Chronic renal disease

Malvinder S Parmar

Early identification and active management of patients with renal impairment in primary care can improve outcomes

Timmins and District Hospital, Timmins, ON, Canada
Malvinder S Parmar *director of dialysis*
Correspondence to: 707 Ross Avenue East, Suite 108, Timmins, ON, Canada P4N 8R1
atbeat@ntl.sympatico.ca

BMJ 2002;325:85–90

The number of patients with end stage renal disease is growing worldwide. About 20-30 patients have some degree of renal dysfunction for each patient who needs renal replacement treatment.[1] Diabetes and hypertension are the two most common causes of end stage renal disease and are associated with a high risk of death from cardiovascular disease.

Mortality in patients with end stage renal disease remains 10-20 times higher than that in the general population. The focus in recent years has thus shifted to optimising the care of these patients during the phase of chronic kidney disease, before the onset of end stage renal disease. This review summarises current knowledge about the various stages of chronic renal disease, the risk factors that lead to progression of disease, and their association with common cardiovascular risk factors. It also provides strategies for intervention at an early stage of the disease process, which can readily be implemented in primary care, to improve the overall morbidity and mortality associated with chronic renal disease.

Summary points

- Significant renal dysfunction might be present even when serum creatinine is normal or only slightly abnormal
- Renal function declines progressively once creatinine clearance falls by about 25% of normal, but symptoms are often not apparent until renal failure is advanced
- The baseline rate of urinary protein excretion is the best single predictor of disease progression
- The prevalence of common cardiovascular risk factors is high in chronic renal disease; early identification and effective control of these risk factors is important to improve outcomes
- Cardiovascular disease accounts for 40% of all deaths in chronic renal disease
- Potentially reversible causes should be sought when renal function suddenly declines
- Irreversible but modifiable complications (anaemia, cardiovascular disease, metabolic bone disease, malnutrition) begin early in the course of renal failure

Sources and search criteria

I searched Medline to identify recent articles (1992-2001) related to the management of chronic renal disease and its complications. Key words used included chronic kidney disease, chronic renal failure, kidney disease, end stage renal disease, anaemia, erythropoietin, ischaemic heart disease, cardiac disease, lipid disorders, hyperparathyroidism, calcium, phosphate, nutrition, diabetes, and hypertension in relation to kidney disease. I also referred to the recent clinical practice guidelines published by the National Kidney Foundation.[2]

Diagnosis

Chronic renal failure is defined as either kidney damage or glomerular filtration rate less than 60 ml/min for three months or more.[2] This is invariably a progressive process that results in end stage renal disease.

Serum creatinine is commonly used to estimate creatinine clearance but is a poor predictor of glomerular filtration rate, as it may be influenced in unpredictable ways by assay techniques, endogenous and exogenous substances, renal tubular handling of creatinine, and other factors (age, sex, body weight, muscle mass, diet, drugs).[3] Glomerular filtration rate is the "gold standard" for determining kidney function, but its measurement remains cumbersome. For practical purposes, calculated creatinine clearance is used as a correlate of glomerular filtration rate and is commonly estimated by using the Cockcroft-Gault formula or the recently described modification of diet in renal disease equation (box 1).[w1 w2]

Stages of chronic renal disease

Chronic renal disease is divided into five stages on the basis of renal function (table, fig 1). Pathogenesis of progression is complex and is beyond the scope of this review. However, renal disease often progresses by

P+

Additional references appear on bmj.com

Box 1: Methods for estimating creatinine clearance (glomerular filtration rate) in ml/min/1.73 m²

Cockcroft-Gault formula:[w1]

$$\text{Creatinine clearance} = \frac{(140 - \text{age})(\text{weight in kilograms})}{\text{Serum creatinine } (\mu\text{mol/l}) \times 0.81} \times (0.85 \text{ if female})$$

Modification of diet in renal disease equation:[w2]

Glomerular filtration rate=$186.3 \times (\text{serum creatinine})^{-1.154} \times \text{age}^{-0.203} \times (0.742 \text{ if female}) \times (1.21 \text{ if black})$

