Factors Relating to Urinary Protein Excretion in Children with Autosomal Dominant Polycystic Kidney Disease

CINDY SHARP,* ANN JOHNSON,* and PATRICIA GABOW*†
*University of Colorado Health Sciences Center and †Denver Health, Denver, Colorado.

Abstract. Adults with autosomal dominant polycystic kidney disease (ADPKD) who have overt proteinuria (>300 mg/d) have higher mean arterial pressures, lower creatinine clearances, larger renal volumes, and a more aggressive course of renal disease than ADPKD patients without proteinuria. This study examines the relationship between proteinuria and microalbuminuria and similar factors in ADPKD children. A total of 189 children from 81 ADPKD families was included in the analysis. The ADPKD children (n = 103) had significantly greater urine protein excretion rates than the non-ADPKD children (n = 86) (3.9 ± 0.3 versus 2.8 ± 0.2 mg/m² per h, P < 0.001). Children with severe renal cystic disease (>10 cysts; n = 54) had greater protein excretion than those with moderate disease (<10 cysts; n = 49) (4.4 ± 0.5 versus 3.3 ± 0.2 mg/m² per h, P < 0.05). The ADPKD children had significantly greater albumin excretion rates than the non-ADPKD children (32 ± 6 versus 10 ± 2 mg/m² per 24 h, P < 0.001), and a higher percentage of ADPKD children had significant microalbuminuria (>15 mg/m² per 24 h in boys and >23 mg/m² per 24 h in girls) than their unaffected siblings (30% versus 10%, P < 0.05). Thirty percent of ADPKD children had albuminuria and 23% had overt proteinuria. For all ADPKD children, there was no correlation between proteinuria and hypertension. However, there was a significant correlation between urinary protein excretion and diastolic BP among children diagnosed after the first year of life (r = 0.23, P < 0.05). Therefore, proteinuria and albuminuria occur early in the course of ADPKD and may be markers of more severe renal disease.

Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary renal disease, affecting an estimated half million Americans. In recent years, it has become clear that the disease can affect children as well as adults. However, much remains to be defined regarding the characteristics and natural history of the disease in ADPKD children.

In this regard, it is well known that proteinuria and albuminuria are common laboratory findings of renal disease and may correlate with a worse renal and cardiovascular prognosis (1–7). We have recently reported on the frequency and correlates of proteinuria and microalbuminuria in adults with ADPKD (8). Eighteen percent of adult ADPKD patients have overt proteinuria (>300 mg/d). Hypertensive ADPKD patients had significantly greater protein and albumin excretion than did normotensive ADPKD patients. Patients with overt proteinuria had a greater pack-year smoking history than did patients without overt proteinuria. In addition, those patients with greater protein excretion had larger renal volumes and lower creatinine clearances. Patients with overt proteinuria demonstrated a more aggressive course of renal disease and reached a serum creatinine of 1.5 mg/dl an average of 14 yr earlier than ADPKD patients without overt proteinuria. Since there have been no studies that have examined the frequency and correlates of protein and albumin excretion in ADPKD children, we conducted this study.

Materials and Methods

Children of the adults in the Denver ADPKD study group were asked to participate in an ongoing study of ADPKD. All children who agreed to participate were admitted to the Pediatric Clinical Research Center at the Children’s Hospital for a 2- to 3-d stay. The parents provided informed consent, and children over 7 yr of age signed an assent form. A detailed history was obtained by an interview with the parent and/or the child if he or she was old enough to provide information. A complete physical examination was performed on each child. A complete abdominal ultrasound was performed with a high-resolution real-time scanner (Acuson 1.28 EXP with a 3.5 or 5.0 MHz transducer). Renal cyst number was recorded and renal volume was calculated as described previously (9).

Renal ultrasonography was used to provide the diagnosis of ADPKD. A child was considered to have ADPKD if any renal cyst was found on ultrasound. The ADPKD children were further divided into children with moderate cystic disease (≤10 cysts) and severe cystic disease (>10 cysts). Children who were diagnosed in the first year of life were classified as very early onset ADPKD.

