

benign nature of most of these was ultimately proved, there were some follicular lesions which were initially considered to be benign, but ultimately proved to be malignant. Some were tentatively classified as "atypical" or "suspicious." In some instances a decision that a lesion was malignant was rendered some days later on finding blood vessel or capsular invasion, or atypicality of the cells. Most all of these lesions have proved to have extremely low uptakes of  $^{131}\text{I}$  which can be recognized at the time of the primary operation.

Unfortunately autoradiographs require several weeks to prepare so that they are of no immediate use to the surgeon during a thyroidectomy, but counting of samples of tissue is of great value in warning the surgeon before he concludes the operation that he may be dealing with a carcinoma. The finding of a very low uptake in a neoplasm at the time of operation should arouse serious suspicion of carcinoma and should prompt, not only a further search for lymph nodes which might bear metastases, but also prompt a meticulously complete removal of the entire lobe from which such a neoplasm has been excised. If the final diagnosis then proves to be carcinoma, an adequate procedure will have been done at the first operation.

#### DISCUSSION

DR. OLIVER COPE (Boston): The experience that Dr. Dobyns has just recounted very, very briefly is the most extensive that is available. Two benefits which have resulted from this experience are impressive. The first tells about the biology of these tumors, and the second, explains its practical use in operation.

It is interesting that he has not identified a small percentage of carcinomas that fall into the more active group; if one observes the other endocrine glands he will find hyperfunctioning carcinomas which are encountered from time to time.

Of course, there are rarities, but the fact is interesting that in this enormous series Dr. Dobyns did not encounter a seemingly malignant tumor, which has a function greater than uninvolved tissue.

One of the so-called benign metastasizing tumors, so-called *metastaser adenoma* of the German pathologist, was not listed in Dr. Dobyns' re-

#### Summary

Radioiodine should be given to all patients with nodular goiters shortly before operation. Measurement of  $^{131}\text{I}$  content of neoplasms at the time of operation is a useful adjunct to frozen section diagnosis of some questionable lesions of the thyroid. Approximately 90% of carcinomas of the thyroid encountered will be found to take up 1/100 or less  $^{131}\text{I}$  than an equal weight of paranodular thyroid tissue. Being forewarned of the likelihood of a malignant lesion by precise counting, the surgeon takes particular precautions so that if the diagnosis of a malignant lesion is ultimately made, the most appropriate surgical procedure for that lesion will have been done at the first operation.

#### References

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port, unless it was not so identified. Of course, that theoretically should be the hyperfunctioning lesion and yet occasionally, it gives rise to metastases.

Since Dr. Dobyns is an able expert—an anatomist as well as a functional expert—I suspect he has not overlooked any of these lesions.

The second question is a practical one.

The practical use of this knowledge can be beneficial if the present technic can be developed. This will provide an added dimension at operation, a functional dimension which benefits beyond pathologic findings of frozen section. This usefulness, of course, depends upon rarity of exceptions. We can consider *metastaser adenoma* as a possible one.

The second possibility which is significant, is the functional capacity of the benign papillary tumors. A benign papillary tumor was seen with a high uptake and then a malignant one with zero uptake. Although the benign tumor had not metastasized, is it not possible that it was removed

because of its hyperfunction before it metastasized? I wish you would comment further on the evidence that such functioning papillary tumors are truly benign.

With these two possible exceptions, the suggested technic should help to identify the biologic nature of the tumors at operation, but we should be able to understand these exceptions better.

DR. COLIN G. THOMAS, JR. (Chapel Hill): I would like to compliment Dr. Dobyns on a most excellent presentation, and for calling our attention to this lack of affinity of the thyroid cancer for radioactive iodine. In conjunction with frozen section examination, this may enable the surgeon to make a more definitive diagnosis at the time of operation. Certainly nothing is more disconcerting to the patient than to be told 2 or 3 days after operation that further surgery is necessary.

He pointed out that there are a number of benign lesions that also have this characteristic. I wonder if he could be more specific and indicate what those lesions are and if there are any quantitative differences between the adenoma, the colloid nodule and thyroiditis.

Stimulated by his report, we looked up our own experience which is much more limited. Using the same criteria, that is the ratio of tumor radioactivity to that of perinodular tissue, and found the lowest ratios in carcinoma. Next in line was the adenoma. The colloid nodule had a median of approximately four times that of carcinoma. Our experience would be corroborative.

