetite is lessened.

(b) Psycho-stimulants: compounds which are capable of producing the same generalized psychological stimulation (both mental and emotional) that is possessed by the psychomotor stimulants. The dosages of psychomotor stimulants are limited in large part because of the motor side effects, which are much reduced or absent in the present sub-category. If the psychomotor stimulants could be given in sufficiently high doses the effect might be the same as this group of drugs. In any case, the decreased motor effects would place them in a different sub-category.

(c) Psychic energizers: compounds which tend to “fill the pump” rather than “speed it up”. In the treatment of depressed patients the mood is raised to a normal base-line, producing a feeling of well-being (eudaemonia), rather than elevated above the base-line (euphoria). In contrast to the stimulants, blood pressure usually tends to drop slightly, and appetite increases rather than decreases. Although both the stimulants and the psychic energizers will reduce the need for sleep, prolonged usage of the stimulants tends to produce hyperirritability, whereas with the psychic energizers some patients can go for a year or more on three or four hours of sleep per night. Rather than distractibility, there is an increased capacity to concentrate.

3. *Psychotomimetics*. Professor Delay’s category is “psycho-dysleptic”, which is also satisfactory. Although the term “hallucinogenic” might be applicable to a specific sub-category, it is too limited for the major grouping, since these compounds may produce other types of psychotic manifestations in addition to hallucinations. Although no effort
is made to be fully inclusive, some of the possible sub-categories of this group would be:

(a) Hallucinogens: producers of hallucinations (auditory, visual, sensory, etc.).

(b) Cataplexogenics: producers of rigid or unresponsive conditions in which the subject does not respond to stimuli although he is fully conscious and in no sense comatose.

(c) Euphoriants: agents which elevate mood to an abnormal degree.

(d) Chronoleptogenics: drugs which distort the sense of time.

(e) Depressants: agents which lead to an abnormally "low" mood or emotional state.

(f) Disinhibitors: compounds which remove the normal and customary inhibitions in respect of speech, fantasy, feeling and/or action.

(g) Confusants: preparations which induce in the subject a state of perplexity and/or confusion.

CLINICAL CLASSIFICATION OF PHARMACEUTICALS INFLUENCING PSYCHOLOGICAL STATES

Psychopharmaceuticals (Phrenotropics)

1. Psycho-inhibitors (Psycholeptics)
   (a) Hypnotics
   (b) Sedatives
   (c) Muscle relaxants
   (d) Ataraxes (neuroleptics)
   (e) Unclassified

2. Psycho-activators (Psycho-analeptics)
   (a) Psychomotor stimulants
   (b) Psycho-stimulants
   (c) Psychic energizers

3. Psychotomimetics (Psycho-dysleptics)
   (a) Hallucinogens
   (b) Cataplexogenics
   (c) Euphoriants
   (d) Chronoleptogenics
   (e) Depressants
   (f) Disinhibitors
   (g) Confusants

CLASSIFICATION OF SPECIFIC DRUGS

Psychopharmaceuticals

I. Psycho-inhibitors (Psycholeptics)
   (a) Hypnotics. Only recently introduced preparations are listed.

   * meprobamate (Miltown, Equanil, Oasol) 400-1200 mg
   * chlorpromazine (Thorazine, Megaphen, Largactil) 50-100 mg
   * glutethimide (Doriden) 0.5-1.0 Gm methylparafynol (Dormison) 500-1000 mg
   * methyprylon (Noludar) 200-500 mg
   * ethinamate (Valmid) 0.5-1.0 Gm ethychlorvynol (Placidy) 0.5-1.0 Gm
   * ectylurea (Nostyn) 300-600 mg (t.i.d.)

   (b) Sedatives—(All dosages are thrice a day (t.i.d.) as required, unless otherwise stipulated)
   * chlorpromazine (Thorazine, Megaphen, Amine, Largactil) 10-50 mg
   * deserpidine (Harmony) 0.1-1.0 mg
   * ectylurea (Nostyn) 150-300 mg
   * ethychlorvynol (Placidyl) 100-200 mg
   * glutethimide (Doriden) .25-.50 Gm
   * hydroxyazine (Atarax, Vistaril) 25-100 mg
   * mepazine (Pacatal) 25-50 mg
   * methyprylon (Noludar) 50-100 mg
   * oxanamide (Quiactin) 150-300 mg
   * perphenazine (Trilafon) 2-4 mg
   * proclorperazine (Compazine, Stemetil) 5-15 mg
   * promazine (Sparine) 10-50 mg
   * promethazine (Phenergan, Lergigan, Atosil) 25-50 mg
   * rauwolfa root (Raudixin) 50-200 mg
   * Rauwolfa serpentina, alseroxylon fraction (Rauwiloid) 2.0 mg
   * rescinnamine (Moderil) 0.1-1.0 mg
   * reserpine (Serpasil, Rau-Sed, Sandril, Eska-serv, etc.) 0.1-1.0 mg
   * thiopropazate (Dartal) 2-5 mg
   * triflupromazine (Vesprin) 10-25 mg

   (c) Muscle relaxants—(Dosages t.i.d.)
   * meprobamate (Miltown, Equanil) 200-400 mg
   * phenoglycodol (Ultran) 300 mg

   (d) Ataraxes (see table below)
   Unless there are reasons to the contrary it is recommended that the intensive treatment dose be reached by the end of the first week. Three months is the minimal period for an adequate clinical trial.

