INDIVIDUALIZATION OF THE PATIENT IN THE TREATMENT OF HYPERTHYROIDISM

GEORGE CRILE, M.D., AND GEORGE CRILE, JR., M.D.

1. INTRODUCTION

The association of hyperthyroidism with old age, extreme youth, heart disease, substernal goiter, or a poor preoperative response of the pulse curve, and with certain complicating diseases, presents a different problem in each instance from the standpoint of surgical treatment. Since it is not possible to set up a routine which is applicable to the management of every case of hyperthyroidism, patients in each of the groups mentioned should be given individual consideration. In short, the problem of the relative prognostic significance of the various factors which constitute warnings in patients with hyperthyroidism will be studied in regard to the specific complications which must be guarded against in each group of patients.

II. TREATMENT OF THYROID CRISIS

It is extremely significant that in the past 10 years, exactly one-half as many patients have died from hyperthyroidism in the Cleveland Clinic Hospital before any operative procedure had been undertaken as have died following operation for hyperthyroidism. This means that the hyperthyroidism which we see has advanced in many instances beyond the stage of curability.

Fifty-eight per cent of these patients who died in the hospital without operation died as a result of thyroid crisis, and ninety-four per cent of the patients who died from thyroid crisis without operation were delirious when they were admitted and died within five days of the time of entry. These figures indicate that if a patient in crisis survives the reaction incident to transportation to the hospital, there is a 94 per cent chance for her recovery. It can be assumed, therefore, that transportation aggravates a thyroid crisis and that a patient already in thyroid crisis should not be transported until the hyperthyroidism is controlled.

In the majority of the cases of fatal preoperative thyroid crisis, long-standing medical treatment had been attempted and often, x-ray or radium treatment had been tried unsuccessfully in the hope that an operation might be avoided. Often an acute infection of the upper respiratory tract or radiation therapy was the precipitating cause of the crisis. These facts emphasize the importance of prompt operation after a definite diagnosis of hyperthyroidism has been made.

Patients who are admitted in thyroid crisis should be given iodine by mouth, or, if the patient is vomiting, iodine should be given by

rectum in doses as great as 30 cc. of Lugol's solution a day. A 10 per cent solution of glucose to which iodine may be added is of great value in combating the tendency to dehydration and acidosis which often is present in patients in thyroid crises.

In a thyroid crisis, a vicious circle of excess metabolism and increase of temperature is present. The elevation of temperature increases the metabolism 7.2 per cent for every degree of temperature centigrade, and the increased metabolism results in greater heat production, and hence in a further elevation of the temperature. By refrigeration, this cycle can often be overcome and the temperature reduced to normal. For this reason, the oxygen tent is a valuable therapeutic agent in the treatment of thyroid crisis. Frequently, the temperature drops several degrees within a few hours of the time of its introduction. It is difficult to say whether this is the direct result of the oxygen or of the refrigeration from the cooled air, but the prompt benefit which the patient appears to experience suggests that the oxygen itself plays a significant rôle in combating anoxemia secondary to excessive metabolism and a failing myocardium. Refrigeration in the form of ice packs should be applied when the temperature is above 102° F. by mouth.

Complete digitalization should, of course, be carried out at once when auricular fibrillation or cardiac decompensation is present. It is extremely important for the patient to obtain rest from the wild and exhausting delirium which often is present. To accomplish this, bromides and morphine are of much more value as sedatives than the barbiturates, and this is true particularly in the older patients who not infrequently become maniacal following the administration of amytal, phenobarbital, etc.

Blood transfusion should be prescribed with caution when the temperature is at its peak. A transfusion reaction may occur as a result of the increased susceptibility of patients with high temperatures to such reactions. However, transfusion is of great value, particularly in elderly patients when the temperature is not too high and when long-standing hyperthyroidism, as is so often the case, has resulted in a lowering of the serum proteins and the production of edema.

III. Routine Preoperative Treatment of Hyperthyroidism

The routine preoperative management of the patient with hyperthyroidism consists in absolute bed rest, quiet surroundings with limitation of visitors, 30 grains of sodium bromide once or twice daily, mild hypnotics at night, and iodine in the form of 1 cc. of Lugol's solution three times daily. The patient should not be told the date of operation because almost invariably if this is done, it will be found that a night of worry will follow and the pulse rate will be elevated above its usual

level on the morning of the operation. One of us, in the earlier days of thyroid surgery, has seen a fatal thyroid crisis precipitated by informing a patient with severe hyperthyroidism of the date of operation, taking her to the operating room fully conscious, and then returning her to the ward without having administered any anesthetic or performed any operation. Therefore, operation is performed in the patient's room without any warning or preliminary psychic disturbance.