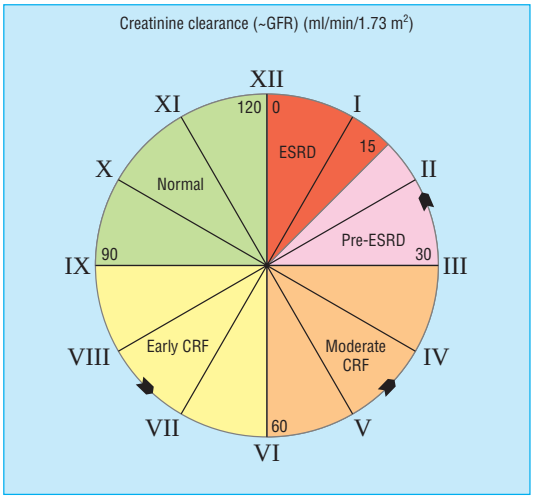

Fig 1 Continuum of renal disease (anticlockwise model) (CRF=chronic renal failure; ESRD=end stage renal disease; GFR=glomerular filtration rate)

"common pathway" mechanisms, irrespective of the initiating insult.[4] In animal models, a reduction in nephron mass exposes the remaining nephrons to adaptive haemodynamic changes that sustain renal function initially but are detrimental in the long term.[5]

Early detection

Renal disease is often progressive once glomerular filtration rate falls by 25% of normal. Early detection is important to prevent further injury and progressive loss of renal function.

Box 2: Risk factors for chronic renal disease

Risk factors
(Factors that increase the risk of kidney damage)
- Age
- Diabetes*
- Hypertension*
- Family history of renal disease
- Renal transplant

Initiation factors
(Factors that initiate kidney damage)
- Diabetes*
- Hypertension*
- Autoimmune diseases
- Primary glomerulopathies
- Systemic infections
- Nephrotoxic agents

Progression factors
(Factors that cause progressive decline in renal function after onset of kidney damage)
- Persistent activity of underlying disease
- Persistent proteinuria
- Elevated blood pressure*
- Elevated blood glucose*
- High protein/phosphate diet
- Hyperlipidaemia*
- Hyperphosphataemia
- Anaemia
- Cardiovascular disease
- Smoking*
- Other factors: elevated angiotensin II, hyperaldosteronism, increased endothelin, decreased nitric oxide

*Common modifiable cardiovascular risk factors

Patients at high risk (box 2) should undergo evaluation for markers of kidney damage (albuminuria (box 3), abnormal urine sediment, elevated serum creatinine) and for renal function (estimation of glomerular filtration rate from serum creatinine) initially and at periodic intervals depending on the underlying disease process and stage of renal disease. Potentially reversible causes (box 4) should be identified and effectively treated if a sudden decline in renal function is observed.

Stages of renal dysfunction (adapted from National Kidney Foundation—K/DOQI)[2]

Stage	Description	Creatinine clearance (~GFR) (ml/min/1.73 m²)	Metabolic consequences
1	Normal or increased GFR—people at increased risk (box 2) or with early renal damage	>90	
2	Early renal insufficiency	60-89*	Concentration of parathyroid hormone starts to rise (GFR ~ 60-80)
3	Moderate renal failure (chronic renal failure)	30-59	Decrease in calcium absorption (GFR<50) Lipoprotein activity falls Malnutrition Onset of left ventricular hypertrophy Onset of anaemia (erythropoietin deficiency)
4	Severe renal failure (pre-end stage renal disease)	15-29	Triglyceride concentrations start to rise Hyperphosphataemia Metabolic acidosis Tendency to hyperkalaemia
5	End stage renal disease (uraemia)	<15	Azotaemia develops

GFR=glomerular filtration rate.
*May be normal for age.