   (e) Undetermined—(Dosages t.i.d.)
   * azacyclonol (Frenquel) 20-100 mg
   * benactyzine (Suavitil, Parason, Suvren) 1.0-3.0 mg
   * phenyltoloxamine (PRN) 200-400 mg
   * acetylpromazine/acepromazine (Notensil, Plegicil)
TABLE

RECOMMENDED DOES OF ATARAXICS

<table>
<thead>
<tr>
<th>Name of drug</th>
<th>Intensive treatment dose</th>
<th>Maintenance dose</th>
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<tbody>
<tr>
<td>* reserpine (Serpasil, Rau-Sed, Sandril, Eskaserp, etc.); *deserpidine (Harmonyl); *rescinnamine (Modenil)</td>
<td>8.0-15.0 mg daily</td>
<td>3-5 mg daily</td>
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<tr>
<td>* chlorpromazine (Thorazine)</td>
<td>150-500 mg t.i.d.</td>
<td>50-100 mg t.i.d.</td>
</tr>
<tr>
<td>mepazine (Pacatal)</td>
<td>100-150 mg t.i.d.</td>
<td>50-100 mg t.i.d.</td>
</tr>
<tr>
<td>* perphenazine (Trilafon)</td>
<td>2-16 mg t.i.d.</td>
<td>2-8 mg twice a day (b.i.d.) or t.i.d.</td>
</tr>
<tr>
<td>* prochlorperazine (Compazine)</td>
<td>50-150 mg t.i.d.</td>
<td>25-50 mg</td>
</tr>
<tr>
<td>* promazine (Sparine)</td>
<td>200-600 mg t.i.d.</td>
<td>50-100 mg</td>
</tr>
<tr>
<td>thalidomide (Dartal)</td>
<td>20-30 mg t.i.d.</td>
<td>5-15 mg</td>
</tr>
<tr>
<td>trifluperazine (Stellazine)</td>
<td>10-20 mg t.i.d.</td>
<td>1-10 mg</td>
</tr>
<tr>
<td>* triflupromazine (Vesprin)</td>
<td>50-200 mg t.i.d.</td>
<td>25-50 mg</td>
</tr>
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II. Psycho-activating Drugs—(Dosages t.i.d. except as noted)

(a) Psychomotor stimulants.
* dextro-amphetamine (Dexedrine) 5-15 mg
* methamphetamine (Methedrine, Desoxyn, etc.) 5-15 mg
* methylphenidate (Ritalin) 5-10 mg
* pipradrol (Meratran) 1.0-2.5 mg

(b) Psycho-stimulants.
* imipramine (Tofranil) 10-75 mg

(c) Psychic energizers.
* iproniazid (Marsilid) 10-150 mg/day
  For severe depressions an initiating dose of 50 mg t.i.d. is recommended. This dose should be halved weekly once improvement is established. A maintenance dose may not be necessary, or may range from 5-10 mg a week to 50 mg or more a day.
* JB516 (Catron) 3-24 mg (initial dose 12-24 mg)
* phenaline (Nardil) 10-120 mg (initial dose 60-120 mg)
* nialamid (Niamid) 25-300 mg (initial dose 75-300 mg)
* RO 50831 (Marplan) 10-20 mg t.i.d.

III. Psychotomimetic Drugs.
(doses not given)

(a) Hallucinogens.
  lysergic acid (LSD)
  mescaline
  harmine

(b) Cataplexogenic agents.
  bulbocapnine

(c) Euphoriant.
  cocaine
  psychomotor stimulants and psycho-stimulants in large doses.

(d) Chronoleptogenics
  mescaline
  opium
  LSD

(e) Depressants

(f) Disinhibitors
  Intravenous barbiturates

(g) Confusants
  bufotenin

IV. Combinations of Psychopharmaceuticals.

There are both advantages and disadvantages in the simultaneous use of several psychopharmaceutical agents. Factors which should govern the decision as to which drug or drugs should be used are: (1) the condition of the patient, (2) the response of the patient to previous psychopharmaceuticals, (3) the experience of the administering physician, (4) the closeness with which the patient can be observed and supervised, and (5) the experience of others as reported in the literature or recounted personally.

Pharmacotherapy in the psychiatric field is oriented toward "target" symptoms (which can be readily observed or ascertained) rather than being
directed at etiological factors (which are unknown, uncertain, or non-responsive). A combination of two drugs with different actions would be indicated if treatment with a single agent provided only partial relief and it was felt that further improvement could be obtained. It should be emphasized, however, that "cure" is not always obtainable, and that reduction of disability, as elsewhere in medicine, is a legitimate goal of treatment.

If the patient is restored to a state of being reasonably happy and socially functional, further changes in medication should be made only if there is considerable certainty that they will lead to significantly greater improvement.

The nature of psychiatric reactions is such that it is often impossible to distinguish a primary from a secondary reaction, and alleviation of one symptom may lead to the clearing up of a number of others. In most circumstances, therefore, I would suggest that the most disabling target symptom be selected and the medication which the physician believes most likely to modify or relieve the condition be given. If no change is seen after the period when it could have been anticipated (which varies from one drug to another), the drug should be withdrawn and another substituted. If partial improvement does occur but then "plateaus" with insufficient remission, the addition of a second preparation that is aimed at the residual symptoms should be considered.

The doses of ataraxics when used in combination are usually less than half of the dose of either preparation used alone, with the consequence that those side effects which are related to dosage can sometimes be eliminated. At other times the side effects of one drug may counteract those of the other and provide another advantage. The opposite, of course, may also be true; some combinations produce more side effects of greater intensity. Of even greater importance is the fact that certain of the combinations produce therapeutic results that neither of the preparations could produce alone.

It is still my opinion that the combination of Rauwolfia derivatives with a phenothiazine is the single most effective overall preparation in the treatment of the disturbed schizophrenic patient of the chronic or semi-chronic variety. The utilization of a psychic energizer along with a phenothiazine derivative seems to open possibilities for treatment of the agitated depressions, the withdrawn psychotic and other syndromes for which neither drug alone seems to suffice.

Other combinations are too frequent to itemize. A distinction should be drawn between combinations capable of producing therapeutic results that could not be obtained by either drug alone and adjunctive medication that serves primarily to rectify the side effects of some other pharmaceutical.

