The concept of tranquilizing drugs in medicine is a new one, going back little more than 5 years. The term itself is essentially a popular one and defies precise definition. In general, however, substances which are included under the general heading of tranquilizers are those which exert a favorable effect on disturbed emotions of human beings, particularly in terms of relieving tension and anxiety. The effect on mood and feeling is presumably potentiated through brain stem and other subcortical mechanisms. In general, the so-called higher cortical functions which are affected by the conventional sedative, hypnotic and intoxicating drugs are uninvolved. The purpose of the present discussion is to offer the pediatrician a frame of reference regarding the classification, nature and mode of action of the more prominent tranquilizing drugs which have already been found useful in altering children’s behavior and to outline some fundamental principles which must be employed in using them effectively.

TENTATIVE CLASSIFICATION
To the best of our present knowledge, tranquilizing drugs fall into no single, clearly defined chemical group, nor do they all exert their clinical influence through the same pharmacologic or neurophysiologic mechanisms. Berger has suggested, however, that they may be classified in four general categories based on chemical structure and in two general groups based on over-all neurophysiologic effect. He suggests the following chemical classification, which for orientation purposes is a valuable one.

Phenothiazine derivatives. The best known preparations falling into this group are chlorpromazine (Thorazine\textsuperscript{®}), proclorperazine (Compazine\textsuperscript{®}), and promazine (Sparine\textsuperscript{®}). Structurally these substances are closely related to some of the antihistaminics. Promethazine (Phenergan\textsuperscript{®}), best known for its antihistaminic properties, is a chemical isomer of promazine (Sparine\textsuperscript{®}).

A second group are those chemically related to reserpine, a crystalline alkaloid derived from the plant species Rauwolfia.

A third group are compounds derived from diphenylmethane and including the preparations hydroxyzine (Atarax\textsuperscript{®}) and azacyclonal (Frenquel\textsuperscript{®}).

A fourth group are derived from sub-
stututed propanediols, the best known of which have some muscle relaxant properties in addition to their tranquilizing effects. Meprobamate (Equanil®, Miltown®) is most prominent in this group, which also includes mephenesin (Tolserol®), introduced earlier as a muscle relaxant.

Various laboratory investigations have been undertaken in an attempt to determine what pharmacologic properties may be common to the substances appearing in these four groups. No tests or group of tests have given identical results with all of them. However, members of the first three groups, the phenothiazine derivatives, reserpine and diphenylmethane derivatives, appear to act as autonomic suppressants insofar as their tranquilizing properties are concerned. The fourth group, of which meprobamate is the outstanding example, appears to act as a central relaxant, of which more details will be given later.

It is quite possible that further knowledge may lead to a more practical classification of tranquilizing drugs for the clinician. At present, however, in introducing a general frame of reference for the clinician, it seems wise to discuss the more prominent tranquilizers in terms of the preceding outline.

INDIVIDUAL TRANQUILIZERS AND THEIR USES

Phenothiazine Derivatives

Chlorpromazine, known in this country as Thorazine®, and in Canada and Europe as Largactil®, is probably the best known of the tranquilizers. By 1956 it was said to have been used in more than 7,000,000 patients and to have been the subject of several hundred published reports.

The use of chlorpromazine as a tranquilizer stemmed from the initial report in 1952 of a French surgeon, Laborit, who had used it as one of several drugs, in addition to surface cooling, to induce artificial hibernation in patients. The procedure was proposed to assist them in withstanding various sorts of stress, including that of psychic trauma. Other French clinicians demonstrated that this method, and then the use of chlorpromazine alone, was effective therapy for manic and agitated patients. After these initial observations the drug became available to psychiatrists in this country and elsewhere. Observations on its use as a tranquilizer have come primarily from psychiatrists working with adult psychiatric patients. The preparation, however, has also had extensive use as an antieptic, as a potentiator of the effect of anesthetics, narcotics and sedatives, and as an adjuvant in the treatment of a wide variety of somatic and psychosomatic disorders, which are, however, not pertinent to the present discussion.

