The query corner

I. I. Rabi, the Nobel prize-winning physicist, has told of an early influence upon his sense of inquiry: On returning from grade school each day, his mother would ask, not “Did you learn anything today?,” but rather “Did you ask a good question today?”

Readers are urged to contribute questions intended to elicit a focus of illumination from an authority. They should often be directed toward “How?” or “Why?”, bridging the field of imaging with normal and pathologic anatomy, physiology, biochemistry, and other clinical disciplines, and may be accompanied, if necessary, by a single illustration and up to three references. If authors wish to have their questions published anonymously, this should be indicated when the question is submitted. The selection of questions published remains an editorial decision.

Acquired cystic kidney disease

In whom and how does acquired cystic disease of the kidneys occur? Does it occur more frequently in some kidney diseases, e.g. glomerulonephritis or reflux nephropathy, than in others, e.g. diabetic nephropathy? Is its incidence greater in patients on dialysis than in those with transplanted kidney? If so, why? Is there an increased risk of renal cell carcinoma (RCC)? What is the interval of danger? Does RCC in these circumstances carry the same prognosis as in other kidneys? Should screening be established for RCC in the native kidneys of patients on replacement therapy?

The Editor-in-Chief

Acquired cystic kidney disease (ACKD) is characterized by the development of many fluid-filled cysts in the kidneys of individuals with chronic progressive renal disorders who have no history of hereditary cystic disease. The severity and duration of azotemia appear to be critical factors in determining the extent of cyst development [1]. ACKD may occur in patients with elevated serum creatinine levels who have never been dialyzed. However, the condition is encountered more commonly in dialysis patients, because dialysis extends the time during which renal cysts can develop [1]. After 3 years on dialysis, the prevalence of ACKD is 40% or higher, rising thereafter to reach 90% between 5 and 10 years on dialysis [2].

The mechanisms underlying the development of ACKD are unknown. However, it is postulated that with progressive destruction of functioning renal tissue, various nondialyzable mitogenic and cystogenic substances accumulate causing hypertrophy and hyperplasia of epithelial cells in surviving nephrons [3]. Anatomic tubular distortion caused by intense interstitial fibrosis and tubular luminal obstruction due to hyperplastic epithelium and oxalate crystal deposition set the stage for fluid accumulation in the hyperplastic renal tubules [3]. The fluid is probably derived from transepithelial secretion and such secretion may be stimulated by parathyroid hormone, which is persistently elevated in chronically azotemic individuals [3]. Under these influences the tubules dilate to form cysts. In some patients multifocal epithelial hyperplasia progresses to adenoma and from there to renal cell carcinoma, a process that may require activation of certain oncogenes as the final step for cancer development [3].

Nephrosclerosis, diabetic nephropathy, and chronic glomerulonephritis account for a large percentage of dialysis patients with ACKD [2]. However, these are the three most common causes of end-stage renal disease (ESRD) in the United States [4] and there is no statistical evidence indicating that any one type of renal disease specifically predisposes to ACKD [2]. Indeed, all kinds of ESRD may be associated with ACKD.

Former dialysis patients with functioning renal transplants sometimes show regression of ACKD on follow-up ultrasound or CT scans. This supports a hypothesis that ACKD is due to circulating blood factors that are not removed by dialysis, but that are removed by successful renal transplants. However, more commonly, the presence of a functioning renal allograft causes only retardation of the progressive cystic changes that characterize ACKD in chronic dialysis patients [2]. Accordingly, most patients with successfully
functioning renal transplants remain at risk for ACKD and its complications [2, 5].

Some investigators have reported that the incidence of renal cell carcinoma in dialysis patients is 57–134 times higher than in the general population [6]. However, such data are at variance with general clinical experience, which does not show many dialysis patients with invasive or metastatic renal cell carcinomas. A reason for this discrepancy may be that small renal tubular neoplasms (≤3 cm) are significantly more common than invasive or metastatic carcinomas in dialysis patients [1]. Indeed, they occur in at least 7% of all dialysis patients and their clinical significance is unknown. As in the nonazotemic general population, many of these “adenomatous” lesions may remain quiescent and never develop into clinically significant carcinomas. Prospective, longitudinal CT studies and population-based studies suggest that the annual incidence of invasive or metastatic renal cell carcinoma among dialysis patients is three to six times greater than among the general population in the United States [1, 7]. Accordingly, the available evidence suggests that there is an increased incidence of clinically significant renal cell carcinoma in dialysis patients, but that the increase is not nearly as high as that stated by several investigators.