SOME CONVENIENT RULES OF THUMB

Both in evaluating the clinical literature and in judging what to expect in terms of your own patients, there exist a number of indices which are usually so well known by those in the field that they are never mentioned and therefore occasionally come as a valuable surprise. As a rule, the longer the duration of illness the more prolonged the treatment must be for an adequate clinical trial. This is particularly true in respect of the ataractic drugs, and although initial sedation and some lessening of the psychopathological state may be evident within the first weeks the full benefits of treatment are sometimes not achieved until after as long as two years. In a case of long standing, certainly anything under three to six months of treatment cannot be regarded as sufficient.

The incidence both of side effects and of favourable therapeutic responses, particularly with the ataraxics, is markedly greater in females than in males. Side effects of virtually every type occur two to three times more frequently in females, so that in evaluating the relative usefulness of different compounds the sex of the patients must be considered. A study done with male subjects only will show a lower incidence of side effects than one done with females. On the other hand the therapeutic response is slightly better in females. There are a variety of sociological, psychological, and biochemical factors which each enter to some degree into the creation of this curious state of affairs. Anything resembling a full discussion of this would easily occupy an entire article.

As a rule (there are exceptions) within a specific category of pharmaceuticals, the greater the potency of the drug on a milligram for milligram basis the fewer the number of side effects, although occasionally those side effects which do occur tend to be more marked than with less "concentrated" preparations. As elsewhere in medicine the real "pay-off" is the therapeutic index (i.e., the therapeutically effective dose divided by the side effects), and one should not be led astray simply because
compound A requires only half the number of milligrams of compound B.

Spontaneous remissions occur in all except the organic psychoses, and even here compensatory factors sometimes bring about clinical improvement. Among first admissions to a mental hospital roughly 50% of those under 60 years of age are discharged within the first year, even without treatment of a specific type. After 2½ years of hospitalization, however, the chances of a spontaneous remission are less than 1 in 100. Accurate figures for patients seen in practice are not available, but the figures for hospitalized patients provide a rough guide. One should not be satisfied, nor too much impressed, by pharmaceuticals “proved” effective because the “average” duration of illness in the group of patients tested was 10.5 years and some patients had been hospitalized for 20 years. This is insufficient information upon which to judge the true effectiveness of the preparation. Let us say that the range of illness was from six months to twenty years. Of two hypothetical groups, the first might consist of 100 patients with the following breakdown: 1 patient hospitalized for six months, 1 patient hospitalized for twenty years, with the remaining 98 all being hospitalized (or ill) between ten and eleven years. The prognosis for spontaneous recovery in such a group would be one or two patients at most. On the other hand, a second group (with the same “average” duration of illness and the same range) might consist of 50 patients hospitalized for six months and another 50 for twenty years, in which case the expected rate of spontaneous remission would be in the order of 25%. Data on duration of hospitalization or illness must be stratified in terms of 1-year, 2-year, 5-year or other similar groupings for comparisons to be made between various drugs or between drugs and placebos. Similarly, when the sex of the patients, their age or other factors are also relevant, even stratification is not sufficient at times, and an analysis of variants or some other appropriate type of factor analysis may be required. Many clinicians have a strong aversion to statistical analysis, but a good statistician, like a good physician, uses the simplest technique appropriate to the occasion. No one would ask an internist or a surgeon to treat every case of abdominal pain with cascara for the sake of statistical simplicity, so that if one is unwilling to accept statistical analysis the obligation is to learn sufficient about it to be knowledgeably critical.

SIDE EFFECTS AND THEIR MANAGEMENT

Drugs with any degree of potency almost invariably act at multiple sites, and therefore, in addition to accomplishing the specific therapeutic objective aimed at, they may produce other reactions. The obvious ways in which these side effects can be handled are: (1) by reduction or elimination of the medication, (2) by providing adjunctive medication to reduce or eliminate them, (3) by substitution of other medication which has the same beneficial effect but not the specific side effect in that particular individual, or (4) by getting the patient to accept the fact that the specific side effect is inevitable and to learn to live with it during the period of treatment.

Irreversible side effects (except in the case of the rare fatalities) are virtually unknown. Therefore the patient can safely be assured that whatever it is that is bothering him will almost certainly clear up at the termination of treatment, if not before. With the more potent preparations which are at present available, some of the side effects appear almost inevitable. I believe it is a wise practice to warn the patient of the probable occurrence of the most frequent and how they can be managed. If they do then occur, the patient is less alarmed than would otherwise be the case, and if they do not, no great harm has been done. If the patient presses for details as to the degree of severity and discomfort they may entail, it seems wise to indicate the actual range but stress the high degree of individual variability, indicating, as is the case, that in most instances they are more annoying than either painful or serious. Unless one chooses to resort to a printed list, it is well to emphasize only the most likely of the side effects, since in addition one should underscore those signs or symptoms which are possible indicators of the serious side reactions and should be reported immediately. Illustrations of the common side effects would be nasal stuffiness in the Rauwolfia group, constipation and dryness of the mouth with the phenothiazines, and extra-pyramidal symptoms in both groups of drugs. The dry and scratchy throat which may be indicative of agranulocytosis or leukopenia (with some of the phenothiazines) should be emphasized, since the patient may otherwise regard this as an unrelated and not too uncomfortable occurrence unworthy of mention. The clinical evidences of jaundice are usually sufficiently dramatic, so that the patient need not be specifically requested to bring them to attention. The general opinion of most clinicians
and investigators is that laboratory tests, unless done on a daily basis, are of relatively small value in detecting the prodromata of most of the side effects.