Multiple BP were obtained during the clinical research stay (range, 3 to 20; mean 14). The measurements were taken with an automatic device (Dynamap; Critikon, Inc., Tampa, FL), using a child-size cuff. Hypertension was defined as 50% or more of systolic and/or diastolic in-house BP higher than the 95th percentile for age-, height-, and gender-matched children (10). Children who were currently receiving antihypertensive medications were also considered hypertensive. Routine chemistry determinations were performed on blood and urine.
samples. Urinary protein concentrations were determined by the Coomassie blue dye-binding method (11).

Overt proteinuria was defined as urinary protein excretion greater than 4 mg/m² per h (12). Urinary albumin concentrations were determined by RIA (Diagnostic Products, Los Angeles, CA), which has a detection limit of 0.3 mg/L and a coefficient of variation of <2.7% (13). Microalbuminuria was defined as a urinary excretion of >15 mg/m² per 24 h in boys and 23 mg/m² per 24 h in girls (14). Urine concentrating capacity was determined in children over 6 yr of age by measuring urinary osmolality after a 12-h overnight fast. GFR was calculated by the formula from Schwartz et al. (15):

\[
GFR = \frac{k \times UPc_r}{L}
\]

where \(GFR\) is expressed in ml/min per 1.73 m², \(L\) is body length in centimeters, \(P_c\) is plasma creatinine in mg/dl, and \(k\) is a constant of proportionality and is a function of urinary creatinine excretion per unit of body size. The use of \(k \times UPc_r\) is superior to \(P_c\) alone because creatinine value is very dependent on the percentage of muscle mass, and the \(k\) constant will account for this in children. Gene linkage analysis with the markers for ADPKD1 and ADPKD2 genes was performed as described previously in all children (16–18). Predictions were made in a subset of study children with sufficient affected family members sampled. An at-risk child having the haplotype transmitted with the disease was considered to carry the ADPKD gene. Clinical information gathered on the children was provided in written form to the parents and the children’s physicians, and all children continued care with their own physician.

Statistical Analyses
Continuous variables were compared between groups using unpaired \(t\) tests. Dichotomous variables were compared using \(X^2\) analysis. Age adjustment was performed using analysis of covariance; least squares means are reported in the text for age-adjusted variables. Pearson’s correlation coefficient was used to evaluate the relationship between two continuous variables. Statistical significance was set at \(P < 0.05\). Significant \(P\) values and \(P\) values <0.10 are reported in the text.

Results
One hundred and ninety children from 82 families participated in this study from July 1990 to March 1997. One child with nephrotic-range proteinuria was excluded from the analysis, because ADPKD adults with nephrotic-range proteinuria who were biopsied had a superimposed renal disease (19–21).

No other children had a history, laboratory data, or ultrasonography suggestive of another superimposed renal disease and are considered to have only ADPKD. Four children who were classified as unaffected by ultrasonography were included in the analysis as unaffected even though they were affected by gene linkage analysis; they were included because ultrasonography was the modality used to define disease in this study. However, the results do not change when they are excluded from the study. Eighty-six children had negative ultrasounds and were classified as unaffected (non-ADPKD); 43 of these children had informative gene linkage analysis and 39 were unaffected by this modality as well. One hundred and three of the remaining 189 children were positive by ultrasound and were classified as affected; 42 of these children had informative gene linkage analysis and were positive by this modality as well. Five (one ADPKD, four non-ADPKD) children were in a known ADPKD2 family. Seven of the 16 very early onset children were informative by gene linkage analysis; all were positive and in ADPKD1 families.

The characteristics of the study subjects are given in Table 1. Non-ADPKD and ADPKD children were similar with regard to age, weight, and body surface area. The non-ADPKD children had a smaller percentage of males than the ADPKD children (33% versus 46%, \(P = 0.07\)). The severe ADPKD children had a tendency to be older than the children with moderate disease (11.9 ± 0.5 versus 10.5 ± 0.5 yr, \(P = 0.07\)).