One may rarely see carcinoma of the thyroid that is functioning. We have seen two patients in a series of 135. One was an individual 18 years of age who was hyperthyroid. The lesion microscopically was invasive but was confined to one lobe of the thyroid. The opposite lobe was suppressed. We have seen a second patient, more recently, who had a functioning mass on radioactive iodine scan and two pulsating metastases, one in the sternum and one overlying the sacrum.

Interestingly enough, these metastases took up not only radioactive iodine but, as we described last year, also concentrated <sup>75</sup>Selenomethionine.

[Slide] On the left is a scan of the thyroid. The mass about which we are concerned is in the right lobe. This picks up iodine.

The "hot spot" below represents the sternal metastasis which obviously functions. Of particular interest was the fact that both of these lesions took up <sup>75</sup>Selenomethionine.

The scan of the pelvis showed similar findings with the metastases taking up radioactive iodine and <sup>75</sup>Selenomethionine.

In summary, Dr. Dobyns has given us a method which facilitates diagnosis at the time of operation and it is entirely possible that with more sophisticated means of scanning, this information may be available preoperatively. In conjunction with complementary scans, using <sup>75</sup>Selenomethionine, we may arrive at a more precise diagnosis

which obviously eliminates unnecessary surgery and to better designate operation when it is deemed necessary.

DR. ROBERT CONDON (Chicago): At the beginning of his report, Dr. Dobyns made a point that preoperative radioactive iodine scans presently have some diagnostic imprecision and occasionally were misleading. I wish to emphasize this point.

A couple of years ago, we became somewhat dubious about the value of radioactive iodine scans in the preoperative diagnosis and management of solitary thyroid nodules.

Our conclusion was based on our clinical experience, an entity that we all recognize is the repository of our therapeutic prejudices, so I decided to check that judgment by reviewing a few facts with Leigh Kendall who was then my chief resident.

We reviewed our experience at the University of Illinois Hospital with the accuracy of radioactive scans in the diagnoses of solitary thyroid nodule.

[Slide] Among our group of patients, there were six in whom a clinical diagnosis of probable malignancy seemed rather obvious because there were palpable metastases in the neck adjacent to the solitary thyroid nodule.

It was of interest to us that among this small group of six patients only two had a cold nodule for an incidence of hyperfunction of 33%.

Perhaps of more interest is the fact that among 72 patients in whom the status of a nodule could not be determined clinically, 64 subsequently proved to be benign on histologic examination following excision and the majority of these lesions, as you can see along the bottom line, also proved to be cold nodules when the scans were reviewed.

In fact, there was no difference in the percentage distribution of cold, cool, warm and hot nodules between patients harboring a malignancy and those who had benign disease.

We concluded, now based on this evidence, that preoperative scans were not really worthwhile in diagnosis of malignancy within thyroid nodules.

Despite this finding, I found that it is very difficult to convince my physician friends who are endocrinologists that this is, in fact, true. They are rather attached to using scans and I am grateful to Dr. Dobyns for showing us a way in which scans may be retained in the management of patients with thyroid disease, but a way in which they can be used with more diagnostic precision.

DR. CHARLES ECKERT (Albany): I believe there is one important question to be asked concerning Dr. Dobyns' excellent work. Does this very accurate diagnostic procedure alter the operation that is performed. Let us say for papillary cancer, and secondly do you believe it will improve the end results? Dr. Dobyns has had a long productive experience in this field, and I hope

this experience will enable him to give us this information.

DR. BROWN M. DOBYNS (Closing): The question that Dr. Cope raised about benign metastasizing stroma in distant bones has interested us. In this series there are quite a number of such lesions. They are composed of rather respectable follicles, but some lesions with good follicles take up  $^{131}\text{I}$  poorly.