The usual range of reactions, including nausea, vertigo, skin manifestations, etc., may occur with almost any of the preparations and should be handled, except in the case of the ataraxics and the psychic energizers, by the customary procedure of withdrawal and substitution of some other compound. The side effects discussed in detail are those commonly seen with the ataraxics and psychic energizers, and are *not* an indication for discontinuance or even reduction of medication (except as noted). Once a specific course of treatment has been started, it should not be interrupted short of a minimal three months trial, unless there are very serious reasons for discontinuance, or therapeutic success has been achieved.

**Physiological side effects which may occur with any ataractic.**

**Reduced resistance to intercurrent conditions.** Although it is customary to list side effects in the order either of their frequency or of their seriousness, I have felt it desirable to start with this important side effect because it is so little known. We have ourselves pointed out that there is reduced resistance to a large variety of intercurrent conditions. Infections, whether local or systemic, require larger doses of antibiotics, and there is some evidence that susceptibility to infection is increased. Cardiac decompensation, when it occurs, seems to proceed more rapidly. Diabetic crises are usually more severe. In some patients there is rapid development of trophic ulcers after only a few days in bed, with an unusual resistance to treatment. There is some evidence that glutethimide (Doriden) serves to counteract some of the somatic as well as the psychological side effects. We have had at least a few patients whose cardiovascular reactions led us to withdraw treatment, and who were subsequently able to complete ataractic treatment successfully after being placed on Doriden. There may be other preparations of this type, but we have not systematically searched for them. The important thing is that intercurrent conditions are apt to develop more rapidly and severely than under ordinary circumstances, and require both unusually prompt and vigorous treatment.

**Drowsiness.** To some extent drowsiness may be induced by any of the ataraxics, but it is particularly characteristic of chlorpromazine and, to a lesser degree, of reserpine. On the doses used for intensive treatment lethargy occurs from time to time with almost all the pharmaceuticals in this group. The use of a psychomotor stimulant as required is usually effective.

**Weakness or fatigue.** As distinct from drowsiness, at times patients will complain of marked fatigue upon the slightest exertion. A fair percentage of these cases can be helped by the psychomotor stimulants, but at other times little relief is obtainable until the intensive treatment phase has been completed and the dosage reduced.

**Extra-pyramidal symptoms.** To date, every drug that has proved useful as an ataraxic has induced extra-pyramidal symptoms in at least a percentage of the patients receiving it. In point of fact, extrapyramidal symptoms are more marked among the newer phenothiazines than in the “older drugs”, although other side effects are much less. The manifestations cover an extremely wide range, which may extend from occasional mild generalized tremulousness to the most extreme board-like rigidity of the well-advanced Parkinson syndrome. For a reason not yet clearly understood, some of the newer phenothiazine derivatives seem selectively to produce extra-pyramidal symptoms involving the neck and face muscles. Severe clenching of the jaw, protrusion of the tongue, torticollis and some syndromes not previously described are not infrequently seen. On occasion the muscular rigidity may affect the abdominal muscles, and there have been cases of “typical board-like rigidity” which on operation revealed nothing pathological internally. It has been our strong conviction that, regardless of their degree of severity, extra-pyramidal symptoms of themselves do not constitute a reason for discontinuing treatment. A number of antiParkinsonian agents have been reported as useful, and we ourselves (having observed what was probably the first case of a drug-induced Parkinson-like syndrome) were forced to extemporize and very happily obtained excellent results with methanesulfonate (Cogentin). We have persisted with the use of this compound, given in doses of 2 to 4 mg once or twice a day. Because our programme of pharmaceutical testing is so busy, we have not yet had an opportunity to do comparative studies with other products. We have, however, also noted some relief of symptoms with glutethimide (Dori-
den), when it was given as a corrective for other side effects.

**Disturbances of vision.** Despite pharmacological “logic”, we have seen both myosis and mydriasis occurring with either reserpine or the phenothiazine derivatives. The usual treatment is by the use of pharmacological pupillary constrictors or dilators. In a number of patients where completely unimpaired vision was essential (for their work or other reasons) and pharmaceuticals were inadequate, the use of corrective glasses proved extremely successful.

**Oedema.** Probably a good 20% of the patients receiving intensive treatment develop oedema of the face and/or extremities. At times this becomes a cosmetic problem, or it may produce acute discomfort if the patient has to stand or walk excessively. Some of the cases of facial oedema respond to antihistamines, but at times such preparations as Diuril, Diamox, or even the mercurial diuretics are necessary. “Concealed oedema” may also produce bloating on occasion.

**Menstrual irregularities.** Almost any menstrual irregularity may occur, although amenorrhrea is by far the most frequent. We have not investigated techniques for correcting this condition, since it has not occasioned discomfort or concern once other causative factors have been ruled out.

**Convulsions.** To a greater or lesser degree some drugs induce convulsions in at least a percentage of patients treated. As a general rule this is a dosage function, and can be handled by either reduction in the amount of medication or, if the individual is unduly susceptible, anticonvulsive agents such as Dilantin or phenobarbital, given concomitantly.

**Lactation.** Considerable embarrassment can be avoided if there is awareness that lactation accompanied by engorgement of the mammary glands may occur. Occasionally a male patient will manifest gynaecomastia. In the main the condition is self-limited, but at times will persist until medication is withdrawn.

**Toxic syndrome.** As with virtually any medication, over-dosage will produce typical symptoms of toxic psychosis. The differential diagnosis is usually not difficult, since the syndrome appears after prolonged administration of substantial doses. There is reduction of appetite, and the appearance of confusion of the organic type. This is one of the few conditions calling for reduction of dosage.

**Mid-brain syndrome.** Under unusual circumstances most of these pharmaceuticals have on a few occasions produced a reaction which resembles that of a marked lesion of the mid-brain. There may be hyperpyrexia, ocular palsy, decerebrate movement, or other signs such as opisthotonus. Two points worth noting are: (1) that individuals with prior brain injury or with mental deficiency seem more prone than the usual patient; and (2) that the reaction occurs most frequently in unusually hot weather, which might indicate some disturbance of the heat-regulatory centre. The occurrence of a mid-brain syndrome calls for immediate withdrawal of the medication and for symptomatic treatment. Pharmaceuticals of the same or related nature may subsequently be re-introduced, but obviously great caution is indicated.