ADPKD children were not significantly more frequently hypertensive compared with non-ADPKD children (15% versus 8%, \(P = NS\)). However, severely affected ADPKD children were more frequently hypertensive than both the moderately affected ADPKD children (24% versus 4%, \(P < 0.005\)) and the unaffected children (24% versus 8%, \(P < 0.01\)). Moreover, the mean systolic and mean arterial BP were significantly higher among ADPKD children compared with non-ADPKD children (Table 2). The systolic, diastolic, and mean arterial BP were all significantly higher in the severe ADPKD children than in the non-ADPKD and the moderately affected ADPKD children (Table 2). The ADPKD children had larger kidneys than the non-ADPKD group after age adjustment (138 ± 6 versus 97 ±

Table 1. Characteristics of ADPKD and non-ADPKD children

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-ADPKD</th>
<th>ADPKD</th>
<th>Severe ADPKD</th>
<th>Moderate ADPKD</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n)</td>
<td>86</td>
<td>103</td>
<td>54</td>
<td>49</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>10.6 ± 0.4</td>
<td>11.2 ± 0.4</td>
<td>11.9 ± 0.5</td>
<td>10.5 ± 0.5(b)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>39.5 ± 2.0</td>
<td>43.8 ± 2.2</td>
<td>46.1 ± 3.2</td>
<td>41.3 ± 2.9</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>1.22 ± 0.04</td>
<td>1.31 ± 0.04</td>
<td>1.36 ± 0.05</td>
<td>1.25 ± 0.06</td>
</tr>
<tr>
<td>Male (%)</td>
<td>33</td>
<td>46(c)</td>
<td>48</td>
<td>43</td>
</tr>
<tr>
<td>Hypertensive (%)</td>
<td>8</td>
<td>15</td>
<td>24</td>
<td>4(d)</td>
</tr>
<tr>
<td>Age-adjusted renal volume (cm³)</td>
<td>97 ± 6</td>
<td>138 ± 6(e)</td>
<td>159 ± 10</td>
<td>122 ± 10(f)</td>
</tr>
</tbody>
</table>

\(a\) ADPKD, autosomal dominant polycystic kidney disease; BSA, body surface area.

\(b\) \(P = 0.07\), severe ADPKD versus moderate ADPKD.

\(c\) \(P = 0.07\), ADPKD versus non-ADPKD.

\(d\) \(P < 0.005\), severe ADPKD versus moderate ADPKD.

\(e\) \(P < 0.001\), ADPKD versus non-ADPKD.

\(f\) \(P < 0.05\), severe ADPKD versus moderate ADPKD.
The mean urinary protein excretion rate was significantly greater in the ADPKD children compared with the non-ADPKD children (3.9 ± 0.3 versus 2.8 ± 0.2 mg/m² per h, \( P < 0.001 \)) (Figure 1). However, the percentage of ADPKD children with overt proteinuria was not significantly greater than the non-ADPKD children (23% versus 13%, \( P = 0.07 \)). The severe ADPKD children had greater protein excretion than the moderately affected ADPKD children (4.4 ± 0.5 versus 3.3 ± 0.2 mg/m² per h, \( P < 0.05 \)) and than the unaffected children (4.4 ± 0.5 versus 2.8 ± 0.2 mg/m² per h, \( P < 0.001 \)). Thirty percent of severe ADPKD children had overt proteinuria compared with 16% of moderate ADPKD children (\( P = \text{NS} \)) and 13% of unaffected children (\( P < 0.05 \)). Seventy-two percent of the ADPKD children had overt proteinuria, and 37% of the moderate ADPKD children had overt proteinuria. Only three of 16 (19%) very early onset ADPKD children had overt proteinuria, and three of the 10 measured had increased albumin excretion.

There were no differences in proteinuria or microalbuminuria between hypertensive and normotensive ADPKD children. However, when the very early onset ADPKD children were excluded, there was a significant correlation between urinary protein excretion and diastolic BP (\( r = 0.23, P < 0.05 \)). Albumin excretion correlated with the calculated creatinine clearance (\( r = 0.35, P < 0.005 \)). Given that maximum urinary osmolality is lower in ADPKD children than in their unaffected siblings (9), and that this reflects in part the severity of the structural disease, we compared this variable with protein excretion. There was no correlation between protein or albumin excretion and maximum urinary osmolality.