Box 3: Definition of urinary albumin or protein excretion

- Normal albumin excretion: <30 mg/24 hours
- Microalbuminuria: 20-200 µg/min or 30-300 mg/24 hour or
  - in men—urine albumin/creatinine 2.5-25 mg/mmol
  - in women—urine albumin/creatinine 3.5-35 mg/mmol
- Macroalbuminuria (overt proteinuria): >300 mg/24 hour
- Nephrotic range proteinuria: >3 g/24 hour

Box 4: Potentially reversible causes of worsening renal function

- Effective circulatory volume depletion: dehydration, heart failure, sepsis
- Obstruction: urinary tract obstruction
- Uncontrolled hypertension
- Toxic causes: nephrotoxic or radiocontrast agents

Box 5: Management strategies for diabetic nephropathy

(Ensure effective control of common cardiovascular risk factors—for example, lipids, smoking—at all times)

- Initial stage (normal albumin excretion, <30 mg/24 hours):
  - Optimal glycaemic control (haemoglobin A_{1c} <7%)
  - Target blood pressure <130/80 mm Hg
  - Monitor urinary albumin excretion
- Incipient nephropathy (microalbuminuria, 30-300 mg/24 hour or 20-200 µg/min):
  - Optimal glycaemic control (haemoglobin A_{1c} <7%)
  - Target blood pressure <125/75 mm Hg
  - Control urinary albumin excretion, irrespective of blood pressure
  - Angiotensin inhibition
- Overt nephropathy (albumin excretion >300):
  - Optimal glycaemic control (haemoglobin A_{1c} <7%)
  - Target blood pressure <125/75 mm Hg
  - Control urinary protein excretion
  - Angiotensin inhibition, irrespective of blood pressure
  - Avoid malnutrition
  - Modest protein restriction, in selected groups
- Nephropathy with renal dysfunction:
  - Optimal glycaemic control; avoid frequent hypoglycaemia
  - Target blood pressure <125/75 mm Hg
  - Angiotensin inhibition
  - Watch for hyperkalaemia
  - Avoid malnutrition; consider protein and phosphate restriction
- End stage renal disease:
  - Renal replacement—transplantation or dialysis
  - Monitor for hyperkalaemia
  - Hold angiotensin inhibition (when glomerular filtration <15 ml/min) in selected patients

Diabetes

Diabetes is a common cause of chronic renal failure and accounts for a large part of the growth in end stage renal disease in North America.[w3] Effective control of blood glucose and blood pressure reduces the renal complications of diabetes.

Meticulous control of blood glucose has been conclusively shown to reduce the development of microalbuminuria by 35% in type 1 diabetes (diabetes control and complications trial)[6] and in type 2 diabetes (United Kingdom prospective diabetes study).[7] Other studies have indicated that glycaemic control can reduce the progression of diabetic renal disease.[8] Adequate control of blood pressure with a variety of antihypertensive agents, including angiotensin converting enzyme inhibitors, has been shown to delay the progression of albuminuria in both type 1 and type 2 diabetes.[9 10] Recently, angiotensin receptor blockers have been shown to have renoprotective effects in both early and late nephropathy due to type 2 diabetes.[11–13] Box 5 shows strategies for managing diabetic nephropathy.

Hypertension

Hypertension is a well established cause, a common complication, and an important risk factor for progression of renal disease. Controlling hypertension is the most important intervention to slow the progression of renal disease.[w4]

Any antihypertensive agents may be appropriate, but angiotensin converting enzyme inhibitors are particularly effective in slowing progression of renal insufficiency in patients with and without diabetes by reducing the effects of angiotensin II on renal haemodynamics, local growth factors, and perhaps glomerular permselectivity.[9 w5] Non-dihydropyridine calcium channel blockers have also been shown to retard progression of renal insufficiency in patients with type 2 diabetes. Recently, angiotensin receptor blockers (irbesartan and losartan) have been shown to have a renoprotective effect in diabetic nephropathy, independent of reduction in blood pressure.[11–13] Early detection and effective treatment of hypertension to target levels is essential (box 6). The benefit of aggressive control of blood pressure is most pronounced in patients with urinary protein excretion of >3 g/24 hours.[w4]

Proteinuria

Proteinuria, previously considered a marker of renal disease, is itself pathogenic and is the single best predictor of disease progression.[w7] Reducing urinary protein excretion slows the progressive decline in renal function in both diabetic and non-diabetic kidney disease.