**Weight changes.** As a rule there is an appreciable weight gain, which does not appear to be primarily related to the retention of fluids. This is true not only in patients who were cachectic or malnourished, but also in those who appeared in good physical condition. In line with the “constant irregularity” of side-reactions, there are occasional patients who show weight loss, and in a few instances anorexia develops, so that medication has to be reduced or discontinued.

**Hypotension.** Although the hypotensive effect is better known with the Rauwolfia derivatives, it can also occur with the phenothiazines. As a rule the blood pressure (although it may appear markedly or even alarmingly low to the physician) does not fall below the level of physiological discomfort to the patient. In some cases, however, there are reactions which may result in mild dizziness or vertigo. In other patients the effect is more marked, and either psychomotor stimulants or a combination of 1/100 grain atropine and 3/8 grain of ephedrine t.i.d. is called for. In the very extreme cases, bed rest plus norepinephrine (Levophed) are required.

**Psychological side effects which may occur with any ataractic**

**Depression.** The incidence of severe depression with Rauwolfia derivatives in the treatment of neuropsychiatric conditions has, in my opinion, been vastly over-rated. Interestingly enough, the depressive reaction is much more frequent in
patients being treated for hypertension, and I have elsewhere indicated that I believe the response is a secondary psychological one rather than a direct drug reaction. Many patients who develop hypertension have a psychological constitution which demands constant activity and proof of competency. Any agent or situation which immobilizes them is apt secondarily to produce depression. The phenothiazines may lead to the same depressive reaction, although at other times they may produce a mild elevation of mood. An interesting exception is mepazine (Pacatal), which rather consistently produces a moderate mood elevation along with its ataractic effect. Occasionally one or two electroshock treatments will relieve the depression, and more recently we have had marked success in combining a psychic energizer with an ataraxic, although such combinations required markedly reduced doses of the phenothiazines because of potentiation. The psycho-stimulants also appear useful as a corrective. A recent paper has reported the success of glutethimide (Doriden) in handling this condition.

Anhedonia. The psychomotor stimulants, the psycho-stimulants, or if necessary the psychic energizers, are quite successful in relieving "lack of feeling", which sometimes proves most disturbing to a patient. It is interesting to note that this condition occurs most frequently in psychotic patients, once the abnormal mental content produced by delusions and hallucinations has been wiped out. Glutethimide (Doriden) has also been reported useful in this situation.

Suicide. In our own very extensive series of several thousand patients treated by ataraxes, we have not found substantial evidence that the rate of suicide is appreciably increased. Care should be taken, as in the treatment of any depressed patient, and special caution should be observed at the period of transition, i.e. when the previously "immobilized" patient begins showing signs of increased activity but is not yet completely relieved of the depression. He has then sufficient energy to put suicidal thoughts into effect. A number of recent papers have stressed the fact that the overwhelming majority of suicidal patients either volunteer information as to their intention, or readily admit it if questioned. The patient who is responding to treatment but who goes through a phase of threatening suicide should be taken seriously and watched with extreme care, and there should be no hesitation in using hospitalization if it appears to be the only way protection can be given through this phase.

Changes in sexual function. Both impotence and increased eroticism have been noted. Increase in eroticism is somewhat more frequent with reserpine, and impotence more common with the phenothiazine derivatives, although the data are too sparse to draw any statistically significant conclusions. No specific method of handling either of these conditions has been evaluated. Reassurance should be given that the impotence is drug-induced, and is either self-limited or will disappear upon reduction or withdrawal of the drug.

Dreams. Great vividness of dream life is noted by many of the patients undergoing treatment, and occasionally they have difficulty in shaking free of these thoughts once awake. Increase in the "frequency" of dreams is common, although this may be due to increased recall rather than to an actual quantitative change. Some patients are disturbed by nightmares, and others have commented on the excitingly erotic nature of their night life.

Insomnia. Although as a rule most patients sleep more easily and with less disturbance, there are occasional patients in whom insomnia develops. We have had very satisfactory results with glutethimide (Doriden), although at times doses as high as 3 grams are needed. If the insomnia is associated with tension and restlessness, methanesulfonate (Cogentin) has proved useful.

Lethargy, retardation and withdrawal. In some cases the patient may pass from a state of reduced agitation to one in which he loses interest and concern with his environment, sometimes to the extent of appearing somewhat dazed. At the extreme this may reach a point where he appears markedly out of contact with his environment and "flat" in affect. The psychomotor stimulants or psycho-stimulants, accompanied, if necessary, by reduction in the dosage of the ataraxic, are recommended as a way of handling this reaction.

Restlessness, agitation and turbulence. Even though a great many patients show lethargy, they may at the same time give evidence of restlessness. With the Rauwolfia derivatives, and in almost equal frequency with the newer phenothiazine derivatives, the patient may pass through a stage of agitation and even turbulence, in which there is
re-activation of disturbed behaviour which had subsided in the "sedative" phase (as originally described by Barsa). During this period the patients may become extremely irritable, and at times hypermotility as well as psychopathological manifestations are greater than they were before treatment. Barbiturates are of practically no use, but occasionally methanesulfonate (Cogentin), and more frequently glutethimide (Doriden), are helpful. In extreme cases hyoscine may also be necessary. The exceptionally important point to be made is that this is a normal development in the course of treatment. It is very definitely not an indication for either withdrawal of medication or reduction of dosage if the patient is being given intensive treatment. The successful patients, after periods of from a few hours to as long as six weeks, pass on to the re-integrative phase, which is the therapeutic desideratum. Only after at least three weeks of this response should the dosage be reduced. It is not at all unusual to find that the patient then begins to improve, since, as we have discussed elsewhere, there are cases characterized by a peculiar "therapeutic lag", which begins when intensive treatment is discontinued. A low maintenance dose following gradual withdrawal is recommended.