IV. Choice of Time of Operation, Type of Operation, and Anesthetic

a. Indications of Unfavorable Prognosis

No standard time of operation, no standard type of operation, and no standard anesthetic should be employed in the operative treatment of patients with hyperthyroidism. Each case should be individualized on its own merits, and the time and the type of operation and the anesthetic should be planned according to the prognosis of the case. In this way only can the maximum safety be assured to the bad risk case, and the minimum hospitalization and discomfort guaranteed to the patient for whom thyroidectomy should present no especial hazard.

The only two absolute contraindications for the surgical treatment of hyperthyroidism are persistent delirium or persistent vomiting. There are, however, certain factors whose presence, although they do not contraindicate surgery, constitutes a warning of an unfavorable prognosis.

In order to determine the relative prognostic significance of the various factors which generally are considered to constitute warnings, an analysis of the fatalities which followed operations for hyperthyroidism in the years from 1924 through 1934 has been made. If these warnings are classified according to the ratio of their occurrence in the group of patients who died following operation as compared to an equal number of patients in each year who were picked at random from those who survived operation, it is found that cardiac complications stand first in importance, and that auricular fibrillation, cardiac decompensation, myocarditis or valvular heart disease occurred seven times as frequently in the patients who died as in those who survived operation. Substernal goiter was present in a ratio of 6:1, a flat pulse curve in a ratio of slightly over 5:1, and age over 60 was present in a ratio of 5:1. The ratio of the presence of severe hyperthyroidism (Grades III and IV) was 3:1. Pulse over 100 at the time of operation was 2.5:1; the presence of complicating diseases, tuberculosis, diabetes, etc., but not including cardiac disorders was in a ratio of 2.5:1; pulse over 120 at entry was 2:1; weight loss of over one-fifth the body weight was 2:1. An analysis of all other factors, such as the presence of

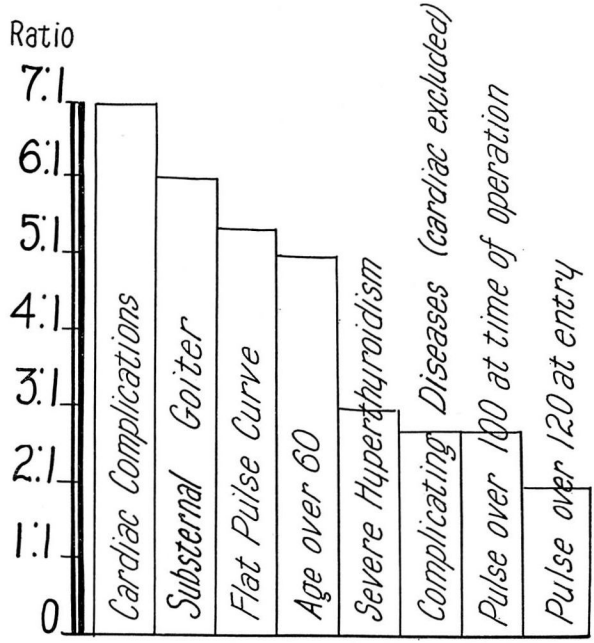
nodular goiter, of a hyperplastic goiter, of preoperative irradiation, of duration of the disease for more than two years, of a history of iodine medication before entry, of a basal metabolic rate above plus 50 per cent, and of sex showed that each occurred as frequently in the patients who survived operation as in those who died following operation (Chart 1).

