The Tranquilizers

and Gertrude Link, R.N.
Cincinnati, Ohio

Any experienced anesthetist knows that it is impossible to positively predict the action and effects of an anesthetic drug upon a given patient. Also, that why many of these drugs act as they do in producing analgesia and anesthesia, has long been a subject of conjecture and theory. No one really knows. It is our feeling that the group of drugs known as "the tranquilizers" can be added to the above, because one can only theorize as to their true mode of action and cannot predict with certainty how they will affect a given patient. In spite of this unpredictability, it has been estimated that some thirty million prescriptions were written last year for these drugs with the expenditure of more millions of dollars—a staggering figure to contemplate. Scarcely a medical periodical is published that does not contain an article on one or more of the tranquilizers, not to mention the articles appearing in lay publications. It is not our purpose to discuss the tranquilizers as they are prescribed as practically a panacea for all ills, but rather to confine our remarks to discussing a few of the more commonly used drugs, and the effect they seem to have on the patient who is to be anesthetized.

In general, the tranquilizers can be divided into two large groups, according to their mode of action, as shown in the following table:

I. Autonomic Suppressants—Thorazine, Sparine, Compazine, etc.
A. Mode of Action:—
1. Antagonize acetylcholine, histamine and serotonin, which regulate certain autonomic functions.
B. Effects:—
1. Produce drowsiness without necessarily inducing sleep.
2. Interfere with memory
3. Prolong or potentiate barbiturate anesthesia and narcotic action
4. Increase excitability; lower electro-convulsive threshold
5. May produce apathy, depression and loss of initiative in normal persons.

II. Central Relaxants; Equanil, Miltown, Tolserol, Myanesin, Etc.
A. Mode of Action:—
1. Produce relief of abdominal responses to tension and anxiety by a muscle relaxant effect, without affecting autonomic function.
B. Effects:—
1. Potentiate barbiturate or narcotic actions only in large doses
2. Excitability not increased

*Director, School of Anesthesia, Cincinnati General Hospital.

3. Do not interfere with normal responses to environment; no depression or apathy.
4. Marked reduction in muscle spasticity
5. Marked diminution of anxiety and tension.

Table 1

Unlike narcotics, the tranquilizers are thought to affect subcortical areas of the brain. Whereas the opiates and barbiturates, while reducing pain and anxiety, also produce drowsiness, lethargy, and even depression of respiration, which may render the patient unable to respond coherently or to cooperate, the tranquilizers, especially those in the central relaxant group, produce relief of pain and anxiety plus a sense of well-being, without accompanying lethargy, inability to cooperate or respiratory depression. Because of this difference in action, many anesthetists feel that the tranquilizers are a valuable adjunct to pre-operative medication. The effects of pre-operative, long term treatment with the tranquilizers, especially chlorpromazine, were probably first noted in mental institutions. Massive doses of this drug were given to psychotic patients over long periods of time. When one of these patients needed surgery and an anesthetic, the problem of hypotension was great and many patients were lost because of the characteristic irreversibility of tranquilizer-induced hypotension which responded poorly to vasopressors. Now, however, with more knowledge of the effects of these drugs, smaller doses are given, less premedication is required and less anesthetic agent is used to maintain general anesthesia. Spinal block and intravenous barbiturate agents are managed with extreme caution, and are used only when other agents are contraindicated.

Four of the most commonly used types of tranquilizers are Chlorpromazine, Promethazine, Reserpine and Meprobamate. Let us start with Chlorpromazine (Thorazine) and briefly discuss each in regard to its place in anesthesia.

Chlorpromazine - Autonomic Suppressant

I. Desirable Effects: -
A. Enhance effects of premedication and of anesthetic agent.
B. Antihistaminic.
C. Anti-emetic.

II. Undesirable Effects: -
A. Hypotension.
B. Tachycardia.
C. Poor response to vasopressors.

III. Choice of Anesthetic: -
Cyclopropane.

Table 2

From the above chart, it would seem that this drug would be ideal as an adjunct to pre-medication because of its desirable effects. However, with practically all anesthetic agents except cyclopropane, the undesirable effects are likely to predominate in a manner which may prove irreversible. In addition to these phenomena seen in conjunction with anesthesia, serious toxicity may be evidenced in some persons. This toxicity may be manifested by obstructive jaundice, blood dyscrasias and dermatitis, in many cases following even small doses.

Studies made on the use of chlorpromazine intravenously as a premedicant, when cyclopropane was used as the anesthetic agent, revealed the following:

1. No significant change in cardiac output; 2. Reduction in peripheral resistance; and 3. Increase in heart rate and some fall in blood pressure.
In contrast with severe hypotension and tachycardia seen when chlorpromazine is used with other agents, the above effects are relatively innocuous.

Promethazine (Phenergan), on the other hand, may be a very useful drug in the hands of the anesthetist. The following table briefly outlines its effects:-

**Promethazine (Phenergan) - Central Relaxant**

I. Desirable Effects:-
A. Enhances effect of premedication and of anesthetic agents.
B. Antihistaminic.
C. Combats emesis and hiccups.
D. Minimal depression of vital functions.
E. Can be used in children and geriatric patients with few side effects.

II. Undesirable Effects - (usually as a result of large dosage):-
A. Hypotension.
B. Tachycardia
C. Respiratory depression.