As a member of the phenothiazine derivative group, it can be considered to function as an autonomic suppressant, although its precise mode of action is still not thoroughly understood. It has been suggested that the drug acts upon the hypothalamus, which regulates autonomic responses and affective discharges, upon various components of the mesodiencephalic activating system, which is responsible for wakefulness, attention and motor initiative, and that it may have some peripheral autonomic effects. It has the capacity to tranquilize without depressing, without clouding consciousness, and without removing inhibitions, in which lies its advantage over traditional sedatives, particularly in the field of psychiatry.

At the present time a great deal more is known about the ability of chlorpromazine to ameliorate symptoms of various psychiatric disorders than about its basic therapeutic effect on the illnesses themselves. In a recent review regarding its use in psychiatry, Winkelman notes that in adults it is more effective in reducing symptomatology which is severe rather than that which is mild. It is most effective when there is overactivity and various forms of psychomotor action, such as anxiety, agitation, panic, hostility, manic behavior and delusional and hallucinatory states. Acute emotional illnesses respond better than chronic dis-
orders in terms of complete symptomatic relief. However, in many hospitalized psychiatric patients, including those with psychoses of long duration, it may bring about sufficient improvement to facilitate their care, not only within the hospital but even at home, as long as the use of the drug is maintained. It may serve an important function as an adjunct to psychotherapy in the psychoneuroses, where it may render patients more accessible to the therapist and reinforce the progress made through psychologic management. It is rarely useful in depressions, however, and these may become worse when the drug is used. Optimal dosage for individual patients varies widely and ranges from 30 to 4,000 mg daily, usually given in divided doses three to four times in 24 hours. Parenterally it may be used for emergency tranquilization, although most patients are maintained with oral dosage. In patients with chronic disease the relapse rate is said to be high when administration of the drug is discontinued. Where one is concerned with the patient's total problem and long-term welfare, all other necessary and available forms of appropriate psychiatric treatment must be used in addition to the tranquilizer, since, as mentioned above, chlorpromazine appears to relieve symptoms rather than "cure diseases."

Occasional side effects have been noted, some of which are toxic and dangerous. While these definitely preclude its indiscriminate use, the incidence of their appearance as weighed against the urgency of the severe problems presented by many psychiatric patients and the wide benefits which have resulted from its judicious employment, must be viewed in practical perspective. Agranulocytosis has been occasionally reported. Jaundice of the bile-regurgitation type is likewise seen occasionally, although this usually subsides promptly if administration of the drug is discontinued. When large doses are employed, extrapyramidal symptoms, particularly Parkinsonism, are occasionally encountered, but these also respond to reduction of dosage. A variety of minor complaints, such as dizziness, nausea and dermatitis, occasionally make it inappropriate for some individual patients.

Clinical hearsay suggests that chlorpromazine has been used widely with children as a tranquilizer, but documentation in the form of published reports is still quite limited. The first report of its beneficial effect in children was published by Heuyer and his colleagues in 1953. Doses as large as 2 mg/kg of body weight were given to 7 agitated children with relief of agitation and hyperactivity in all cases.

Subsequent observations of the tranquilizing effects of chlorpromazine in disturbed children have been reported from inpatient psychiatric units for children, from residential schools for retarded children, from an outpatient psychiatric clinic for children and from studies carried out on children not primarily under psychiatric care. It is of interest that no reports have yet appeared from community-centered child guidance clinics, whose staffs for the most part have been hesitant to incorporate pharmacotherapy into treatment programs traditionally oriented towards modifying the psychodynamic bases of their clients' problems. Likewise, no reports have yet appeared dealing with the use of chlorpromazine as a tranquilizer in pediatric practice.