In the order of frequency with which these warnings of the fatal outcome occurred, we find that age over 50 stands first, severe (Grades

Chart 1

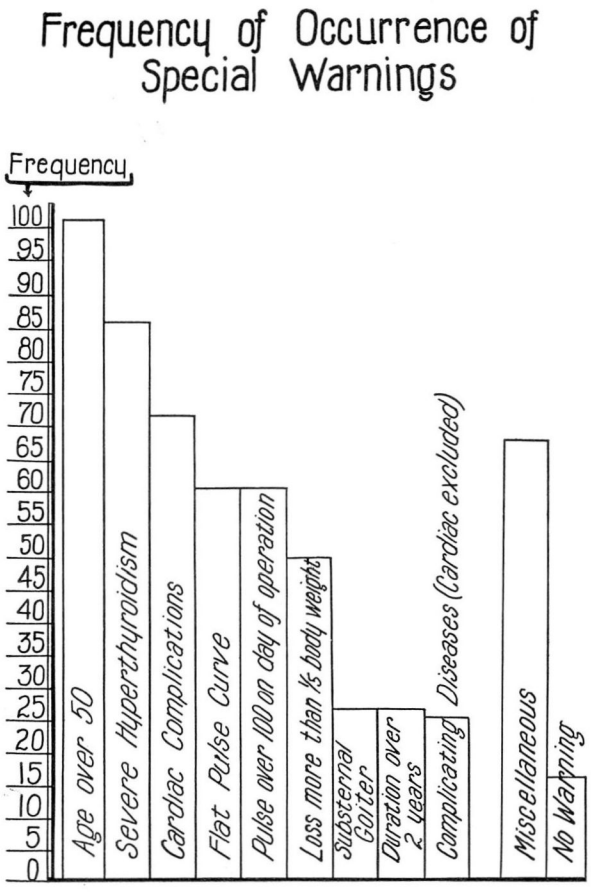
Relative Importance of Various Warnings

(Figures based on ratio of incidence of special warnings in patients who died following operation, to their incidence in patients who survived operation)



III and IV) hyperthyroidism second, cardiac complications third, the presence of a flat pulse curve (in effect a pulse curve which does not fall as rapidly as expected under the preoperative treatment) fourth, pulse over 100 on the day of operation fifth, loss of over one-fifth of the body weight sixth, the presence of a substernal goiter seventh, duration of the disease for more than two years eighth, and the presence of complicating diseases (exclusive of cardiac disorders) ninth (Chart 2).

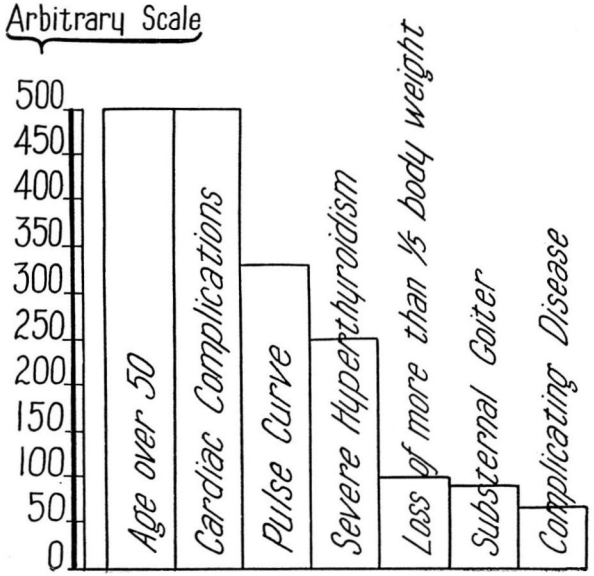
Chart 2



From these figures which represent (1) the frequency of the occurrence of each warning and (2) the ratio of incidence of each warning in patients who died after operation to its incidence in those who survived operation, we can build an arbitrary scale which indicates the probable importance of these various warnings in operative prognosis (Chart 3). It is our belief, however, that in spite of these figures which place age on a par with cardiac disease, age should stand first, because in the majority of instances, a cardiac disorder is the direct result of the arteriosclerotic processes that come with advancing years. Although the presence of a substernal goiter appears to be of little significance on the arbitrary scale, we believe that when this complication is present, it is of definite prognostic importance because it occurred six times more frequently in patients who died following operation than in those who survived operation.

Chart 3

Relative Importance of Various Warnings on an Arbitrary Scale Based on the Incidence and Prognostic Importance of Specific Warnings



Our final evaluation of these prognostic factors in the order of their importance is therefore (1) age, (2) cardiac condition, (3) pulse curve, (4) severity of hyperthyroidism, (5) substernal goiter, (6) loss of weight, and (7) complicating diseases (Chart 4). The final criterion on which we base the contention that age is the most significant prognostic factor is the fact that we have been able to perform as many as 1758 consecutive operations on patients under 45 years of age without a single fatality.