Side reactions peculiar to Rauwolfia derivatives

**Flushning.** If parenteral preparations of the Rauwolfia derivatives are used, it is very frequent with the initial doses to observe a marked flushing reaction, which usually does not recur after the first few treatments.

**Nasal stuffness.** Apart from the direct discomfort resulting from oedema of the mucous membrane of the nares, this "stuffiness" sometimes requires the patient to breathe with open mouth, and produces a dry throat which interferes with sleep. Anti-histamines are not of much help. Nasal decongestants such as nephalone (Privine) have proved more useful, although the usual precautions accompanying prolonged usage should be observed. Other Rauwolfia alkaloids such as deserpidine or recanesine are at times successful.

**Bradycardia.** There is no specific discomfort connected with bradycardia per se, but it is important to be aware of the likelihood of this response. In point of fact, this side effect makes the preparation particularly valuable in patients with tachycardia or palpitations.

**Gastro-intestinal symptoms.** In contrast to the phenothiazines, not infrequently there may be mild cramps, diarrhoea, and even occasionally nausea and vomiting, which are rapidly self-limiting. Methanesulfonate (Cogentin), which has an anticholinergic radical, usually alleviates these symptoms. If this is inadequate, a more direct anticholinergic preparation is almost invariably successful, whether it be belladona, atropine, or one of the synthetics.

**Ptyalism.** Although excessive salivation and, occasionally, drooling are undoubtedly part of the extra-pyramidal syndrome, I believe that they deserve separate mention because of the frequency with which the condition occurs, particularly with the Rauwolfia derivatives. Here again methanesulfonate (Cogentin) is the treatment of choice in our experience.

**Side effects peculiar to the phenothiazines**

**Gastro-intestinal reactions.** Whereas the Rauwolfia derivatives tend to produce hyper-activity of the gastro-intestinal tract, the phenothiazines usually induce obstipation or constipation. The symptoms are particularly common in the older age groups, and if not attended to promptly may produce severe distension and faecal impaction. Hagopian recommends bi-weekly administration of one to one and a half ounces of equal parts of mineral oil and milk of magnesia.

**Dryness of the mouth.** In contrast to the ptyalism of the Rauwolfia derivatives, patients on phenothiazines are frequently disturbed by extreme dryness of the mouth. Treatment is local, with preparations such as lozenges or oil of lemon.

**Dermatological reactions.** A large range of reactions, including urticarial, macular, papular, vesicular and even scarlatiniform, have been reported. At times antihistamines plus local antipruritants are helpful, although in other cases the drug must be withdrawn and an alternative substituted. The occurrence or exacerbation of seborrhoeic dermatitis is relatively frequent, and the use of selenium sulfate (Selsun) or an equivalent should be used promptly to prevent spread of the condition.

It is extremely essential to keep in mind the photosensitivity induced by some of the phenothiazines (particularly chlorpromazine), which is related both to dosage and duration of exposure. Lotions containing para-amine-benzoic acid seem to provide adequate protection, and it has been
reported that gradual exposure may also reduce over-reaction. It should also be well noted that not only direct sunlight, but heat produced by diathermy, by a beauty shop hair dryer, or by prolonged proximity to a kitchen oven, may also induce this extremely painful reaction.

**Jaundice.** There are varying estimates of the frequency of clinical jaundice, but the most probable figure is 1.5% plus or minus 0.5%. The jaundice is almost invariably of the obstructive type. In 98% of cases it occurs during the first two months of treatment, so that after that length of time the patient does not have to be followed nearly so closely. The condition is definitely not related to dosage and has been reported to occur in cases with a single dose of 25 mg and, in one case, 10 mg of chlorpromazine. The very much lower incidence or absence of jaundice with the newer phenothiazines is a distinct improvement. For research purposes we have followed a variety of liver function tests over extended periods of time on a very large number of patients, but in our opinion none of these has sufficient predictive value to be clinically useful. The yellow conjunctiva, the itching, and the other signs of jaundice usually appear even prior to abnormal elevations in the liver function tests or in the alkaline phosphate. At the first clinical sign the drug should be promptly withdrawn and supportive treatment administered. On occasion patients have been re-started on the same medication, and patients have even been continued on chlorpromazine with disappearance of jaundice, but in view of the large number of phenothiazines now available it is suggested that an alternative would be preferable, since the occurrence of jaundice with one phenothiazine gives no indication that the same reaction will necessarily occur with a (chemically) closely related compound. Some interesting evidence has been presented that if the patient is kept well hydrated there is significantly less likelihood of jaundice occurring. Many recommend for treatment of jaundice diets of high protein, high carbohydrate and low fat content together with vitamin K (5 mg intramuscularly daily), Plebex (2 ml daily), a cortisone preparation such as Cortef (50 mg eight-hourly intramuscularly) and, if necessary, blood transfusion. Metacorten (10 mg six-hourly) has also been suggested.

Care should be taken in the interpretation of liver function tests in the absence of clinical symptoms. We have routinely done four liver function tests at weekly intervals in several thousand patients for three weeks prior to starting medication, and found at least one test to show abnormal results in over 80%.