Gatski and Flaherty from the Governor Bacon Health Center in Delaware; Freedman, Effron and Bender, Bender and Nichtern, and Silver from the Department of Psychiatry, Children's Service, Bellevue Hospital, New York; Hunt, Frank and Krush from the Children's Unit of the Metropolitan State Hospital in Massachusetts; and Mikształ from the New Jersey Neuropsychiatric Institute at Princeton, have all reported on the tranquilizing effects of chlorpromazine on children hospitalized for psychiatric reasons. For the most part these were severely disturbed patients. In all these series the observers had the advantage of fairly intimate knowledge of their patients, were able to evaluate other
factors which might influence their results, and could, with the assistance of other members of the hospital staffs, carefully observe day-to-day changes and compare them with the children's behavior prior to receiving medication. In general, their results agree. Chlorpromazine was of definite assistance in reducing overactivity and in relieving anxiety, hostility and aggression in the majority of children to whom it was given, usually within 24 hours of the time administration was started. Several groups noted that it was particularly helpful in relieving the agitation of schizophrenic children. Freedman and his co-workers felt that its beneficial effects tended to diminish after 6 to 8 weeks of administration. This is not mentioned by other workers. The Bellevue group noted that 25 to 50 mg parenterally was useful as an emergency measure to tide children over particularly difficult times, such as the disturbances attendant to hospital admission. Maintenance doses varied. Bender and Nichtern suggested 1 mg/kg of body weight daily as an average dose. Hunt and his co-workers used 10 to 20 mg three times daily, and Flaherty reported wide ranges of dosage, from 40 to 1,000 mg daily. In approximately 200 children discussed in these combined reports no serious adverse effects were noted. A minority did not respond with significant improvement. Hunt's group noted that when a depressive element is present in a child, chlorpromazine is not helpful and may accentuate the maladjustment. None of the observers noted other particularly significant correlations between the symptomatic relief afforded and the clinical classification of children involved. It may be noted that in some of the groups children were selected for study on the basis of their overactivity and aggression.

A number of observations have been reported on the effect of chlorpromazine when administered to overactive mentally retarded children in residential schools. The drug produced fairly consistent reduction of overactivity and improved ease of management in the approximately 100 children included in these reports. Observers varied in their opinions of the type of retarded children most benefited. Bair and Herold and Esen and Durling noted improvement in intelligence quotient in a small series of patients. Most of the observers detected no improvement in learning ability of the patients.

Freed and Peifer noted diminution in overactivity and facilitation in school progress in a group of 25 boys treated with chlorpromazine in a child's psychiatric outpatient clinic, where, for the particular children in question, intensive psychotherapy was not possible. Freed later reviewed the advantages of chlorpromazine and other tranquilizers in maladjusted children and particularly noted that disturbing side effects are rare.

In observations on 18 children with cerebral palsy attending a day school, Denhoff and Holden noted that a significant number improved in mood and general adaptation while receiving chlorpromazine in doses of 10 to 20 mg three times daily. No adverse effects were noted.

In reports dealing with the use of chlorpromazine in children for purposes other than tranquilization comments are occasionally encountered as to its effect on the patient's mood. These observations are difficult to summarize and evaluate, particularly when the drug's use, for instance as an antiemetic, brings relief from distressing symptoms.

The absence of reported serious side effects in children in the reports discussed above must be taken at face value. In terms of the rather low incidence of toxic effects in adults, it is not surprising that in the 200 or 300 cases reported in children no serious complications were encountered. The results do not indicate that toxicity is not a hazard. They do suggest that the likelihood of its occurring is to be weighed against the advantages of tranquilization in some of the more serious emotional problems where chlorpromazine gives promise of bringing symptomatic relief.

Prochlorperazine (Compazine) and promo-
zine (Sparine®) are two other phenothiazine derivatives which have been widely used as tranquilizers in adults. Their general effects are said to be similar to those of chlorpromazine. Their advantages are claimed to lie in their relative freedom from toxic side effects. To date, reports of their use as tranquilizers in children have not appeared.