Despite the general conception that a history of long duration of the disease, a history of iodine therapy, or a high basal metabolic rate constitute danger signs, we have not, in this analysis, been able to find supportive evidence for such opinions. The average basal metabolic rate of the patients who survived operation was only 3.4 per cent higher than that of those who died after operation; moreover, the incidence of the basal metabolic rates above plus 50 per cent was nearly twice as great in the survivors as in the dead.

b. Determination of the Time of Operation

The time of operation is determined by the evaluation of the risk of the patient as judged by the presence or absence of the above warnings. The exact date is never set until the night before the operation, and should the patient's pulse rate on the morning of operation be elevated above its usual level, the operation is postponed. Under these conditions, the preoperative routine should be continued until the pulse curve has responded satisfactorily. In cases in which this curve is flat and does not come down in response to the preoperative routine, the minimum operation should be performed, and this should be performed only after prolonged observation of even three or four weeks has shown that the pulse rate will not fall below 100 in spite of adequate treatment. In this type of case, although the pulse may be only 100, the prognosis unquestionably is less favorable than in cases in which the pulse rate is higher but the drop in the pulse curve has been abrupt.

c. Choice of Operation

The minimum operation which is reserved for those patients who are judged to be the worst risks, is a single "trial ligation" of the superior thyroid artery under local anesthesia. If the reaction from this ligation is minimal, it is a good indication that the patient will be able to withstand a more extensive procedure, and that in a few days, a lobectomy can be performed with safety. If, however, the patient has a marked reaction following the ligation, it is best to wait until this reaction has subsided and then ligate the artery on the other side. The patient then is sent home to rest for three months, at the end of which period she returns for the completion of the operation.

If a lobectomy is performed, the wound is packed open with acroflavin gauze until the next morning. At this time, if the patient's condition is satisfactory, the second lobe is removed, thus completing the operation at one hospitalization. If, however, the reaction has been severe, the incision is closed, and the patient is sent home for three months before the other lobe is removed. It is interesting to note that we never have lost a patient following the second lobectomy when the patient has been sent home between the stages of the operation. Thus, when lobectomies are performed three months apart, even though it may seem inconvenient to the patient, it constitutes the safest method of thyroidectomy. One stage thyroidectomy, of course, is performed in the great majority of cases (85.7 per cent) and the above procedures are reserved only for those cases which present especial operative hazards.

d. Choice of Anesthetic

The choice of the anesthetic necessitates careful study, not only of the objective findings in the case, but also of the patient's personality, mentality, and emotional control. There can be no question but that when a local anesthetic is administered to an extremely nervous and emotionally uncontrolled patient, a psychic reaction occurs which may be more alarming than the depression which follows some types of general anesthesia. However, in the majority of cases, adequate and skillful infiltration of the local anesthetic supplemented by gas oxygen analgesia can make the operation so completely devoid of sensation that thyroidectomy can be performed without "psychic trauma." A basal anesthesia of 60 milligrams of avertin per kilogram of body weight has been used in selected cases since 1932 with good results.

A wide block with local anesthetic (three-fourths of one per cent novocain) supplemented with gas oxygen analgesia results in the ideal anesthesia for those patients who are cooperative and have good emotional control. These patients are carried in a stage of pleasant unconcern in which they are led by the anesthetist to discuss any subject that will divert their attention from the operation. This, of course, can be accomplished without depression of respiration and intracellular metabolism, and hence without the increased operative risk that necessarily accompanies a general anesthesia.

e. Management of the Patient between Stages of a Divided Operation

In the management of patients who are sent home between stages of a divided operation, either following ligations or between lobectomies, it is important to bear in mind the possibility that if iodine medication has been administered for a long time before the patient

entered the hospital, the disease may be partially under control and may actually be more severe than is apparent clinically. Therefore, if the patient is sent home following, for example, a ligation, and iodine is withdrawn, it is possible that an exacerbation of the hyperthyroidism may occur incident to the withdrawal of iodine, and that this exacerbation may be more severe than the remission induced by the ligations. If this is the case, a thyroid crisis may ensue at home, or the patient may go on to cardiac decompensation. We believe, therefore, that following the first stage of a divided operation, iodine should be administered until the remission induced by the operation is well established, and that it should then be withdrawn so that for the final six weeks before re-admission, the patient will have had no iodine and hence will be susceptible to iodine control. We believe that iodine loses its maximum effectiveness after protracted use, and although iodine undoubtedly does exert a slight effect in the control of hyperthyroidism for an indefinite period of time, the maximum benefit occurs in from two to four weeks. After this period, the continued use of iodine may be followed by the phenomenon of "iodine escape" and an exacerbation of the hyperthyroidism. For this reason the use of iodine is discontinued six weeks before the patient returns for the completion of the operation so that the maximum preoperative response to iodine may be attained.