Angiotensin blockade with angiotensin converting enzyme inhibitors or angiotensin receptor blockers is more effective at comparable levels of blood pressure control than conventional antihypertensive agents in reducing proteinuria, decline in glomerular filtration rate, and progression to end stage renal disease.[11–14 w5 w8-w10]

Intake of dietary protein

The role of dietary protein restriction in chronic renal disease remains controversial.[15 16 w4] The largest con-

Box 6: Target blood pressure in renal disease[w6]

- Blood pressure of <130/85 mm Hg in all patients with renal disease
- Blood pressure of <125/75 mm Hg in patients with proteinuric renal disease (urinary protein excretion ≥1 g/24 hours)

trolled study initially failed to find an effect of protein restriction,[17] but secondary analysis based on achieved protein intake suggested that a low protein diet slowed the progression. However, early dietary review is necessary to ensure adequate energy intake, maintain optimal nutrition, and avoid malnutrition.

Dyslipidaemia

Lipid abnormalities may be evident with only mild renal impairment and contribute to progression of chronic renal disease and increased cardiovascular morbidity and mortality. A meta-analysis of 13 controlled trials showed that hydroxymethyl glutaryl coenzyme A reductase inhibitors (statins) decreased proteinuria and preserved glomerular filtration rate in patients with renal disease, an effect not entirely explained by reduction in blood cholesterol.[18]

Phosphate and parathyroid hormone

Hyperparathyroidism is one of the earliest manifestations of impaired renal function,[19] and minor changes in bones have been found in patients with a glomerular filtration rate of 60 ml/min.[20] Precipitation of calcium phosphate in renal tissue begins early, may influence the rate of progression of renal disease, and is closely related to hyperphosphataemia and calcium phosphate (Ca×P) product. Precipitation of calcium phosphate should be reduced by adequate fluid intake, modest dietary phosphate restriction, and administration of phosphate binders to correct serum phosphate. Dietary phosphate should be restricted before the glomerular filtration rate falls below 40 ml/min and before the development of hyperparathyroidism. The use of vitamin D supplements during chronic renal disease is controversial.

Smoking

Smoking, besides increasing the risk of cardiovascular events, is an independent risk factor for development of end stage renal disease in men with kidney disease.[21] Smoking cessation alone may reduce the risk of disease progression by 30% in patients with type 2 diabetes.[22]

Anaemia

Anaemia of chronic renal disease begins when the glomerular filtration rate falls below 30-35% of normal and is normochromic and normocytic. This is primarily caused by decreased production of erythropoietin by the failing kidney,[23] but other potential causes should be considered. Whether anaemia accelerates the progression of renal disease is controversial. However, it is independently associated with the development of left ventricular hypertrophy and other cardiovascular complications in a vicious cycle (fig 2).[24]

Treatment of anaemia with recombinant human erythropoietin may slow progression of chronic renal disease but requires further study. Treatment of anaemia results in partial regression of left ventricular hypertrophy in both patients with pre-end stage renal disease and patients receiving dialysis and has reduced the frequency of heart failure and hospitalisation among patients receiving dialysis.[25 26]

Both National Kidney Foundation and European best practice guidelines recommend evaluation of anaemia when haemoglobin is <11 g/dl and consideration of recombinant human erythropoietin if haemoglobin is consistently <11 g/dl to maintain a target haemoglobin of >11 g/dl.[27 28]

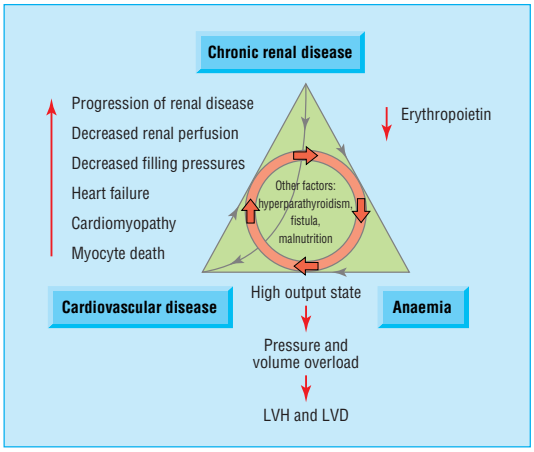

Fig 2 Perpetuating triad of chronic kidney disease, anaemia, and cardiovascular disease (LVH=left ventricular hypertrophy; LVD=left ventricular dilatation)