Forty-three ADPKD children and 36 non-ADPKD children had two separate visits. The average time interval between

### Table 2. Blood pressures (BP) in ADPKD and non-ADPKD children

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non-ADPKD</th>
<th>ADPKD</th>
<th>Severe ADPKD</th>
<th>Moderate ADPKD</th>
<th>( P ) Value (ADPKD versus non-ADPKD)</th>
<th>( P ) Value (severe versus non-ADPKD)</th>
<th>( P ) Value (severe versus moderate ADPKD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>( n )</td>
<td>86</td>
<td>103</td>
<td>54</td>
<td>49</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>106 ± 1</td>
<td>110 ± 1</td>
<td>113 ± 2</td>
<td>108 ± 2</td>
<td>&lt;0.05</td>
<td>&lt;0.005</td>
<td>0.06</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>62 ± 1</td>
<td>64 ± 1</td>
<td>66 ± 1</td>
<td>61 ± 1</td>
<td>NS</td>
<td>&lt;0.005</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean arterial BP (mmHg)</td>
<td>77 ± 1</td>
<td>79 ± 1</td>
<td>82 ± 1</td>
<td>76 ± 1</td>
<td>0.06</td>
<td>&lt;0.001</td>
<td>NS</td>
</tr>
</tbody>
</table>

Because our previous studies had suggested that very early onset ADPKD children may represent a unique set of ADPKD children (22), we examined this group in detail. The 16 early onset children were significantly younger (8.6 ± 1.0 versus 11.7 ± 0.4 yr, \( P < 0.005 \)), were more frequently hypertensive (44% versus 9%, \( P < 0.001 \)), and had larger age-adjusted renal volumes (213 ± 17 versus 128 ± 7 cm³, \( P < 0.001 \)) than the other ADPKD children. Only three of 16 (19%) very early onset ADPKD children had overt proteinuria, and three of the 10 measured had increased albumin excretion.

Figure 1. Urinary protein excretion in autosomal dominant polycystic kidney disease (ADPKD) children versus non-ADPKD children.

Figure 2. Urinary albumin excretion rates in ADPKD children versus non-ADPKD children.

6 cm³, \( P < 0.001 \)); the severe ADPKD children had larger kidneys than the moderate ADPKD children (159 ± 10 versus 122 ± 10 cm³, \( P < 0.05 \)).
visits was 3 yr and was similar for the ADPKD and non-ADPKD children (3.2 ± 0.1 versus 3.1 ± 0.1 yr, P = NS). Both ADPKD and non-ADPKD children had significant increases in their urinary protein excretion; however, there was no significant difference in the rate of increase between the two groups (ADPKD +0.4 ± 0.1 mg/m² per h per yr versus non-ADPKD +0.2 ± 0.1 mg/m² per h per yr, P = NS). There may have been a tendency for the children with severe ADPKD to have a greater increase in protein excretion than the moderate ADPKD children (0.5 ± 0.2 versus 0.1 ± 0.1 mg/m² per h per yr, P = 0.09). For the entire group of ADPKD children, there was no significant relationship between increases in urinary protein excretion and changes in BP. However, the increase in urinary protein excretion in the non-very early onset ADPKD children correlated with increases in systolic BP (r = 0.33, P = 0.05). Microalbuminuria was not routinely measured during the initial visit for many of these children, so the rate of change in albumin excretion cannot be determined at this time.

Discussion

Nephrologists have long viewed proteinuria as a marker of significant renal disease. In the early 1980s, excretion of subclinical amounts of albumin, called microalbuminuria, was also found to predict overt nephropathy in insulin-dependent diabetes mellitus (IDDM) (1). Moreover, a number of recent studies have identified the severity of proteinuria as a risk factor for renal functional loss (23–25). This association has been found with IgA nephropathy (26), membranous nephropathy (27,28), hyperinsulinemia (29,30), and ADPKD (8). The prognostic value of microalbuminuria has been extended to the cardiovascular system as well (31,32).

A post hoc analysis of the Modification of Diet in Renal Disease study by Peterson et al. revealed that proteinuria is an independent risk factor for the progression of renal disease (33). When the patients in this study were divided into four groups based on BP and amount of proteinuria, there was no evidence that patients with hypertension and <0.25 g of protein per day had any decline in renal function. In contrast, patients with greater baseline proteinuria had faster declines in GFR and more benefit from BP reduction. This suggests an important interaction between BP, proteinuria, and renal function deterioration.