**Leukopenia and leukocytosis.** Some degree of leukopenia is relatively common, occurring in perhaps 15% of all patients on many of the phenothiazines. This reaches the point of agranulocytosis in 1-2% of the patients, and fatalities with chlorpromazine and some of the analogues should be considered as part of the therapeutic risk. Most of the newer phenothiazines have either no, or a much lower occurrence of, leukopenia, and for this reason are frequently preferable. The one therapeutic advantage of chlorpromazine is that it induces a certain amount of somnolence and lethargy, which at times is clinically desirable, but since this can be achieved in other ways it does not make chlorpromazine the most desirable of the phenothiazines. Prochlorperazine (Compazine), triflupromazine (Vesprin), perphenazine (Trilafon) and numbers of others appear to be much safer, and equally effective. The occurrence of marked leukopenia or agranulocytosis is an indication for immediate withdrawal of medication. With agranulocytosis, protective antibiotics should be instituted at once in significant doses, and a variety of adrenocortical preparations have been recommended by various authors. If the case is diagnosed early enough fatal termination can usually be avoided. It is therefore extremely important to stress to the patient that the clinical signs of agranulocytosis, such as scratchy throat, extreme fatigue, etc., should be promptly reported. It is also advisable to have a base-line haematological examination to provide a standard against which to judge subsequent laboratory data, should this prove necessary.

**Side effects of psychic energizers**

The psychic energizers represent by far the most potent group of pharmaceuticals in the psychiatric field. They have frequently not been treated with the respectful caution which is their due. This in part has been due to the fact that even the ataraxics are relatively "non-explosive" compounds. Since dosage recommendations for most of the other psychopharmaceuticals definitely tend to lean to the conservative side, many practitioners have found it expedient to double or even triple recommended dosages. In turn patients have had the same venturesome spirit, and not infrequently doubled or even tripled the prescribed dose. As a consequence occasional patients have taken, fairly regularly,
five to ten times the dose suggested by the pharmaceutal house. When iproniazid (Marsilid) was introduced, the practice was so well established that, despite the extremes of caution recommended, the optimal dose was quite frequently exceeded. Since the pharmaceutical dose was a cumulative one, sometimes not reaching its onset of action for as long as three weeks or more, there was a natural tendency to keep on increasing the dosage in the hope of achieving a therapeutic response. With this type of loading, when the drug did begin to act, it was at levels far above the optimal. No sensible physician would either prescribe digitalis for a patient in cardiac decompensation, or suggest that a diabetic patient take insulin according to an initial maximum recommended dose and return in a month or two. Unfortunately, because the other psychopharmaceuticals had such a large margin of safety this actually was done with iproniazid.

Some of the psychic energizers now on clinical trial (but not yet on the market) have a potency ranging up to roughly fifty times that of iproniazid, so that in the future even greater care will have to be exercised.

Potentiation of other medications. The greatest caution must be observed by keeping constantly in mind the ability of these drugs to potentiate many other medications. To a small extent this is true of some of the phenothiazine derivatives, but compared with the psychic energizers other potentiating agents are comparatively inert. On three or four occasions I have failed to find the response I had anticipated, and only after close questioning did the patients admit that they were continuing their "small dose of barbiturate", which they had been using regularly for from ten to twenty years. They had felt that my insistence that all other medications be discontinued for the time being could not possibly have applied to their "sleeping pill", even though it had been particularly mentioned. In effect, they had unknowingly raised their dose of barbiturate by five to ten times, and as a consequence barely managed to stagger through the day. The phenothiazine derivatives are also increased in potency, and doses no more than a quarter of the customary should be used for initiation of treatment. As a result of failure to note this potentiation, I have been called in consultation to see a full-blown case of a Parkinson-like syndrome who was on long-term treatment with perphenazine (Trilafon). When a psychic energizer was added the extrapyramidal symptoms developed in a few hours.

Since certain foods have a pharmacological effect they should not be overlooked. It was a patient who brought to my attention the reason for her extreme jitteriness, which is not typical of these medications. She had sworn that she had not touched any other medication—but finally asked me whether the fact that she drank ten or twelve cups of coffee a day might have any effect, adding that under normal circumstances she had no reaction to this. When the coffee was reduced to two or three cups a day excessive irritability disappeared. Subsequently I have observed the same reaction not only with tea but also with some of the "cola" drinks, which contain caffeine. In one extreme case, a single cup of coffee taken in the morning kept the patient not only jittery all day but up the entire night. The reaction was repeated on three different occasions in the same patient, so that the effect was probably a real one.

Anaesthetics taken for dental work have also occasioned marked reactions. In part these appear related to the adrenaline present in most such solutions, but one would also suspect that any substance resembling cocaine might be another factor. Therefore, dental work should be avoided if possible. Similarly, if an operative procedure requiring general anaesthesia is needed, the anesthesiologist should be warned of possible extreme reactions. The patients themselves should be cautioned of this, since it might otherwise occur without the physician being given prior warning.

As yet we do not know the exact degree to which all other common medications are potentiated, so that they should be administered circumspectly with small initial doses if their use is indicated.

Liver toxicity. On April 1, 1958 (a few days short of a year after we had pointed out the specific psychopharmacological action of iproniazid (Marsilid) on depression), the US Food and Drug Administration estimated that 400 000 to 500 000 patients had been treated with these drugs, with a total of 33 fatalities associated with jaundice. Since both clinically and pathologically the symptomatology cannot be distinguished from that of infectious hepatitis, it is almost certain that some of these patients died from the viral infection, and certainly others, for whom permission for an autopsy was not obtained, must also have died from other causes. On the other hand there were almost certainly more fatalities than reported, which would tend to increase the number of cases. The total number of cases of jaundice (roughly 100) does not
seem out of line with what might have been expected from infectious hepatitis. The mortality rate does seem unusual, if it is assumed that both figures are roughly accurate. I am therefore left with the impression that, just as resistance to intercurrent conditions is lowered with the ataraxics, there is here a similar weakening of resistance, which may even show some particular susceptibility in respect of specific virus conditions.

