according to the anticipated changes in behavior likely to result from using each drug. Among these classifications are the major tranquilizers, the minor tranquilizers, certain narcotics, the antidepressants, psychomotor stimulants, and the psychotomimetics.[1] In connection with this request, we have limited the discussion of origins to the major and minor tranquilizers. In the case of the major tranquilizers, the references are to the phenothiazines and also to the rauwolfia alkaloids, the latter being included because of the role they have played in the development of psychopharmacology. As far as the minor tranquilizers, the drugs for which references are provided are meprobamate and the benzodiazepine derivatives.

Among the drugs included in the phenothiazine category are chlorpromazine hydrochloride (Thorazine, Largactil, Megaphen), promazine hydrochloride (Sparine), trifulpromazine hydrochloride (Vesprin), fluphenazine hydrochloride (Permitil, Prolixin), perphenazine (Trilafon), prochlorperazine maleate (Compazine), triflurperazine hydrochloride (Stelazine), and thioridazine hydrochloride (Mellaril).[2]

Among the rauwolfia alkaloids are rauwolfia serpentina (Raudixin, Rauserpa, Rauval), alseroxylon (Rauwiloid), reserpine (Serpasil, Serpate, Sandril, reserpoid, Rau-sed Serfin, Vio-Serpine), deserpidine (Harmonyl), rescinnamine (Moderil, and syrosingopine (Singoserp).[3]

Among the minor tranquilizers, the references are to meprobamate (Miltown, Equanil) and to the benzodiazepines, such as chlordiazepoxide hydrochloride (Librium, Libritabs) and diazepam (Valium).[4]

The Phenothiazines.—According to the *Pharmacological Basis of Therapeutics*, phenothiazine itself was synthesized in 1883, but it was not until 1934 that it was first used as an anthelmintic, urinary antiseptic, and insecticide.[5] In the late 1930's a derivative of phenothiazine, promethazine, was found to have antihistamic properties, and like many antihistamines, a strong sedative effect. The French had made some unsuccessful attempts at treating psychoses with antihistamines in 1943, and others attempted to use promethazine in the treatment of agitation in mental disease in 1950.[6]

The developments leading to the findings associated with chlorpromazine are recounted as follows:[7]

> Meanwhile, the ability of promethazine to cause a marked prolongation of barbiturate sleeping time in mice was discovered, and in 1950 the French surgeon Laborit introduced the drug into clinical anesthesia as a potentiating agent. This prompted a search for other phenothiazine derivatives with potentiating actions as well as greater central activities, and in the same year Charpentier synthesized drug number 4560 RP, or chlorpromazine. Two years later, Laborit and co-workers (1952) described the ability of this compound to potentiate anesthestics and produce "artificial hibernation." They noted that chlorpromazine by itself did not cause a loss of consciousness but produced only a tendency to sleep and a marked lack of interest in what was going on.
>
> In 1952, Courvoisier and her associates described an amazingly large number of actions manifested by chlorpromazine (hence *largactil*, the French trade name). These included gangliolytic, adrenolytic, antifibrillatory, antiedema, antipyretic, antishock, anticonvulsant, and antiemetic properties. In addition, chlorpromazine was found to enhance the activity of a number of other analgesic and central depressant drugs.

The first use of chlorpromazine alone in the treatment of mental illness was undertaken by Delay and his associates in 1952.[8] Not until 1954 did there appear

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[1] See, for example, "A Rational Framework for the Development, Evaluation, and Use of Psychoactive Drugs," in *Drug Therapy—Supplement to the American Journal of Psychiatry;* vol. 124, No. 8, February 1968.

[2] List is not exhaustive. See the *Pharmacological Basis of Therapeutics*, the MacMillan Company, New York, or *New Drugs*, American Medical Association, Chicago. Words in upper-case designate trade-names of drugs within class. (See Appendix A.)

[3] See Footnote No. 2 above.

[4] There are a large number of other agents used as anti-anxiety drugs, many of which resemble meprobamate in their actions. See Footnote No. 2.

[5] "The Phenothiazine Derivatives," *The Pharmacological Basis of Therapeutics*, The MacMillan Company, 1965; page 163.

[6] "Essai de therapeutique abortive d'access maniacodepressifs par le 2339 RP (antergan)." Annls med.-psychol, 1943, 101, 432–435, Daumezon, G. and L. Cassan. "Traitement de l'agitation motice par un antihistaminique (3277 RP ou phenergan)," XLVIII Congres des Al. et Neurol; Paris 1950, Guiraud, P., and C. David.

[7] See Footnote No. 5.

[8] See footnote No. 5.