Although renal cancer may develop in azotemic patients who have never been dialyzed, the highest prevalence of renal cancer associated with ESRD is seen among patients treated with dialysis for prolonged periods [6]. Lifetable survival curves of patients with cancer of the end-stage kidney show that their 5-year survival rate for all stages of cancer combined is about 35%, which is similar to the corresponding 42% survival rate reported in 1989 for renal cancer in the general population [2]. Renal cancers in dialysis patients may therefore be biologically similar to those occurring in non-uremic patients. However, renal neoplasms associated with ACKD are more frequently bilateral and multifocal than those encountered in the nonazotemic general population.

Various investigators have recommended that periodic imaging using ultrasound or CT should be used to monitor the status of the native kidneys of dialysis patients for the development of carcinoma [6]. Because the frequency of ACKD increases significantly after 3 years of dialysis, it is often recommended that screening should begin after completion of the third year of dialysis. An effective screening program requires at least annual screening. In the United States, the long-term dialysis program is mostly funded by Medicare and it has been estimated, based on 1987 figures, that annual CT screening of all long-term dialysis patients after 3 years would add at least $36 million to the Medicare budget [1]. Current costs may be even higher.

Despite improvements in survival in recent years, overall mortality in the dialysis-treated ESRD population in the United States is high relative to the general population. In 1991, the expected average remaining years of life for dialyzed ESRD patients aged 30–49 years ranged from about 5–10 years [4]. The average remaining years of life for patients 50 and older ranged from about 1.5 to 6 years. Acute myocardial infarction, cardiac disease, infection, cerebrovascular accidents and withdrawal from dialysis account for most deaths among dialysis patients [4]. Malignancy of all types is not a frequently reported cause of death in dialysis patients [4]. It is therefore unlikely that an aggressive renal imaging program with early tumor discovery and nephrectomy will significantly improve the survival of dialysis patients. On the contrary, the mortality and morbidity associated with radical nephrectomy necessitated by the discovery of small asymptomatic renal tumors may reduce the survival of dialysis patients at increased surgical risk, because of severe cardiovascular disease [8]. Accordingly, it seems that diagnostic screening for renal cell carcinoma of the native kidneys of all dialysis patients is neither medically nor economically justifiable [1, 8], although there are strong advocates for such screening programs [6].

However, physicians treating dialysis patients should have a high awareness of the risk of renal cell carcinoma in dialysis patients. The occurrence of hematuria, flank pain, or any unexplained fever or systemic illness in dialysis patients constitutes a definite indication for renal imaging. Also, it is possible that further research may identify a subset of dialysis patients in whom annual renal imaging may be performed in a cost-effective manner. A primary consideration should be the general medical condition and life expectancy of each individual patient [1]. Discovery of a renal cell carcinoma in an elderly unfit patient may have no effect on patient management or prognosis. On the other hand, a young patient with a good general medical condition may benefit greatly if imaging shows a renal neoplasm when it is still localized to the kidney and can be resected completely [1].

Known risk factors for carcinoma may also help identify those patients who may benefit from renal imaging. These include prolonged dialysis, the presence of ACKD, large kidneys, and male gender [1, 6]. About 86% of renal carcinomas occurring in dialysis patients affect those with ACKD, and carcinoma occurs four to seven times more commonly in men than in women [2]. The mean age at diagnosis of patients with ESRD and renal cancer is about 49 years, as compared with 62 years for renal cell carcinoma occurring in nonazotemic patients [7]. Accordingly, with a consideration of general medical condition in dialysis patients and with knowledge of risk factors for carcinoma, it may be possible ultimately to define a subset of dialysis patients in whom serial renal imaging may be performed in a cost-effective manner. Such a selective screening program may reduce preventable deaths due to renal cell carcinoma in dialysis patients.