aldosterone excretion halved when we removed about half of her widely scattered tumor nodules. Her symptoms are now relatively well controlled on spironolactone.

Two patients had apparently normal adrenals removed. One was operated upon early in the series when assay techniques were not as accurate as they are now. The other was operated upon a year before plasma renin activity assay became available. Retesting of this patient when the assay became available showed an extremely high plasma renin and a renin-secreting tumor was localized in the right kidney and removed with cure of his hypertension.[12]

Discussion

There is, as yet, no explanation of why adrenal hyperplasia behaves differently than adenoma or whether the two forms of the disease are even causally related. Unfortunately, the diurnal variation and postural tests have not been done on any of the 4 patients who had both adenoma and hyperplasia. We assume that these patients basically are suffering from bilateral hyperplasia.

The accumulated evidence of most reported series indicates that efforts to discriminate among the types of hyperaldosterone continue to improve the efficacy of adrenalectomy. Nevertheless, the safety of operative procedures in experienced hands contraindicates excessive efforts to avoid operation.

There seems relatively little difference in safety between the anterior, lateral, and posterior operative approaches. Each has its indications. The anterior approach in which both glands can be seen easily is particularly helpful in patients with suspected IHA, indeterminate primary aldosteronism, and patients with cancer. The surgeon who deals with this disease should be familiar with all three approaches to the adrenals. This is especially important when reoperations in the adrenal area are contemplated as was the case in three of our patients. These operations have been facilitated by using an approach opposite to the previous one so that the adrenals can be reached through unscarred tissue.

As our experience has developed, and testing procedures have become more sophisticated, the efficiency and safety of adrenalectomy has increased. It seems possible to approach the ultimate cooperation between endocrinologist and surgeon: perfection in diagnosis, absolute localization of disease, and surgery with minimal complications, no mortality, and excellent results. It is tempting for the surgeon to claim credit for the paucity of operative complications in this series. However, it is very plain that some of the major reasons why surgery of aldosteronism is far safer than adrenalectomy for advanced cancer or Cushing's disease is because the metabolic abnormality of primary aldosteronism can be overcome prior to operation and associated problems can be minimized. When the physiology of the operated patient is as predictable as it has become for us in this disease, problems can be corrected before they become serious; and excessive therapeutic reactions to physiologic changes can be avoided.

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Discussion

Dr. William Silen (Boston): In 1966, as Dr. Hunt mentioned, we reported with Dr. Biglieri before this society a group of 24 patients with hyperaldosteronism. We suggested, on the basis of differential levels of aldosterone determined on blood taken from the inferior vena cava and directly from the adrenal vein at operation in a small number of patients, that preoperative catheterization might be of value in determining the side of the lesion. Since then we have found that indeed such determinations are in most cases correctly predictive and enable the surgeon to confine his activities to the side of the lesion.

Therefore, whereas we had in 1966 advocated transabdominal bilat-

eral adrenal exploration, we would now agree with Dr. Hunt that more sophisticated radiologic techniques and adrenal vein catheterization with assay of aldosterone make unilateral operation feasible in most cases. We happen to be blessed with a superb radiologist who can catheterize the adrenal veins essentially 100% of the time. If doubt exists, however, on the basis of catheterization data and/or the scan, then I think that the bilateral transabdominal exploration still has probably a place.

One other caution, however, in our recent experience. Namely, retrograde venous injection of dye, although it may outline the lesion and has done so in our hands, is potentially hazardous and is probably unnecessary.

There are two reasons for this: First, that adrenal infarction of the normal adrenal can occur if retrograde injection is done and therefore render the patient susceptible to adrenal insufficiency after removal of the contralateral abnormal gland; and secondly, infarction of the affected gland can make its subsequent removal extremely difficult from a technical standpoint because of severe fibrosis and reaction in the surrounding tissue.

DR. RICHARD H. EGDAHL (Boston): At Boston University, we have considerable interest in this disease and our experience pretty much bears out his conclusions.

(Slide) One of the things we found, and this goes along with what Tom Hunt said, is that we must look on this disease of primary aldosteronism as perhaps even more complicated than has ever been suggested. It is more like hyperparathyroidism and the problem of differentiating hyperplasia and adenoma.

We have now studied a fairly large number of cases. We have almost 90% good results within the first three months for the standard syndrome of solitary adenoma; 30% are hypertensive at one year.

However, it is ominous that if you follow these patients for five years, about 50% of them are hypertensive and this in the presence of normal adosterone secretion rates. In other words, at 5 years post-op, the incidence of hypertension in patients who appear to be cured by removal of a solitary adenoma seems very much higher than would occur in the normal population. This is reminiscent of a paper from P&S long range results following presumable curative surgery for islet cell adenoma.

So there's something funny about the long range followup solitary adenomas in terms of recurrent hypertension.

(Slide) This shows a point of disagreement that we may have with some of the other groups concerning results for bilateral nodular hyperplasia as compared to solitary to tumors. Approximately 30% appear to be cured of hypertension following removal of one adrenal with a dominant nodule or by bilateral adrenalectomy.

The fascinating thing is that in 30% of the cases with hyperplasia followed for five years, the cure of hypertension seems to hold up. Quite clearly, the patients had hyperaldosteronism and were severely sick from their hypertension. I think it's going to be ten or more years for us to know the full spectrum of this complicated disease.

(Slide) This simply points out that measurement of plasma aldosterone with the radioimmunoassay technique, along with sampling of plasma renin, makes it possible to do a complete diagnostic workup for aldosteronism on ambulatory patients. So the patients who has high aldosterone levels in peripheral blood and low renins, has primary aldosteronism.

I think this means we can begin to develop criteria and look at the necessity for hospitalization in the diagnostic workup of this rather complex endocrinopathy. This observation has pertinence to issues of quality and cost, and to PSROs and their functions of utilization review and medical audit.

DR. THOMAS K. HUNT (Closing discussion): We agree in general with the comments that have been made. We have not been as good at adrenal vein catheterization as has the Boston Group, and we're jealous of your results. We've learned to be wary of interpreting the results of a unilateral catheterization. On one occasion, a unilateral catheterization with a good step-up of aldosterone concentration led us into believing there was an adenoma on one side, and a potentially useless adrenalectomy was done in a patient with bilateral hyperplasia.

We have not done the angiography because there is a real chance that the normal gland can be infarcted and instead of having a cured patient with a normal adrenal function postoperatively, you have an Addisonian.

Our indications for operation are very much as Dr. Egdahl suggested. In general, we operate on those patients with biochemical evidence of adenoma whose blood pressure cannot be controlled with less than 150 mg of spironolactone a day because over that level the side effects become very difficult, particularly in men. We also select those patients who on any dose of spironolactone show deterioration of target organ function. A segmental resection of one adrenal to remove just the adenoma has been suggested recently, but we wonder, based on our observation that the adenomatous adrenal is often also hyperplastic, if leaving behind this hyperplastic tissue might have functional significance and lead to a quick return of the syndrome.

Secondly, can an adenoma with hyperplasia in the same gland foretell the future that the other gland will be similarly affected in future years with return of the syndrome? So far, our followup of almost fifteen years has not disclosed such a trend.

Thirdly, what do we do with hyperplasia since obviously even with the adrenals removed, there's still some stimulus to hypertension.

I think all these questions must be answered before we can really promise the perfection that I hinted at.