Reserpine

In 1582 Rauwolf, a German physician and botanist, published the results of his studies while on a trip to Asia and Africa to investigate certain medicinal plants which had been mentioned by early Greek and Arab physicians. Several years later, when a new genus was added to one of the plant families he had studied, it was called Rauwolfia. Today between 40 and 50 species of this plant have been described, growing mainly in India and adjacent countries. In ancient Indian literature it was one variety of this plant, Rauwolfia serpentina, which was particularly mentioned as having medicinal properties, including beneficial effects in insomnia, hypochondria and insanity. About 25 years ago its use was mentioned by modern Indian clinicians as a hypotensive and as a therapeutic agent in psychiatric conditions. On the basis of some of their reports of its value in the treatment of schizophrenia, studies were undertaken in the United States about 5 years ago. Various preparations from the plant have been known as tranquilizers since that time. It is now available in three forms of varying potency. The whole powdered root is known as Raudixin®. A partially purified mixture of alkaloids of the alseroxylon fraction is known in this country as Rauwiloid®. The purified alkaloid is known as reserpine, and most of the recent clinical contributions are concerned with the use of this fraction.

The various forms of reserpine were introduced into this country primarily as hypotensive agents. Experience indicated that their major importance in this field was in relieving the anxiety and tension in hypertensive patients and that it was an effective drug when used in combination with other more potent hypotensive preparations. Its mode of action is not entirely understood. As indicated in Berger’s general classification, it operates as an autonomic suppressant. It has been suggested that the central sympathetic depressant effect is not due to a direct depression of central sympathetic structures but rather to a blockade or inhibition of afferent impulses which activate these centers under normal conditions. It has also been found to stimulate the reticular formation, which perhaps gives a clue to why subjects who are tranquilized can be easily awakened. Studies on serotonin (5-hydroxytryptamine) indicate that reserpine may bring about a release of this substance from brain tissue and thus produce its clinical effects.

Reserpine has proved efficacious in the treatment of chronic psychotic patients. The observed results are somewhat similar to those noted with the use of chlorpromazine. It does not act as promptly as this drug and after administration is discontinued there may be some persistence of effects, suggesting that reserpine acts indirectly (possibly through serotonin release) rather than through a direct effect on neural mechanisms. The general procedure in adults has been to start with a minimal dose and gradually increase it to the point of tolerance or beneficial clinical effects. Initial doses of Raudixin® (the whole root) are conventionally 100 mg twice daily, of Rauwiloid® (the partially refined alkaloid), 4 mg daily, and of reserpine, 0.5 to 1.0 mg daily. Untoward effects are minimal and usually consist of nasal congestion, gain of weight and laxative effects. Lassitude and drowsiness have been noted with larger doses, as have the extrapyramidal symptoms of Parkinsonism, similar to those seen with the use of chlorpromazine. Reserpine is not useful in depressions, and depressive symptoms have indeed been complications of its use in hypertensive patients. There is no evidence that tolerance is definitely established.

As in the case of chlorpromazine, hearsay reports suggest that reserpine has been
TRANQUILIZING DRUGS

used widely in children, but publications concerning its effect as a tranquilizer in youngsters are relatively few.

A number of reports have come from psychiatric hospital units for children and are of the same quality and significance as those noted in the case of chlorpromazine. At the Rockland State Hospital in New York, Nicolaou and Kline19 reported a study outstanding in its design and clarity of presentation involving 39 boys hospitalized for psychiatric reasons. In their initial study a dose of 1.0 mg of reserpine was given daily for 10 weeks, with no adverse changes noted. A significant number of the patients tended to show more conscious awareness of their anxiety, and where overanxiety and lack of co-operation were important symptoms there tended to be improvement. They further studied 11 schizophrenic, and 14 overactive, boys with behavior problems, using parenteral as well as oral dosage. The schizophrenic boys all improved with parenteral dosage, particularly in terms of diminished overactivity. The improvement was not maintained with oral dosage. Regressed patients became more alert. Overactive boys with behavior problems all responded to parenteral dosage. Most of them continued their improvement with oral dosage, and in the case of several it was possible to discharge them to the community. An improvement in interpersonal relationships was conspicuous. Since emotional lability was frequent at the height of the pharmacologic response, the authors suggest that the drug cuts through psychologic defenses which psychodynamically may have been set up to allay anxiety. A more conscious awareness of this anxiety, and possibly lessened need for defenses, may account for the improvement. A convulsive-like attack in one patient and Parkinsonism in another were complications.

