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DISCUSSION

DR. PAUL C. KIERNAN (Washington, D. C.): Washington, and Georgetown University, are greatly privileged to have Dr. Coffey as a surgeon. His many contributions are well known to all of you. In part, this is due to his ability to stimulate and work closely with such individuals in the Medical Department as Drs. Canary and Mackin. His work in acute hyperparathyroidism, tumors of the pancreas and adrenal, have been in part due to this close association. One other of his assets, which is apparent to you, is his ability to select and train such attractive and well-qualified surgeons as Dr. Lee.

The lack of cushion and the quick ability to escape from the effect of Propranolol, I think, should not disturb us. Those of us who continue to be impressed with the efficacy of iodine in the preparation of patients with hyperthyroidism for surgery are pleased to have another agent which can so quickly prepare them.

The speedy control of the hypermetabolism with Propranolol allowing subtotal thyroidectomy to affect the desired surgical remission of the hyperthyroidism has great appeal.

I would like to ask about one group of patients, the asthmatic, and the use of Propranolol.

DR. BENJAMIN F. BYRD, JR. (Nashville): Dr. Coffey and Dr. Lee were kind enough to let me look over a copy of this paper, and there were two or three remarks that I thought the organization might benefit from in enlarging on their observations, and there are some questions I would like to ask—three questions and three observations, if I may.

One of the most interesting things is the fact that there were failures of preparation with Propranolol; and they were able to recognize these failures in preparation and to avoid the hazard of operating on the unprepared patient. The ability is present with this method of preparation to rapidly reduce the patient to a euthyroid state to avoid the dreaded complication of thyroid crisis in the postoperative period and to manage crisis when it did occur in one patient in their series, because of failure to take the drug. I think that the problems of operation which can be avoided with this technic are really remarkable.

I would like to ask them: Were their patients hospitalized throughout the entire administration of Propranolol?

I would like to ask just a little further about the reduction of vascularity and friability of the gland which was observed in the operating room, and I would have thought that these physical characteristics of the gland would have been more difficult to alter than a rapid 5 to 7-day period, and it is astonishing that without added iodine this was changed favorably.

Finally, do you expect any difference in the treatment of nodular and diffuse goiter?

I think that with this rapid preparation we may expect that the benefits of surgical treatment will be returned to common use, in view of the multiple complications of medical therapy, which are well known to us all through past experience.

DR. COLIN G. THOMAS, JR. (Chapel Hill): I, too, wish to compliment the authors on a very carefully performed and superb study, with respect to the effect of Propranolol in thyrotoxicosis and the role of this drug in surgical treatment.

Although thyrotoxicosis is thought to be dependent upon increased levels of thyroxin and triiodothyromine, many of the effects appear to be the augmented physiologic effects of catecholamines. For example, the adrenergic receptors in the heart are strictly beta receptors. Thus the increased heart rate, cardiac output, and ventricular stroke work may be mediated by catecholamines rather than the direct action of thyroid hormones.

It, thus, becomes logical to treat the symptoms of thyrotoxicosis by agents which interfere with catecholamines; namely, via beta adrenergic blockade.

The authors have emphasized that, using this method, one must rely completely upon clinical criteria for adequacy of control. At the same time, we should all realize that this drug does compromise normal homeostatic mechanisms. Those responses which may follow stress or shock may no longer appear. With the use of this drug we have to have careful monitoring, both in the pre- and postoperative period. Although intraoperative complications are rare with surgical treatment, nevertheless, they do occur.

For these reasons, we have elected to use the drug not as a sole means of preparation, but as an adjunct to standard methods of preparation with antithyroid drugs. It has been particularly useful in the following groups of patients: (1) the patients who have had toxic reactions to Tapazole or propylthiouracil; (2) those individuals in whom large doses have been required to control the disease—for example, over 800 mg. of propylthiouracil; (3) patients who are unreliable and uncooperative, and have not taken their antithyroid drugs. This is particularly true of some of the children; and (4) the pregnant patient, in whom doses of antithyroid drugs are undesirable because of their ability to cross the placental barrier and perhaps affect the fetus.

Another indication which would certainly be reasonable would be the patient who was thyrotoxic and who required an unrelated operative procedure. It would seem to me this would be an ideal approach under these circumstances.

For most surgeons, I believe a reasonable course of therapy would be to utilize this drug as an adjunct to present methods and allow individuals with the competence of the authors to continue their studies to identify the over-all usefulness of this drug in the management of patients with thyrotoxicosis.

One of their points was the decreased cost of this approach. However, I note that the over-all length of hospitalization was approximately 11 to 12 days, whereas with other means of preparation this is usually between 4 and 6 days.