Prevention or attenuation of complications and comorbidities

Malnutrition

The prevalence of hypoalbuminaemia is high among patients beginning dialysis, is of multifactorial origin, and is associated with poor outcome. Hypoalbuminaemia may be a reflection of chronic inflammation rather than of nutrition in itself. Spontaneous intake of protein begins to decrease when the glomerular filtration rate falls below 50 ml/min. Progressive decline in renal function causes decreased appetite, thereby increasing the risk of malnutrition. Hence early dietary review is important to avoid malnutrition. Adequate dialysis is also important in maintaining optimal nutrition.

Cardiovascular disease

The prevalence, incidence, and prognosis of clinical cardiovascular disease in renal failure is not known with precision, but it begins early and is independently associated with increased cardiovascular and all cause mortality.[w11] Both traditional and uraemia specific risk factors (anaemia, hyperphosphataemia, hyperparathyroidism) contribute to the increased prevalence of cardiovascular disease.[29] Cardiac disease, including left ventricular structural and functional disorders, is an important and potentially treatable comorbidity of early kidney disease.

No specific recommendations exist for either primary or secondary prevention of cardiovascular disease in patients with chronic renal disease. Current practice is mostly derived from studies in patients with diabetic or non-renal disease. At present, in the absence of evidence, clinical judgment indicates effective control of modifiable and uraemia specific risk factors at an early stage of renal disease; definitive guidelines for intervention await well designed, adequately powered prospective studies.

Preparing patient for renal replacement treatment

Integrated care by the primary care physician, nephrologist, and renal team from an early stage is

vital to reduce the overall morbidity and mortality associated with chronic renal disease. Practical points helpful at this stage of renal disease include

- Patients should be referred to a nephrologist before serum creatinine is 150-180 µmol/l
- Patients receiving comprehensive care by the renal team have shown slower rates of decline in renal function, greater probability of starting dialysis with higher haemoglobin, better calcium control, a permanent access, and a greater likelihood of choosing peritoneal dialysis[w12]
- Patients with progressive renal failure should be educated to save vessels of the non-dominant arm for future haemodialysis access; they should have a permanent vascular access (preferably arteriovenous fistula) created when the glomerular filtration rate falls below 25 ml/min or renal replacement treatment is anticipated within a year
- Patients starting dialysis at relatively higher levels of residual renal function (early starts) have better solute clearance, less malnutrition, better volume control, and less morbidity and mortality than patients starting at traditional low levels of renal function (late starts).[w13]

Conclusion

Chronic renal failure represents a critical period in the evolution of chronic renal disease and is associated with complications and comorbidities that begin early in the course of the disease. These conditions are initially subclinical but progress relentlessly and may eventually become symptomatic and irreversible. Early in the course of chronic renal failure, these conditions are amenable to interventions with relatively simple treatments that have the potential to prevent adverse outcomes. Fig 3 summarises strategies for effective management of chronic renal disease. By acknowledging these facts, we have an excellent opportunity to change the paradigm of management of chronic renal failure and improve patient outcomes.

Competing interests: None declared.