The group at Bellevue Hospital who reported on chlorpromazine,6,7 also discussed the use of reserpine in dosage of 0.3 mg daily the first week, increasing to 3.0 mg daily the fourth week in hospitalized children. They did not feel that reserpine benefited a significant number of their patients, although they suggested that limited dosage and exclusive use of the oral route of administration may have precluded maximal effects. Bender and Nichtern17 note that in autistic schizophrenic children the results were completely unpredictable. They felt that dosage schedules had to be highly individualized and that tolerance of the drug was variable. Mikształ,18 who also reported on chlorpromazine, noted comparable results when reserpine was used with children hospitalized for psychiatric reasons.

In children seen largely on an outpatient basis, Lambros20 found that in a large series of children with convulsive disorders reserpine was beneficial in reducing irritable behavior. It was also of assistance in relieving the restlessness of a number of children immediately after head injury and temporarily improved enuresis in other children. Zimmerman and Burgemeister,21 reporting on a large series of children with convulsive disorders, noted that 6 of 10 improved as far as their behavior responses were concerned, although two-thirds of this and a larger group were unimproved, or worse, as far as the seizures were involved. In a group of 10 mentally retarded children no change in ability to perform psychologic tests was noted, but overactive and psychotic behavior, when it existed as a complicating problem, was somewhat relieved. Timberlake and his associates22 noted that 1.0 mg daily of reserpine resulted in improvement of the behavior of 40% of overactive, abusive, destructive, impulsive or withdrawn mentally retarded children during 2 months of administration. Intellectual capacity was not altered. There have been other reports of the use of reserpine in mentally retarded individuals, but the majority of these have not been children, and it is difficult to know whether results in various age groups are strictly comparable.

In a study of 15 children with cerebral palsy, Watkins23 noted that parents were more impressed by changes in children's behavior at home than the therapists were at a treatment center.

Talbot24 administered reserpine in elixir form, 0.1 mg three times daily, to 29 irrita-
ble, hypertonic infants between 7 weeks and 12 months in age, with reduction of symptoms in all. His comments on the general effect of the medication, not only on the infant but on the family and distraught parents are worthy of attention by pediatricians.

It is more difficult to evaluate the efficacy and general acceptance of reserpine as a tranquilizer in children than is the case with chlorpromazine. The need for parenteral use for prompt response may be one reason for this, as well as the occasional depressive effects and discomfort associated with nasal congestion and gastrointestinal disturbance.

**Diphenylmethane Derivatives**

Two drugs from the diphenylmethane group are fairly widely known for their tranquilizing effects. They have apparently not been used as extensively as the substances already discussed, and reports concerning their effect on children are correspondingly limited.

Azacyclonol (Frenquel®) is an isomer of a mildly stimulating, antidepressive drug, Meratran®, which had been introduced somewhat previously. Despite its chemical similarity to Meratran®, Frenquel® has very different pharmacologic properties. It is apparently not a depressant of the mesodiencephalic activating system but may act through its inhibiting effect on serotonin. It has been noted to have a blocking effect on the so-called model psychoses induced by the administration of lysergic acid diethylamide (LSD) and has been found beneficial in relieving adult psychotic patients with hallucinations. In general, its effect on chronic hospitalized adult psychiatric patients somewhat parallels the clinical effects of chlorpromazine. A conventional dose for adults is 10 mg twice daily by mouth. No untoward side reactions have been observed. While no detailed reports of its effect on children have appeared, Bender and Nichtern7 indicated that it had been used on seriously maladjusted children at Bellevue Hospital and that it seemed to decrease the impulsivity of some of them, to integrate their total functioning, rendered some more amenable to therapy, and reduced diffuse anxiety in some schizophrenic children and others suffering from organic brain disorders. They do not mention the dosage used with children.