The Ramipril Efficacy in Nephropathy Study (REIN) examined the decline of GFR and proteinuria in a large cohort of nondiabetic patients with chronic renal disease (creatinine clearance 20 to 70 ml/min per 1.73 m²) with and without hypertension (34). Patients with non-nephrotic-range proteinuria (<2.5 g/24 h) had the lowest rate of decline in GFR, and kidney survival was >90% over a 3-yr follow-up period. The patients with nephrotic-range proteinuria (>4.3 g/24 h) lost more than 10 ml/min per 1.73 m² of GFR per year and had a 3-yr kidney survival of <50%. Therefore, the higher the urinary protein excretion rates, the faster the progression to end-stage renal disease (ESRD). Underlying renal disease was not predictive of the progression of decline in GFR. Although the BP increased the predictive value of the protein excretion rate on the GFR decline, it was not an independent risk factor. This study showed that urinary protein excretion rate was the strongest baseline predictor of progression of nondiabetic proteinuric nephropathies.

Iseki et al. performed a community-based screening of more than 100,000 individuals, assessing their systolic and diastolic BP and amount of proteinuria by the dip stick method (35). Proteinuria was the most potent predictor of ESRD.

In a study by Agrawal et al. (36), a cohort of 11,343 nondiabetic hypertensive patients were screened for microalbuminuria. Thirty percent of these patients had microalbuminuria, and 24% of patients with isolated systolic hypertension had microalbuminuria. Patients with microalbuminuria were more likely to have coronary disease, left ventricular hypertrophy, lipid disturbances and peripheral vascular disease, and stroke. A multiple regression analysis with these complications as dependent variables indicated that microalbuminuria was the next strongest predictive factor second only to BP. In addition, Goetz et al. found an 8% prevalence of microalbuminuria in 455 adults in Minnesota (37). Systolic BP and decreased creatinine clearances were correlated with microalbuminuria independently of diabetes mellitus.

Microalbuminuria has been associated with a worse renal prognosis and a higher cardiovascular mortality among individuals with diabetes. The presence of microalbuminuria in normotensive individuals with either insulin or non-IDDM is associated with a three- to fivefold increased risk of cardiovascular mortality and a greater than 10-fold risk of progression to ESRD when compared to subjects without microalbuminuria (38–41).

Proteinuria has been shown to be a risk factor for cardiovascular mortality. In the Multiple Risk Factor Intervention Trial (MRFIT), the benefit of modifying risk factors (BP, blood cholesterol, and cigarette smoking) in men ages 35 to 57 was examined (42). Men were excluded from the trial if they already had evidence of end-organ damage on history, physical, electrocardiogram, or had a serum creatinine >2.0 mg/dl. Proteinuria was quantified by urine dip stick and was reported as 1 to 4+. Predictive factors for baseline proteinuria included elevated diastolic BP and serum cholesterol, ethnicity (black), antihypertensive therapy, and diabetes. After adjustment for these factors, the presence of proteinuria still strongly correlated with cardiovascular disease (CVD) and coronary heart disease mortality and was weakly associated with non-CVD mortality. Both the level and the persistence of proteinuria increased the risk of mortality. This study demonstrated a strong and independent relationship of proteinuria to CVD.

The data in children with microalbuminuria are much more limited. Karlen et al. examined the incidence of microalbuminuria in children with pyelonephritic scarring. Children with scarring had significantly lower GFR and excreted more albumin than control individuals. Children with a GFR below 90 ml/min per 1.73 m² had a higher prevalence of microalbuminuria compared to children with a GFR above this level (70% versus 40%) (43).

In children and adolescents with IDDM, the data are not uniformly supportive of microalbuminuria as a prognostic indicator for nephropathy. In 1990, 81 children with IDDM were
studied by Shield et al. for early signs of diabetic nephropathy (44). Nine patients were identified as having microalbuminuria, and these subjects were reexamined 3 yr later. In five cases, the albuminuria resolved on the second examination and in three cases the albumin excretion had decreased. Improved glycemic control or interventional drug treatment could not explain the improvement in albumin excretion rates. This suggested that the progression of nephropathy in childhood might be slower or more irregular than later in life.