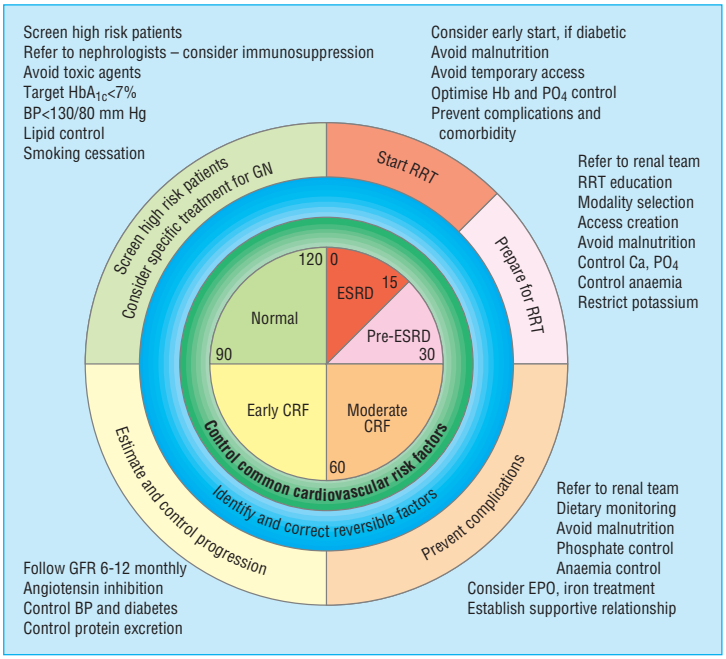

Fig 3 Strategies for active management of chronic renal disease (BP=blood pressure; Ca=calcium; CRF=chronic renal failure; EPO=erythropoietin; ESRD=end stage renal disease; GN=glomerulonephritis; GFR=glomerular filtration rate; Hb=haemoglobin; PO_4=phosphate; RRT=renal replacement treatment)

1 Jones C, McQuillan G, Kusek J, Eberhardt M, Herman W, Coresh J, et al. Serum creatinine levels in the US population: third national health and nutrition examination survey [correction appears in *Am J Kidney Dis* 2000;35:178]. *Am J Kidney Dis* 1998;32:992-9.
2 National Kidney Foundation—K/DOQI. Clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. *Am J Kidney Dis* 2002;39(suppl 1):S1-266.
3 Walser M. Assessing renal function from creatinine measurements in adults with chronic renal failure. *Am J Kidney Dis* 1998;32:1-22.
4 Remuzzi G, Bertani T. Pathophysiology of progressive nephropathies. *N Engl J Med* 1998;339:1448-56.
5 Brenner BM, Meyer TW, Hostetter TH. Dietary protein intake and the progressive nature of kidney disease: the role of hemodynamically mediated glomerular injury in the pathogenesis of progressive glomerular sclerosis in aging, renal ablation, and intrinsic renal disease. *N Engl J Med* 1982;307:652-9.
6 The Diabetes Control and Complications Trial (DCCT) Research Group. Effect of intensive therapy on the development and progression of nephropathy in the DCCT. *Kidney Int* 1995;47:1703-20.
7 UK Prospective Diabetes Study Group. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *BMJ* 1998;317:703-13.
8 Wang P, Lau J, Chalmers T. Meta-analysis of the effects of intensive blood-glucose control on late complications of type I diabetes. *Lancet* 1993;341:1306-9.
9 Lewis E, Hunsicker L, Bain R, Rhode R. The effect of angiotensin converting enzyme inhibition on diabetic nephropathy. *N Engl J Med* 1993;329:1456-62.
10 Parving H-H, Osterby R, Anderson P, Hsuech W. Diabetic nephropathy. In: Brenner B, ed. *The kidney*. Philadelphia, PA: Saunders, 1996:1864-92.
11 Parving H-H, Lehnert H, Brochner-Mortensen J, Gomis R, Anderson S, Arner P for the Irbesartan in Patients with Type 2 Diabetes and Microalbuminuria Study Group. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 Diabetes. *N Engl J Med* 2001;345:870-8.
12 Lewis EJ, Hunsicker LG, Clarke WR, Berl T, Pohl MA, Lewis JB, et al for the Collaborative Study Group. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. *N Engl J Med* 2001;345:851-60.
13 Brenner BM, Cooper ME, Zeeuw D, Keane WF, Mitch WE, Parving H-H, et al for the RENAAL Study Investigators. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med* 2001;345:861-9.
14 Mogensen CE, Neldam I, Tikkanen I, Oren S, Viskoper R, Watts RW, et al. Randomised controlled trial of dual blockade renin-angiotensin system in patients with hypertension, microalbuminuria, and non-insulin