Another drug of this group which has had wide publicity but limited careful clinical documentation is hydroxyzine (Atarax®). Bayart,25 reporting from a pediatric service in Belgium, indicated that on 30 mg daily there was 90% reduction in tics in a series of children treated for this symptom and that in another group of children with poor school records the calming effect of the drug brought about improvement in scholastic performance within 10 to 15 days. Nathan and Andelman26 used hydroxyzine in the form of a syrup, 20 to 60 mg daily, in a series of 58 children seen in private pediatric practice for a variety of behavior and emotional problems. The responses to the medication were definitely individualized, but a large majority of the patients showed striking improvement, in the opinion of their physicians, their parents and their teachers. The lack of toxicity of the preparation and minimal side effects was impressive. Ayd27 noted similar effects in children, particularly in terms of decreasing tension, relieving disturbed autonomic function, and calming hyperkinetic behavior. He suggested doses larger than those currently recommended for children and indicated that 200 to 300 mg daily may be needed in some hyperkinetic children. He suggested that single or repeated doses of 25 mg orally or intramuscularly a few hours before unpleasant, fear-provoking situations, such as diagnostic tests in the hospital, might suffice to relieve anxiety and secure the child's co-operation. Its effect on schizophrenic children has been inadequately studied and results are not clear. He wisely indicates in a review of tranquilizing therapy in general that it should be a part of the total therapeutic attack on a child's problem.

The paucity of controlled and documented information regarding the use of diphenylmethane derivatives as tranquil-
izers in children suggests the need for more investigation as to their value as compared with other tranquilizing agents.

**Substituted Propanediols**

Drugs of the substituted propanediol group were originally introduced into psychiatric practice because of their muscle relaxant effect. The first prominent preparation of this type was mephenesin (Tolserol®). In one report of the use of this drug with children, Freedman and his collaborators reported a study of its use on children hospitalized for psychiatric reasons. In some of the patients there was an improvement in relationships with others. In some there was a relief of anxiety, and in a few, diminished sense of depression, and in others decreased hyperactivity. Its effect on schizophrenic children was not striking. Doses up to 1,500 mg three times daily were employed. Because of the brevity of the action of this preparation, the size of the doses needed, and the frequent occurrence of gastrointestinal disturbances, interest in the use of mephenesin as an adjuvant in psychiatric treatment is already waning. A more recently introduced and chemically related compound, meprobamate (Equanil®, Miltown®), which has a much greater tranquilizing effect, is at present receiving wide attention.

Meprobamate is considered a central relaxant, in contrast to the autonomic suppressant effect of the drugs in the first three groups which have already been discussed. It seems to have a selective blocking action in interneuronal reflexes and in this way may block some of the activity of the reticular (activating) systems of the brain stem and thalamus. It is also known to reduce muscle tension. Although its mode of action differs from those of the other drugs which have been discussed, its clinical effect is not dissimilar. It is said to have special value for psychoneurotic patients who react in an abnormal way to somatic stimuli. It has little or no demonstrable effect in so-called “normal” human subjects. While it reduces excess anxiety and tension, it does not produce depression and is relatively free of toxic effects. The possibility of the establishment of tolerance and habituation in some adults has recently been reported. Initial fatigue, dizziness and occasional headache in adult patients usually wear off with continued use of meprobamate, but rarely nausea is a reason for discontinuing it. The adult dosage is 400 to 2,400 mg daily, divided over the 24 hours.