Chiarelli et al. examined IDDM children with an elevated GFR (>140 ml/min per 1.73 m²) and compared albumin excretion rates, BP, and HbA1 to age- and gender-matched cases, the albuminuria resolved on the second examination and (45). They discovered that seven of the 23 patients with hyperfiltration developed persistent microalbuminuria, and two of these patients had overt proteinuria. Only one of the diabetic patients with a normal GFR developed persistent microalbuminuria.

This relationship between proteinuria and microalbuminuria and renal functional deterioration is complex, with data supporting both a causal and sequential relationship between the proteinuria and functional impairment (46,47). To the extent that proteinuria and/or microalbuminuria contributes to the renal deterioration, identification of patients with these findings has prognostic implications.

This information initially prompted us to evaluate systematically protein and albumin excretion in adults with ADPKD (8). The findings of proteinuria and microalbuminuria in these patients and their correlation with markers of severity of renal disease and with hypertension were comparable to data noted above in other renal diseases. This prompted us to extend the study to ADPKD children.

Notably, 30% of ADPKD children had microalbuminuria and 23% had overt proteinuria. In addition, there was a significant increase in the excretion of protein and albumin in children with ADPKD compared to their unaffected siblings. In many ways, this is a remarkable observation. The course of this renal disease is extraordinarily long, with only about 50% of individuals with ADPKD entering ESRD by age 60 (48). Moreover, compared with adults, children tend to have a paucity of renal cysts, which suggests that abnormalities in protein excretion precede severe structural alterations. However, as in adults, those children with the most severe structural involvement do manifest more frequent and a greater amount of proteinuria and albuminuria.

One somewhat unexpected observation was the low frequency of proteinuria and microalbuminuria among the very early onset ADPKD children. By other parameters, these children appear to have a more severe disease than other ADPKD children (22). They are diagnosed in the first year of life with ultrasonographic evidence of the disease. Moreover, they demonstrate early progression to bilateral cysts, are more frequently symptomatic, and more frequently demonstrate hypertension than the children diagnosed later in life (49). In addition, it appears that it is these children who may enter ESRD in childhood or early adolescence. Hence, we would have predicted a higher frequency of proteinuria due to their higher frequency of hypertension and their more severe structural disease. However, because these children are considerably younger than the other ADPKD children, it may be that the end-organ effect of hypertension has not yet had sufficient time to be manifested and that these children will demonstrate a high frequency of these abnormalities over time.

However, it is also important that proteinuria correlates with the diastolic BP in non-early onset ADPKD children. In fact, when hypertension was defined as greater than the 95th percentile for age- and gender-matched children (50), rather than the current methodology, which also includes height (10), the non-early onset ADPKD children with hypertension had greater proteinuria than the normotensive children (6.2 ± 1.7 versus 3.7 ± 0.3 mg/m² per h, P < 0.05). This underscores that even in children, there may be an important end-organ effect of hypertension in ADPKD. This is supported by our data (9) and the results of Zeier et al. (51), which demonstrate a significant correlation of BP with left ventricular mass in children and young adults with ADPKD.

Our previous study in adult ADPKD patients demonstrated a correlation of pack-year smoking history with proteinuria. However, only four children in each of the ADPKD and non-ADPKD groups were current or former smokers. Given the increased frequency of smoking in teenagers, it would be wise for physicians to specifically counsel against smoking in these children.

At this point, it is not possible to know whether the occurrence of microalbuminuria in ADPKD children will predict those patients who go on to develop overt proteinuria or whether those children with proteinuria, particularly those with coexisting hypertension, will have a worse long-term renal and cardiovascular prognosis. However, given the emerging body of data in this area, it is not unreasonable to hypothesize these relationships. Therefore, it would appear prudent to document urinary protein and albumin excretion in ADPKD children and more closely follow the children with these abnormalities. Moreover, given the relationship of proteinuria and microalbuminuria with hypertension and renal disease progression, it would seem appropriate to consider this information as one piece of data in determining when to treat BP elevation in ADPKD children. The practice of measuring urinary protein and albumin excretion in ADPKD children should not be interpreted as a blanket recommendation for screening all at-risk asymptomatic children in ADPKD families. As in making any diagnosis in a child, the parents and the children (to the extent that their age permits) should participate in the decision with an understanding of potential psychologic implications for all members of the family, the effects on insurability, and the clinical implications of a positive diagnosis of ADPKD.

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