Additional educational resources

- Tomson CRV. Recent advances: nephrology. *BMJ* 2000;320:98-101
- Mason PD, Pusey CD. Glomerulonephritis: diagnosis and treatment. *BMJ* 1994;309:1557-63
- Walker R. Recent advances: general management of end stage renal disease. *BMJ* 1997;315:1429-32
- Ifudu O. Care of patients undergoing hemodialysis. *N Engl J Med* 1998;339:1054-62
- Remuzzi G, Schieppati A, Ruggenenti P. Clinical practice: nephropathy in patients with type 2 diabetes. *N Engl J Med* 2002;346:1145-51
- National Kidney Foundation—K/DOQI. Clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. *Am J Kidney Dis* 2002;39(suppl 1):S1-266

Patient information

- Kidney School (www.kidneyschool.org)—an interactive, web based program designed to help people learn what they need to know to understand renal disease and its treatment, adjust to renal disease, make good medical choices, and live as fully as possible
- Doc-To-Me (www.doctome.com)—presents concise, informative, and authoritative pre-end stage renal disease lectures: "Staying healthy with bad kidneys"
- Kidney Incorporated (www.hdialysis.com)—provides general information about kidneys, pre-end stage renal disease care, and dialysis treatment

dependent diabetes: the candesartan and lisinopril microalbuminuria (CALM) study. *BMJ* 2000;321:1440-4.
15 Klahr S. Is there still a role for a diet very low in protein, with or without supplements, in the management of patients with end-stage renal disease? *Curr Opin Nephrol Hypertens* 1996;5:384-7.
16 Levey AS, Adler S, Caggiula AW, England BK, Greene T, Hunsicker LG, et al. Effects of dietary protein restriction on the progression of advanced renal disease in the modification of diet in renal disease study. *Am J Kidney Dis* 1996;27:652-63.
17 Modification of Diet in Renal Disease Study Group. Effects of diet and antihypertensive therapy on creatinine clearance and serum creatinine in the modification of diet in renal disease study. *J Am Soc Nephrol* 1996;7:556-66.
18 Fried LF, Orchard TJ, Kasiske BL. Effect of lipid reduction on the progression of renal disease: a meta-analysis. *Kidney Int* 2001;59:260-9.
19 Martinez I, Saracho R, Montenegro J, Llach F. The importance of dietary calcium and phosphorus in the secondary hyperparathyroidism of patients with early renal failure. *Am J Kidney Dis* 1997;29:496-502.
20 Coen G, Mazzaferro S, Ballant P, Sardella D, Chicca S, Manni M, et al. Renal bone disease in 76 patients with varying degrees of predialysis chronic renal failure: a cross-sectional study. *Nephrol Dial Transplant* 1996;11:813-9.
21 Orth S, Stockmann A, Conradt C, Ritz E, Ferro M, Kreusser W, et al. Smoking as a risk factor for end-stage renal failure in men with primary renal disease. *Kidney Int* 1998;54:926-31.
22 Ritz E, Ogata H, Orth SR. Smoking a factor promoting onset and progression of diabetic nephropathy. *Diabetes Metab* 2000;26(suppl 4):54-63.
23 Eschbach JW. The anemia of chronic renal failure. *Kidney Int* 1989;35:134-48.
24 Foley RN, Parfrey PS, Harnett JD, Kent GM, Murray DC, Barre PE. The impact of anemia on cardiomyopathy, morbidity and mortality in end-stage renal disease. *Am J Kidney Dis* 1996;28:53-61.
25 Portoles J, Torralbo A, Martin P, Rodrigo J, Herrero J, Barrientos A. Cardiovascular effects of recombinant human erythropoietin in predialysis patients. *Am J Kidney Dis* 1997;29:541-8.
26 Eschbach JW, Aquiling T, Haley NR, Fan MH, Blagg CR. The long-term effects of recombinant human erythropoietin on the cardiovascular system. *Clin Nephrol* 1992;38:S98-103.
27 National Kidney Foundation—Dialysis Outcomes Quality Initiative. Guidelines for the treatment of anemia of chronic renal failure. *Am J Kidney Dis* 1997;30(suppl 3):S150-91.
28 European best practice guidelines for the management of anaemia in patients with chronic renal failure. *Nephrol Dial Transplant* 1999;14(suppl 5):1-50.
29 Foley RN, Parfrey PS. Cardiac disease in chronic uremia: clinical outcomes and risk factors. *Adv Ren Replace Ther* 1997;4:234-8.