Selling, who reported some of the earliest clinical observations with meprobamate, included mention of 10 children. He mentions briefly that six of these showed a decrease in activity, better concentration and diminished disruptive influence in the classroom as a result of their medication. Litchfield reported his observations on a group of children seen in a general pediatric clinic because of behavior disturbances. In younger children the administration of meprobamate resulted in a decrease of restlessness, irritability and sleeplessness, and older children were more responsive to parental discipline. Several older children with irritability associated with petit mal convulsive disorders (in whom the seizures had been controlled) were also improved as far as behavior was concerned. Dosage varied with age, but approximately 400 mg daily, divided throughout the 24 hours, was considered optimal for most of the patients. No side effects, aside from occasional drowsiness, were noted. Possible psychodynamic factors involved in the patients’ problems were not discussed. Perlstein gave meprobamate to a group of children suffering from convulsive disorders and other neurologic disturbances. Petal mal attacks were favorably influenced in some. It was noted that one reason for this may have been the tranquilizing effect on their emotional disorders which might have triggered individual seizures. Initial dosages of 200 mg twice daily were gradually increased to a maximum of 100 to 800 mg two to four times daily. Aside from drowsiness, no side effects were noted. Gillette discussed the effects of meprobamate on 53 patients with cerebral palsy, the majority
of whom were children. While she focuses her discussion on the response of these patients in terms of muscular function, she notes that emotional control was improved in 40% of the children and overactivity reduced in 25%. Kugelmass reported a diminution in the incidence of a wide variety of undesirable and irritating behavior characteristics in 250 mentally retarded children who received this drug.

In contrast with what has been reported concerning the other tranquilizers under discussion, meprobamate has apparently not been studied, insofar as children are concerned, in the controlled setting of a children's psychiatric hospital ward.

**DISCUSSION**

At the present time the physician who is looking for a synoptic comprehensive review of significant information about tranquilizing drugs is bound to be disappointed. A great deal has been learned about them, and while much of it has been published, the literature is widely scattered. Much of what has been learned is of too recent origin to have appeared in textbooks, and the time is not yet ripe for definitive review monographs. A considerable amount of basic and clinical data on some of the more widely used compounds is available in the reports of symposia published by the New York Academy of Sciences and research reports issued by the American Psychiatric Association. These are valuable initial sources of reference, as is Bakwin's review article on chlorpromazine.

The use of tranquilizing drugs to modify children's behavior difficulties is only one aspect of a much larger field dealing with the chemotherapy of children's behavior disorders in general. This has been a matter of interest to pediatricians and child psychiatrists for some 20 years and is briefly summarized in the review by Bender and Niehtern, to which reference has already been made.

The treatment of emotionally disturbed children is of course the special province of the child psychiatrist and the child guidance clinic. Where these are available to the pediatrician as sources of consultation or referral, he will presumably enlist their aid in management. However, many clinicians do not have ready access to such resources and must handle their patients' problems as part of a busy pediatric practice. In such instances, the use of tranquilizers which reduce or eliminate many troublesome behavior symptoms offers a valuable supplement to the guidance of parents, counseling of children, and helpful advice to teachers and community agencies, which make up a significant portion of every pediatrician's daily activities. If the use of the drugs makes some children "easier to live with," and thereby contributes to an improved social adjustment, to better scholastic success, or wider social acceptability, their use is well worthwhile. The indirect effects of improvements in children's behavior upon the attitudes toward them of their parents, teachers, and playmates may well be far more important in the long run than the direct effect of medication upon the children themselves.

We still need a great deal more information regarding the precise mode through which various tranquilizers alleviate certain specific behavior symptoms. Until this is available it will be impossible to select accurately a particular drug for use in a particular clinical problem. It is to be hoped that in future studies with tranquilizers, particularly in the field of pediatrics, as much attention will be paid to psychologic processes which are modified as to the conspicuous symptoms which are relieved.