The only near-effective alternative for many of these patients was electroconvulsive therapy, where the generally accepted mortality rate is 1 in 1000. On the semi-official estimate of the number of cases treated with iproniazid (Marsilid), if the mortality were comparable to that of electro-shock therapy, one would anticipate four to five hundred deaths directly related to the drug. At the worst, therefore, on the basis of available data iproniazid is ten to fifteen times as safe as electro-shock therapy. In view of the furore created about this jaundice a misquotation comes to mind: "Never has so much been said so frequently about so little."

Various adrenocortical products have been suggested by way of treatment, but no definitive evidence exists that they are consistently of help. Obviously withdrawal of the drug and supportive treatment are mandatory.

**Hypotension.** Evidence would seem to indicate that these drugs are even more regularly hypotensive in their action than the Rauwolfia derivatives, although here the drop below the limits of physiological functioning is more frequent. As a general rule the drop in blood pressure is associated with postural changes, and at times becomes so marked that complete bed rest is required. These changes disappear with reduction or withdrawal of medication, although a number of clinicians have insisted that administration of cortisone (12.5 mg twice daily) or ACTH relieves the postural hypotension and enables the patient to continue medication without difficulty. My own experience has been limited to a number of patients who received a few milligrams of thyroid daily before or after treatment was begun with the psychic energizers. In each of the three cases seen the psychic energizer either failed to work, or it lost its therapeutic action after the thyroid was added. In view of the f easness of the cases one cannot draw conclusions as to incompatibility, but I would certainly advise caution in the use of endocrine products of any sort until more is known.

**Neuralgias.** On prolonged administration of moderate or high doses neuralgias may occur. These range from "earaches" to "arthritis", and if the patient is not cautioned he or she may also end up with completely unnecessary dental extractions. There has been no difficulty in managing this reaction; this is usually done by a temporary lowering of dosage plus the administration of 25 to 50 mg of pyridoxin (vitamin B₆).

**Changes in bowel habits.** Obstipation or constipation are very frequent to at least some degree, and occur very markedly in the sensitive patient. In some individuals faecal impaction or congestion seems to be associated with vasomotor instability, and it is therefore recommended that some method of bowel evacuation be utilized approximately twice a week.

**Changes in sexual function.** The occurrence of temporary impotence in the male is not at all infrequent, although this may be more marked in attaining orgasm than in achieving erection. It is not unusual to hear a patient complain that three hours of intercourse were required in order to reach a sexual climax, which proved to be a rather exhausting experience. Using this experience as a base, I have successfully treated a number of cases of *ejaculatio praecox*. On some of the newer psychic energizers a number of female patients have commented on their increased sexual sensitivity. Also after a period of reduced sensitivity while on the drug, there have been cases of marked responsiveness upon withdrawal.

**Weight changes.** There is quite frequently an increase in appetite, characterized by a positive nitrogen balance. After an early rise, the weight usually drops slightly. Since cosmetic or other problems may be involved, it is suggested that caloric intake be watched if there is reason for concern.

**Oedema.** As with ataraxics, the occurrence of oedema is best handled by the use of Diuril, Diamox, or the mercurial diuretics, if the condition reaches the point of cosmetic or physiological discomfort.

"**Insomnia**". A reduced need for sleep is among the most characteristic of responses to the psychic energizers. This is not true insomnia since there is no concomitant fatigue. Whether one chooses to regard this as a side effect, with the implication that it is something undesirable, or it is looked upon as a bonanza, is in part dependent upon how the possibility of this reaction is presented by the
physician. Although meprobamate and other of the non-barbiturate hypnotics can be used in lower than usual doses without great danger, this to some extent tends to counteract the effect of the medication. My own approach has been to point out that two or three extra hours of waking life per day, if someone is feeling in a good frame of mind, constitute a remarkable gift. The patients have been encouraged to organize their life around the fact that there will be reduced need for sleep, and discussion of what can be done that is interesting and constructive during these periods has also proved helpful.

We have elsewhere discussed the use of these drugs for the treatment of drug addiction, and it has been interesting to watch patients who have been on nightly barbiturates for twenty or more years find that they can get on perfectly well without them. As might be anticipated, there is also a paradoxical response in some patients who have previously suffered from marked insomnia. They find that for the first time they are able to sleep well when placed on these medications.

In summary then, rather than "treating" this side effect in an effort to eliminate it, I would encourage its presence and help the patient make use of it.

Miscellaneous. A variety of other side effects have been reported occasionally. These include: hyperaesthesia, paraesthesia, perspiration, altered dependent reflexes, reduced tolerance to cold, possible skin rashes, transient nausea and pyrosis.

How regularly these are associated with the drug is unknown, and we have had no particular experience which would lead us to other than the normal medical recommendations for handling such reactions.

RÉSUMÉ

Il existe une telle abondance de noms et de termes désignant les médicaments modifiant les fonctions psychologiques que même les spécialistes peuvent se sentir par moment débordés. L'auteur donne une liste des désignations usuelles en indiquant celles qui lui paraissent les plus appropriées et pourquoi.

En ce qui concerne l'ensemble des médicaments ayant une influence sur les états psychologiques, le terme que propose l'auteur est celui de médicaments "psycho-pharmaceutiques", le mot "tranquilisants" étant inacceptable puisque parmi ces médicaments il y a non seulement des tranquillisants, mais également des excitateurs. L'adjectif "phrénotropiques" est parfaitement acceptable, celui de "neurotropiques" trop limitatif.

Les trois catégories principales de "psychopharmaceutiques" sont les psycho-inhibiteurs ou psycholeptiques, les psycho-activateurs ou psycho-analeptiques, les psychotomimétiques ou psycho-dysleptiques. L'auteur donne une liste des médicaments appartenant à chacun de ces trois catégories, en les classant selon leur action principale, et en indiquant pour chacun d'eux les doses d'attaque et les doses d'entretien. Cette classification est suivie de conseils sur leur utilisation, d'une étude détaillée des effets secondaires propres à chaque groupe de substances et des différents moyens de combattre ces effets.