(Accepted 31 May 2002)

Lesson of the week

Antenatal screening for rubella—infection or immunity?

Nilesh M Mehta, Roslyn M Thomas

Interpret antenatal screening tests for rubella cautiously in recent immigrants and in women with a rash in early pregnancy

Neonatal Intensive Care Unit, Northwick Park Hospital, Harrow HA1 3UJ
Nilesh M Mehta *specialist registrar*
Roslyn M Thomas *consultant paediatrician*
Correspondence to: R M Thomas ros.thomas@nwlh.nhs.uk

BMJ 2002;325:90–1

Rubella vaccination among schoolgirls and susceptible women in the United Kingdom since 1970 has dramatically reduced the number of cases of congenital rubella syndrome and terminations of pregnancies related to rubella infection.[1] In 1988 the combined measles, mumps, and rubella vaccine was introduced for children aged 12-15 months. Reported cases of congenital rubella syndrome declined significantly, with only a few notified cases of infection among immigrants and in infants whose mothers acquired the infection while travelling overseas in early pregnancy. Immune status of pregnant women is determined by routine antenatal screening for rubella IgG antibody, so that susceptible women can receive postpartum vaccination.

We report two infants with congenital rubella syndrome whose mothers had recently arrived from abroad. Both mothers had a rash in early pregnancy in their country of origin, which was not elicited when they booked for antenatal care in the United Kingdom.

Case reports

Case 1

A 22 year old primiparous Sri Lankan woman had routine antenatal screening tests at 20 weeks' gestation, soon after her arrival in the United Kingdom. The laboratory reported presence of rubella IgG antibody, "consistent with immunity." The infant was born with severe symmetrical intrauterine growth restriction, purpura, thrombocytopenia, and a patent ductus arteriosus. Cranial ultrasonography showed bilateral periventricular calcification (fig 1). Skeletal radiographs showed linear radiolucencies in the metaphyses of the long bones and lucent areas in the iliac bones, consistent with osteitis (fig 2). Ophthalmological examination showed a unilateral cataract on the first day after birth and progressive bilateral cataracts by 3 weeks of age. Congenital rubella syndrome was suspected, and the mother confirmed that she had had a transient rash at 6-8 weeks' gestation in Sri Lanka. Rubella specific IgM was detected in the infant's blood taken at 11 days of age, and excretion of rubella virus was subsequently confirmed in the infant's saliva and urine. Audiological testing showed major bilateral sensorineural hearing loss by 12 weeks. Retesting of the mother's antenatal serum with IgM and IgG avidity tests gave results compatible with acquired rubella infection during early gestation.

Case 2

Soon after her arrival in the United Kingdom a 29 year old primiparous Nigerian woman gave birth at 38 weeks' gestation to an infant with severe symmetrical intrauterine growth restriction. The woman's antenatal tests in Nigeria did not include rubella screening. The infant had interstitial pneumonitis, thrombocytopenia, and a patent ductus arteriosus. Ophthalmological examination showed bilateral cataracts by 3 weeks of

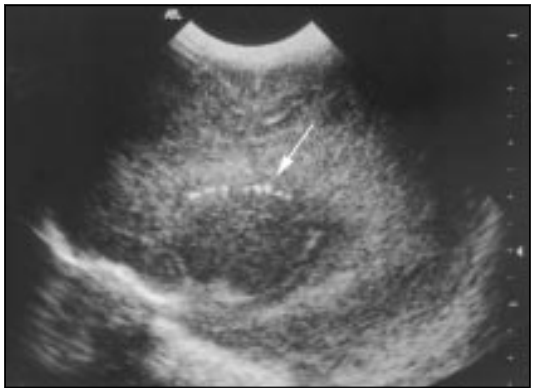

Fig 1 Cranial ultrasound scan showing linear calcification in the brain parenchyma in the parasagittal plane