We have occasionally thought on preliminary consideration that a distant metastasis, identified before thyroidectomy, was hyperfunctioning because it seemed to have a great deal of  $^{131}\text{I}$  in it. However, when biopsied at the same time that some normal tissue was obtained at thyroidectomy, we were surprised to find that the uptake in these "benign metastasizing stromas" was not nearly as high as it was in the normal tissue. Thus, it should be reemphasized that even though the uptake in a malignant lesion may seem to be considerable (and indeed be effectively treated with  $^{131}\text{I}$  if there is no normal thyroid tissue to compete with the neoplasm), the uptake at best may be only 1/50 or 1/100 that of the normal tissue (gram for gram). In the vast majority of the malignant lesions, the uptake is relatively far less than this, hence the value of the assay.

I pointed out that among a large number of papillary lesions with radioautographs, the hot papillary lesions, so far as we have observed them, have not metastasized. Dr. Cope has asked the interesting question whether we have just happened to remove them before they metastasized. This is difficult to say. Certainly they must be extremely rare.

Perhaps I should say that we define a hyperfunctioning or hot lesion as one which takes up more  $^{131}\text{I}$  than an equal weight of normal thyroid tissue from the same individual. This does not necessarily imply that the individual has thyrotoxicosis. Since we have found no papillary tumors with intermediate function and since no metastases so far have been associated with the hot papillary lesion, it seems very worthwhile to pay special attention to the cold papillary ones at the time of the initial operation.

Dr. Thomas has described his experience with two carcinomas that have very considerable function. These are extremely important cases. I think one is in the literature, and the other should be. Some other hyperfunctioning carcinomas have been described. Most are not conclusively documented. Certain things should be kept in mind in the documentation of a hyperfunctioning carcinoma. The uptake of the metastasis must be compared to the normal thyroid tissue. A scan is not reliable for this comparison because, as happened to me recently, a flattened hyperfunctioning adenoma was lying in front of the carcinoma. Preoperatively, the mass which was carcinoma received the credit for the uptake. Some distant metastases seem very hot especially if a large tracer dose is used, but if the counts over the

metastatic carcinoma are in the thousands, the counts will be in the millions over the normal thyroid tissue. Finally some metastases, although they take up far less  $^{131}\text{I}$  (gram for gram) than the normal tissue, may become so wide spread that the total output of hormone is sufficient to make the individual mildly thyrotoxic. Such a lesion is not hyperfunctioning by definition.

Dr. Condon's remarks were very pertinent. I share the feelings about inaccuracies of scanning. I also further share his feelings about the inappropriateness of turning the job of scanning of the thyroid over to a technician; and later a physician who is experienced in the physical examination attempts to orient and correlate his findings to the picture of the scan. The actual size and precise location of each palpable mass must be determined and drawn on the scan at the same time the scan is made. Many of these scans must be done obliquely or one mass pushed and held away from another to avoid superimposition and to distinguish the uptake of one mass from another. This is not done adequately unless it is done by a physician who is experienced in examination of the thyroid.

Dr. Thomas has asked for an opinion regarding the uptake in tissue from adenoma, colloid nodules, and thyroiditis as compared to carcinoma. Probably no more than 5 to 7% of benign adenomas have as low an uptake as the most functional carcinomas. Essentially all colloid nodules will have more  $^{131}\text{I}$  than carcinomas. Most all will take up  $\frac{1}{2}$  to  $\frac{1}{10}$  that of the normal thyroid. In thyroiditis there are most always enough small islands of functioning follicles, even in the most extensively replaced gland, to make the count well out of the range of carcinomas.

Dr. Eckert has asked how these interpretations have affected the procedure that one carries out and the outcome of that procedure. The assay of  $^{131}\text{I}$  in a neoplasm at the time of the operation serves as a guide to the surgeon during the operation. If when the gland is exposed and there are no gross features that suggest malignant disease, then the mass or masses may be excised sacrificing only enough normal thyroid tissue to avoid getting next the capsule of the lesion, rather than remove a whole lobe just to remove a single mass. This permits conservation of normal tissue. If the lesion has very little  $^{131}\text{I}$  in it (and you have this information in 2 or 3 minutes) then the remainder of that lobe is totally removed and with meticulous care. There should be far fewer unnecessary wide excisions; those that are likely to be malignant are more widely excised; and I can say from experience, there are far fewer surprises several days after operation when the pathologist reports carcinoma and we wish we had done more. At present, we have no way of proving that the eventual outcome of the surgical procedure done with this additional information is better than in the past, but from the reasoning presented, we feel more secure in what we are doing.