III. Choice of Anesthetic:-
Any agent except intravenous barbiturates.

*Table 3*

With this drug, the desirable effects outweigh the undesirable effects since the latter become apparent only as a result of large dosage. This drug has been found valuable as premedication in conjunction with meperidine. It has been found to relieve fear and apprehension and promote a feeling of well-being and relaxation in patients coming to surgery. As a result, as with any satisfactory pre-medication, reflex irritability is reduced and less anesthetic agent is needed. Care, however, must be taken in the use of promethazine with intravenous barbiturates since it markedly enhances their action. Complications of hypotension, tachycardia and respiratory depression may intervene with this combination; however, response to treatment of these untoward effects is much more predictable with promethazine than with other tranquilizers. It is also claimed to be of value in postoperative sedation, lessening pain and apprehension and stabilizing of vital signs. When given in conjunction with narcotics however, the narcotics should be administered in smaller dosage.

This drug is of particular value in combination with spinal and local anesthesia. Most adult patients given 25 milligrams, will become calm and drowsy, although easily aroused. Vital functions are affected minimally, if at all. With promethazine as an adjunct, many surgical procedures which might otherwise require addition of intravenous barbiturates in anesthetic dosages, can be made possible under local anesthesia.

It is worthy of note that chlorpromazine, promethazine and meperidine can be successfully combined in what is known as a “lytic cocktail”. The dosage of each drug is as follows: Chlorpromazine - 25 mgm.; Promethazine - 25 mgm., and Meperidine - 100 mgm.

This combination yields 4 c.c. of solution which may be administered intramuscularly ninety minutes preoperatively to the adult who is to have procedures such as carotid angiogram, femoral arteriogram, cardiac catheterization or even closed reduction of some minor fractures. It has been used with phenomenal success at the Cardiac Clinic, Children's Hospital, Cincinnati, Ohio for cardiac catheterization of children of all ages with congenital heart disease. In children, the dose is estimated giving 1 c.c. of the “cocktail” for each twen-
ty pounds of body weight. With the lytic cocktail the children are drowsy but cooperative and come through the procedure with few complications and minimal discomfort.

In the adult, it has been occasionally necessary to repeat meperidine 50 mgm. and promethazine 25 mgm., half intramuscularly and half intravenously, to maintain good analgesia and cooperation of the patient during the procedures. However, with this supplement, the pain and discomfort of intravenous or intra-arterial dye injection is reduced to the extent that satisfactory X-ray films can be obtained for diagnostic studies.

In our opinion, Reserpine is one of the most dangerous of the tranquilizers in combination with anesthesia. In the table below its effects are outlined:

**Reserpine** - Autonomic Suppressant

I. Desirable Effects:
   A. Reduction in nervous tension plus sedative effect.
   B. No significant change in arterial O₂ tension.
   C. Pulmonary ventilation not affected.
   D. Increases appetite.

II. Undesirable Effects:
   A. Hypotension during and after anesthesia.
   B. Bradycardia — cholinergic effect.
   C. Peripheral edema.
   D. Prolonged effect even after withdrawal.
   E. Poor response to vasopressors.

III. Choice of anesthetic:- (if any) Cyclopropane.

Table 4

Reserpine is a Rauwolfia derivative, used extensively for reduction of blood pressure in the hypertensive individual. It is also used as a tranquilizer, per se, because of its similarity in action to that of chlorpromazine. Its undesirable effects may become apparent, when anesthesia is superimposed, for as long as two weeks after withdrawal of the drug. If the anesthetist is not informed of the fact that a patient has been receiving Reserpine, irreversible hypotension may take place following induction of anesthesia with any agent. This may hold true even under the lightest plane of anesthesia with nitrous oxide and oxygen. It is our conviction that at least three weeks should be allowed to intervene between withdrawal from Reserpine therapy and the administration of an anesthetic. Overdosage with Reserpine has been known to result also in serious psychological complications such as suicidal tendencies and marked depression.

The fourth and last type of tranquilizer which we will mention here is Meprobamate. This is one of the least noxious when used in average dosage, as shown in the outline below:

**Meprobamate** - Equanil, Miltown - Central Relaxant

I. Desirable Effects:
   A. Low toxicity; four to five times less toxic than most barbiturates.
   B. Skeletal muscle relaxant, with little, if any, action on diaphragm.
   C. Anticonvulsant.
   D. Can be used as pre-operative sedation without producing hypotension or respiratory depression.
   E. Minimal, if any, action on vital functions.

II. Undesirable Effects: - (Probably due to idiosyncrasy)
   A. Allergic dermatitis with pruritus, fever, chills.
   B. Diarrhea.

III. Choice of Anesthetic:
   Any agent.

Table 5

Meprobamate is used orally and cannot be given parenterally; therefore, it has a greater margin of safety
and fewer side effects. There is relatively little danger of untoward responses in patients coming to surgery who have been medicated with Meprobamate and no special anesthetic agent is contraindicated. This drug is actually the most widely used of all the tranquilizers, being prescribed for any number of psychosomatic disorders with good results.

CONCLUSION
1. It is extremely important that the anesthetist be made aware that a patient has been treated with tranquilizers. 2. The anesthetist should know in what way the drug may affect the action of the anesthetic agent; therefore it is imperative the physiological effects of these drugs be known. 3. Vasomotor depression seen following the administration of some of the tranquilizers may be extremely difficult to treat, responding only to the use of the most potent vasopres-
sor drugs. 4. Extreme caution should be observed with any change of the patient's position, especially when the patient must be in Fowler's or head-up position, because of the frequent occurrence of postural hypotension. 5. Any anesthetic agent which has a ganglionic blocking effect, such as deep ether or high spinal, should be avoided. It is still our contention that there is no drug, or combination of drugs, which can ever afford the wide margin of safety provided by a skillfully administered inhalation anesthetic.

BIBLIOGRAPHY