V. Discussion of Efficacy of Specific Agents in the Prophylaxis and Treatment of Complications

Iodine, refrigeration, intravenous glucose, and blood transfusions are all indicated in the management of a postoperative thyroid reaction in exactly the same way as they are in the management of a thyroid crisis.

Preoperative digitalization is reserved for those patients who show evidences of myocardial failure or who have auricular fibrillation. We believe that it is not necessary to administer digitalis routinely to every patient before operation.

Since 1930, bad-risk patients have been placed in an oxygen tent immediately following operation and kept there until the reaction has begun to subside. We believe that this procedure has resulted in a definite reduction in the incidence of thyroid crisis. As mentioned before, it is difficult to state definitely whether or not much of this effect is not the result of refrigeration. During the past 10 years, there have been, on the average, twice as many deaths from thyroid crisis during the hot months of the year—June, July, and August—as in the colder period of the year. This in itself shows the necessity for refrigeration. But the oxygen tent appears, as above stated, to have a more specific effect on the thyroid reaction. The incidence of pneumonia

has not diminished as a result of the prophylactic use of the oxygen tent, but the relative incidence of mortality from pneumonia has diminished 50 per cent since its use was adopted in 1930.

VI. Application of Specific Therapeutic Measures to Special Groups

We have mentioned the various factors which constitute warnings in regard to operative risk and have discussed the therapeutic measures by which these risks can be minimized. The question next arises as to how we can apply these therapeutic measures to specific groups of patients so that the individual patient will have the maximum safeguard against the complications which occur most commonly in her specific group.

Further analysis of the cases which have terminated fatally following thyroidectomy shows that the presence of a flat pulse curve, of a basal metabolic rate of over plus 50 per cent, of a psychosis, or of severe hyperthyroidism, especially in young patients, constitutes a special warning against the development of the postoperative thyroid crisis which is the commonest cause of death in patients in these groups. In substernal goiter and in old age, the greatest risk is pneumonia. Myocardial failure is the most frequent cause of death in patients with auricular fibrillation, cardiac decompensation or evidences of chronic myocardial damage and also in those patients in whom the disease has been present for more than two years, and in those with low grade hyperthyroidism (Chart 4).

a. Severe Hyperthyroidism

In the first group—those patients who have an excessively high basal metabolic rate, a flat pulse curve, or in those who have a psychosis—all our therapeutic measures against thyroid crisis including blood transfusion, parenteral fluids, the oxygen tent, and morphine in doses sufficient to insure comfort and rest, should be used immediately following the operation.

While we believe that small amounts of iodine should always be continued after operation, we never have felt that the postoperative use of large doses of iodine exerted any striking effect on the thyroid reaction of a patient who had received the maximum amount of iodine. One of us has shown in the experimental laboratory that the administration of iodine exerts no effect on the elevated metabolism of completely thyroidectomized dogs fed on large quantities of desiccated thyroid. The effect of iodine is, therefore, not on the tissues of the body in general or on the thyroid hormone circulating in the blood, but its action is rather directly on the secretory activity of the thyroid gland. For this reason, large doses of iodine cannot be expected to cause any effect on