There are three types of situation in which the pediatrician may find tranquilizing drugs particularly useful. One of these involves children who are acutely disturbed, anxious, tense, agitated or overactive to a degree that emergency relief is indicated. Another occurs where children are about to face a potentially disturbing experience such as hospitalization or various treatment procedures. Here temporary tranquillization may not only help put a child at ease and assure his co-operation...
but may result in his being less apprehensive regarding future measures of the same sort. The third situation involves children who are chronically emotionally disturbed and whose overt symptoms of anxiety, hostility or overactivity make it impossible for them to participate successfully in the conventional childhood activities, and thus deprive them of many experiences which are important factors in promoting healthy personality development.

Conclusive evidence as to the relative value of the various tranquilizers in each of these situations is not yet available. Most of these drugs, regardless of their mode of action, produce symptomatic improvement of the same sort—reduction in overactivity, diminution in tension or lessening of anxiety. This leaves the pediatrician with a choice of substances from which he may choose, but no clear cut indications that a particular preparation is essential to meet a very special need. The fact that when reserpine is used orally there is a definite time-lag, both as to when it becomes effective and when it ceases to be effective, may influence its selection in some instances. Annoying and at times dangerously toxic side effects are a possibility with most of the drugs which have been mentioned. In none of them, however, is the hazard so great that their use is seriously contraindicated when the need is urgent.

Many clinicians when using drugs primarily to relieve symptoms which in themselves are not potentially lethal employ unusually conservative dosage. When drugs are used to prevent or relieve emotional disturbances in children, too cautious an approach is a serious obstacle to consistently good results. The drugs which have been discussed have far more than placebo value. However, the assurance with which they are prescribed will frequently be reflected, particularly in children's parents, in attitudes of confidence and acceptance which contribute a great deal to the total treatment situation.

For the emergency management of acutely disturbed children it is suggested that a potent tranquilizer, in form designed for parenteral use, be given generously, promptly and by injection. If the child has already received sedative drugs it must be remembered that tranquilizers potentiate their effect, and dosage must be scaled down accordingly. It must also be remembered that chlorpromazine and reserpine may lower the convulsive threshold, so that if the child also requires treatment for epilepsy, administration of anticonvulsive medication should be continued.

For prophylactic use in the face of impending special procedures which may be disturbing, a tranquilizing drug is best given by mouth in full dosage 1 or 2 hours before the effect is needed. If the procedure is also to involve an anesthetic, consultation should be held with the anesthetist since most of the tranquilizers compound or complicate the effect of many anesthetic agents.

The effective use of all drugs, including the tranquilizers which are used to relieve the symptoms of children with chronically disturbed behavior, is an art which usually improves with experience. Oral preparations in reasonably palatable form adapted to the age of the child are preferable. Adequate uninterrupted dosage is desirable. Changes in dosage should be a decision for the physician, not the parent, and should not be made too frequently. If the therapeutic results are good, medication should be maintained for a period of weeks or months. The likelihood of children becoming habituated to or dependent upon any of the tranquilizers in common use is very slight, thanks to the lack of enthusiasm of most youngsters for medications in general. A major objective for the use of pharmacotherapy of children with behavior problems is to enable them to be free of disturbing symptoms for a period long enough to permit them to build up confidence in themselves. To insure this objective, the use of medication must always be accompanied by other available forms of guidance and psychologic management as has been repeatedly mentioned earlier in this discussion.
SUMMARY

The availability of so-called tranquilizing drugs as adjuncts to the therapy of emotionally disturbed children is of such recent origin that few reviews of their use in this regard have as yet appeared. The present article discusses a tentative classification of these substances, their general effects, probable mode of action and potential hazards. Included is a brief review of the literature concerning the use of the following preparations as tranquilizers for children: chlorpromazine, reserpine, aza-cyclonol, hydroxyzine and meprobamate. Indications for their use are briefly outlined, as are some of the principles of their effectiveness. Emphasis is placed upon the fact that tranquilizing drugs may be useful for the relief of symptoms, but that in the total treatment of emotionally disturbed children all other available means of psychologic management should also be employed.

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