I have two questions: What would they consider the contraindications to the use of the drug, other than those patients who do not respond? I have in mind in particular individuals who have thyrocardiac disease. Secondly, it seemed from their observations that the incidence of hypothyroidism might be somewhat higher in this patient group. Have they compared their incidence of hypothyroidism in patients treated this way with those managed by more standard methods of preparation?

DR. CHARLES WRAY (Augusta): Dr. Thomas has reviewed the manner in which we have thought about the use of this drug. I would like to mention that we are indebted to Dr. Raymond Alquist, who is Professor of Pharmacology at the Medical College of Georgia, for the development of the concepts of alpha and beta

receptors, and, consequently, all of us who were subjected to his mind have been very interested in these kinds of drugs.

My own experience with the use of Propranolol in thyrotoxicosis has been limited to three cases. Two patients developed skin rashes, and one a decrease in white count in relatively usual doses of propylthiouracil. We had chosen to follow the outline of Piimston, and had treated these patients for 2 weeks preoperatively and 2 weeks postoperatively with Propranolol and iodine.

I had always been very interested in listening to surgeons discuss the bleeding problems that are encountered during thyroidectomy. Since I have never seen a patient operated on who was completely unprepared, I have never been able to evaluate this. I suspect that perhaps these problems have been overemphasized, and our experience in recent years—in particular with these three patients—would indicate that patients can be prepared with Propranolol without bleeding, and Dr. Lee and Dr. Coffey have mentioned this.

We too have been looking for patients, as Dr. Thomas mentioned, who were in severe heart failure, and recently none have presented themselves. Our medical colleagues, however, are taking the opportunity to control the patients' symptoms quickly with the use of Propranolol.

I would like to compliment the authors for their courage in using this technic. I would like to thank the society for this opportunity to participate in the program and to enjoy this meeting.

DR. ROBERT J. COFFEY (Closing): In response to Dr. Kieran's question, we currently consider a history of asthma as a contraindication to the use of Propranolol. In two such cases the drug promptly provoked severe asthmatic symptoms.

I might say at this point that Dr. Lee and I would like to recognize the original impetus that Dr. John Canary, who is Director of our Division of Endocrinology, and his associate, Dr. Mackin, have given to this study. Of course, it is an outgrowth of their interest in the use of this drug in the thyrotoxic patient.

Dr. Byrd raised the question as to whether these patients had been hospitalized during the entire period of treatment. I believe Dr. Lee mentioned that all were hospitalized preoperatively for about 5 days and postoperatively for 6 to 7 days.

The consistency of the gland after Propranolol treatment was commented on by both Dr. Byrd and Dr. Wray. I have been im-

pressed in the cases that I have personally operated on that the gland was handled with no technical difficulty. There has been no problem with bleeding or with friability. We have employed the conventional subtotal thyroidectomy, and we encountered none of the difficulties that had been occasionally observed in the patient who had been prepared with propylthiouracil.

Dr. Canary is of the opinion that there is no difference in the application of this therapy to the diffusely involved versus the nodular gland associated with thyrotoxicosis.

I certainly enjoyed Dr. Thomas' remarks. They were very pertinent. He obviously is very familiar with this drug, and has brought out some very interesting points. I think that the question of the thyrocardiac is an interesting one. Our endocrinologists do not feel that this poses any contraindication to the use of Propranolol unless evidence of heart failure exists.

Of course, this series is too small, and the follow-up too short, to make any comments about the ultimate incidence of hypothyroidism; however, I would expect that it would not be materially influenced by the Propranolol therapy.

In closing, I would like to make several observations. First, this is strictly a preliminary report. We are making no sweeping recommendations for its general use. We are going to continue our studies in the hope of more clearly delineating the limitations of this drug, its applications, and possibly its dangers.

We are prompted to report these early experiences because it is evident at this time that there are several very clearcut and useful indications for this therapy.

In the first place, I think the patient who has manifested an intolerance or refractoriness to the conventional antithyroid drug therapy should be prepared for operation in this manner.

Secondly, I think if a patient who is thyrotoxic requires control of the thyrotoxicosis quickly, rapidly, and faster than propylthiouracil or other therapy would permit, this is the preferred method. This situation might arise clinically either in the patient who is being prepared for thyroidectomy or perhaps in the thyrotoxic patient who requires operation for another condition or is being exposed to some other stressful experience.

Finally, in the patient who develops either threatened or real postoperative thyroid storm, the symptoms can be controlled by appropriate Propranolol therapy in a matter of 30 minutes to 1 hour. This, I think, is one of the most valuable uses of Propranolol.