Chart 4

Causes of Death in Patients with Specific Warnings

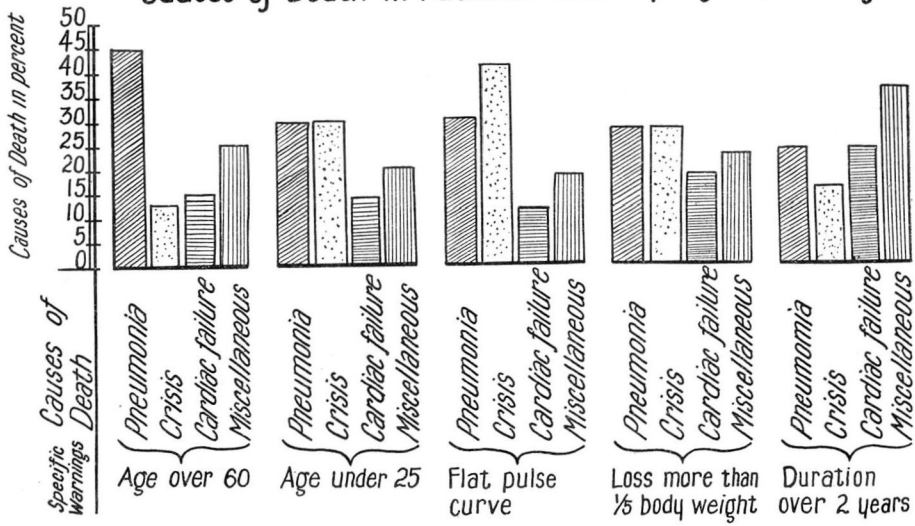
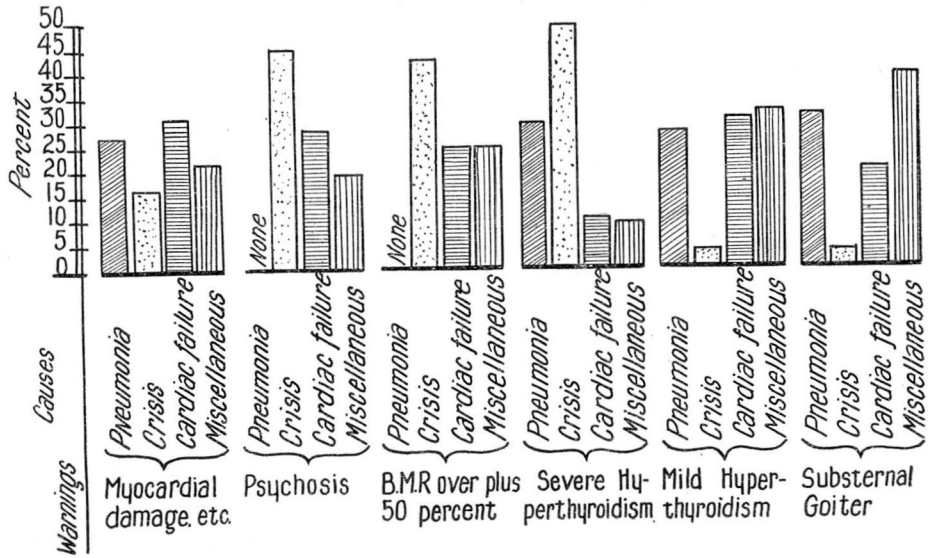


Chart 4 (continued)



the postoperative reaction of a fully iodized patient. The best we can do is to carry on with the routine small dose of iodine so that at least there will be no exacerbation of symptoms incident to the withdrawal of iodine.

If the surgeon believes that the patient's greatest hazard is from the severity of the hyperthyroidism and if the patient is relatively young and otherwise in good condition, a basal anesthesia of avertin is of definite value in calming the patient and minimizing the postoperative reaction. If, however, the patient is old or debilitated, the use of this drug is contraindicated as will be explained later.

In all cases, the temperature should be watched carefully and taken at least every two hours during the first two days after operation. This is particularly true in hot weather when the rise of the patient's temperature may be almost as rapid as that following a chill. If 12 ice caps are placed on the patient's extremities and about the sides of the body when the temperature reaches 102° F., its further elevation can usually be controlled. Additional ice caps are added and an alcohol sponge bath is given if the temperature reaches 103° F. If it should continue to rise to 104° F. or above despite these measures, the patient literally is packed in cracked ice so that more heat is abstracted than can be created. In this way only can the patient be saved from "burning herself up" in a crisis of chemical hypermetabolism.

b. Hyperthyroidism in Old Age

The management of the aged patient, in whom pneumonia is the greatest hazard, is quite different. We have seen that sedation and avoidance of psychic disturbances are fundamental principles in the management of severe hyperthyroidism in the young adult. But in the aged, we must not depress the respiration or the internal metabolism of the body because of the danger of inducing a terminal pneumonia. Depressant drugs are tolerated well in the young but easily force the aged below the critical threshold at which resistance cannot overcome the ever-present tendency to pneumonia. Every resource at our disposal must be utilized to build up the resistance of the aged patient and stimulate the vital functions. Preoperative and postoperative blood transfusions are of especial value in the aged, and there can be no question as to their value in increasing the resistance and strength of the patient.

As we have shown already, the chief hazard in the aged is pneumonia, while death from thyroid crisis is relatively rare. Hence, in the aged, it is better to perform the operation under local anesthesia with a minimum of gas oxygen analgesia. Avertin or any general anesthesia with its secondary depression of respiration, the cough reflex, and of the internal metabolism should be avoided even at the expense of an occa-

sional mild psychic reaction. Similarly, the postoperative use of morphine should be limited to the minimum requirements.

In old age, the principle of the multiple stage operation should be followed, and a trial ligation should be performed if there is any question in the mind of the surgeon in regard to the ability of the patient to withstand a more radical procedure. Pneumonia may follow even a relatively mild thyroid reaction, and the general condition of the patient as well as her status in regard to hyperthyroidism, should be given prime consideration in the choice of both the time and type of operation.

As has been shown before, the use of the oxygen tent has lessened the mortality rate from pneumonia. The aged patient with hyperthyroidism therefore should have oxygen therapy at least as soon as any signs of pulmonary congestion occur. In addition, we believe that the severity of the thyroid reaction has been reduced by the use of the oxygen tent, and that bad-risk patients of all ages make better progress when oxygen therapy is started immediately after the operation.

In the aged, ice packs should be applied only when absolutely necessary so that chilling with its attendant liability to pulmonary complications may be avoided.

c. Hyperthyroidism with Cardiac Complications

Preoperative digitalization, as we have mentioned above, should be reserved for those patients who show evidence of severe myocarditis, or who have auricular fibrillation or cardiac decompensation. As soon as either of the latter two complications are discovered, the patient should receive digitalis immediately. Oxygen therapy is of value in these cardiac complications as is morphine in doses adequate to insure rest. In this way, the failing myocardium is strengthened by the digitalis, the efficiency of the oxygen-distributing function of the heart is increased by the oxygen tent, and the metabolic demands of the organism as a whole are decreased by the morphine to the point that a balance between oxygen supply and demand is struck and cardiac compensation restored. Blood transfusion of course is contraindicated in the presence of acute cardiac decompensation.

d. Intrathoracic Goiter with Hyperthyroidism

The presence of an intrathoracic goiter in a patient with hyperthyroidism demands special consideration. Pneumonia again is one of the greatest hazards and the same routine measures for its prevention should be applied as have been suggested for the prevention of pneumonia in the aged. The multiple stage operation, however, increases the technical difficulties in the removal of an intrathoracic goiter, and this type of operation is not performed except in cases in which it is felt that a one stage operation would involve an unjustifiable

risk. The technical difficulties in the delivery of a substernal goiter may be increased enormously by adhesions and scar tissue secondary to the first stage of a divided operation.

e. Hyperthyroidism Complicated by Chronic Nephritis

In the presence of chronic nephritis, avertin should not be used. The patient should be treated before and after the operation with large quantities of a 10 per cent solution of glucose administered intravenously.

f. Hyperthyroidism Complicated by Liver Damage

When hyperthyroidism is complicated by liver damage, such as alcoholic cirrhosis, the chief cause of death is a peculiar type of toxemia which is characterized by stupor and alterations of the blood chemistry, which perhaps are incident to hepatic insufficiency. This complication is best averted by the pre- and postoperative administration of a high carbohydrate diet and large quantities of a 10 per cent glucose solution intravenously.

g. Hyperthyroidism Complicated by Diabetes

The postoperative management of the diabetic patient with hyperthyroidism may also be difficult and the attention of a competent specialist in diabetes is desirable. The most important principle involved is the constant maintenance of oxidation of relatively large quantities of glucose.

h. Hyperthyroidism Complicated by Pulmonary Disease

In the presence of chronic pulmonary disease, the incidence of postoperative pneumonia is high, and the same precautions which were recommended in the treatment of patients with substernal goiter with hyperthyroidism should be taken.

VII. Conclusions

1. The prophylaxis of postoperative complications in patients with hyperthyroidism is more important than treatment after such complications have developed.

2. An accurate knowledge of the postoperative complications to be expected in each type of case is essential if the proper prophylactic measures are to be taken before dangerous complications develop.

3. The recognition of the presence of certain warning factors is of value in prognosis and in the anticipation and prophylaxis of specific complications.

4. The surgical management of patients with hyperthyroidism should be based on an appreciation of the complications to be guarded against in each group of patients as well as a familiarity with the value of the specific forms of prophylaxis and therapy available for each group of patients.