Preventive Nephrology: A Time for Action

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The incidence of new end-stage renal failure (ESRF) treated with dialysis in Singapore has risen from 96 per million population (pmp) in 1992 to 167 pmp in 2000.[1,2] This near-doubling is not unique to Singapore, and many other Asian countries have seen a similar increase in the incidence of ESRF, in large part due to an increasing incidence of the risk factors for renal disease. Consequent to this high incidence of ESRF, at the end of 2002, an estimated 301,649 patients were on dialysis in Asia.[3]

The options available to treat ESRF are dialysis and renal transplantation. Though dialysis is life-saving, there are many adverse consequences of dialysis. Cardiovascular and infectious complications are the leading causes of morbidity in dialysis patients. Indeed, dialysis patients have an annual mortality of 8% in Singapore with reported rates ranging from 6.1% in China to 19.2% in New Zealand.[2] Dialysis patients are also less well rehabilitated than their transplant counterparts due to underlying poor health and co-morbidities. Time spent on the dialysis procedure itself is also a hindrance to the full rehabilitation of the dialysis patient. Equally important are the consequences of dialysis on the financial health of the individual patient and the nation. Treating renal failure is a costly enterprise and cost of treatment of ESRF exceeds the per capita income in many nations across Asia. Indeed, many developing nations in Asia are unable to bear the costs of treating ESRF with dialysis; patients with no access to transplantation often die. On the other hand, renal transplantation is limited by the lack of renal donors. Given these facts, prevention of ESRF is a national imperative.

In this issue on 'Preventive Nephrology' in the *Annals*, the focus is on prevention of renal failure. Early detection of renal disease, determination of its underlying cause, treatment of correctible abnormalities, and retardation of progression to ESRF are the cornerstones of prevention of renal failure. Identification of urinary abnormalities of haematuria and proteinuria, and diagnosis of hypertension are the key features of a screening programme for renal disease. In an effort to detect renal disease as early as possible, a pilot screening project was initiated among 12 year olds in Singapore between 1999 and 2000.[4] Although the screening programme was successful in that it detected early renal disease, as Yap and her co-authors point out, the overall incidence of urinary abnormalities in Singapore among children is low at 1.25 per 1000 children screened. In this study, low body weights and low birth weights in children were associated with a higher risk for proteinuria, suggesting that reduced renal mass at birth together with environmental influences may predispose to earlier presentation of renal disease. As the cost-benefit ratio of screening for renal disease in all children may not be optimal, an alternative approach would be to screen selective cohorts, for example, children with low birth weight and those with lower body weights.

Likewise, in adults, mass screening may not be cost-beneficial. Opportunistic screening of healthy individuals and screening of higher risk individuals such as those older than 50 years old, hypertensives, diabetics, those with family history of renal disease and smokers is recommended.[5] From the 2000 Census, 20.9% (681,282 of 3.26 million) Singaporeans/permanent residents were older than 50 years of age.[6] From the 1998 National Health Survey, 9% of Singaporeans aged 18 to 69 and 32.4% of those aged 60 to 69 were diabetic, 27.3% of Singaporeans aged 30 to 69 were hypertensive and 15% of those aged 18 to 64 were cigarette smokers.[7] Based on these statistics, a significant proportion of the Singaporean population are at high risk for renal disease and should be screened.

Once detected, the next area of focus is to diagnose and treat the underlying cause of chronic renal disease, treat co-morbid conditions and retard its progression. In this issue, several authors have discussed the treatment strategies that may be useful in retardation of progression of chronic kidney disease (CKD). Hypertension plays a key role not only in the progression of renal disease, but also contributes to cardiovascular disease, the major cause of morbidity in renal disease. In this issue, Whitworth[8] summarises the recommendations for treatment of hypertension in renal disease with either angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB). Most patients will require combination anti-hypertensive drug therapy to control blood pressure and reduce both progression of renal failure and the associated cardiovascular morbidity and mortality. Harris and Rangan[9] review the success of proven strategies, such as adequate blood pressure control with angiotensin blockade (in all renal diseases) and good glycaemic control (in diabetic nephropathy), in slowing progression of CKD. They also discuss other potentially beneficial strategies such as smoking cessation, lipid control and aldosterone blockade. In fact, they suggest that eradication of type 2 diabetes and obesity (through improvement of lifestyle factors), and adequate treatment of hypertension, have the potential to eliminate up to half of the most common causes of ESRF in developed countries. Also in this issue, Lee[10] elaborates on the retardation of progression of renal failure in type 2 diabetic nephropathy, focusing especially on control of hypertension and proteinuria. These three papers echo the need for tight control of blood pressure to <130/80 mm Hg for all patients with CKD and the need for multiple antihypertensive agents, especially those that block angiotensin to achieve this goal. Taking therapy from guidelines to practice, Woo et al[11] demonstrate the success of combination therapy with ACEI and ARB in retarding renal disease progression. Finally, Chan[12] elaborates on the potential for hyperlipidaemia to exacerbate cardiovascular morbidity in renal disease and the renal disease itself. As a corollary, aggressive treatment of hyperlipidaemia in patients with renal disease may not only reduce the cardiovascular morbidity but also reduce progression of renal disease.

This issue of the Annals also highlights the potential of new therapies to reduce the burden of renal failure. In Singapore, renal transplant recipients constitute approximately a quarter of the total number of patients receiving renal replacement therapy. As a group, all renal allograft recipients have CKD as they have a single functioning kidney. The article by Vathsala[13] reviews the relationship of immunological and non-immunological risk factors in the development of transplant failure and highlights the potential for novel immunosuppressive therapies such as sirolimus and mycophenolate to improve renal allograft function and survival in this select population. In a tantalizing article on herbal treatment for renal diseases, Peng et al[14] present evidence demonstrating the potential benefit of Chinese herbal medicines such as *Astragalus* or a mixture of various herbs in slowing the progression of CKD. They suggest that the anti-inflammatory effects of these herbal remedies may reduce fibrosis independent of any effects on blood pressure. Though they point out that some Chinese herbal remedies are toxic to the kidney, more research is clearly needed to further elucidate the potential for use of these traditional remedies in treating chronic renal disease.

The message in these articles must be viewed especially in the context of the prevalence of diabetes and hypertension and their treatment in Singapore. In 2000, 47% of all new ESRD in Singapore were due to diabetic nephropathy, earning Singapore its notoriety for the second highest incidence of ESRF due to diabetic nephropathy in the world.[2,15,16] These statistics are hardly surprising given that 62% of the diabetics identified in the National Health Survey of 1998 had not been diagnosed prior to the survey and that 53% of those with known diabetes had poorly controlled diabetes, defined as HbA1c >8% (American Diabetes Association in 1998).[7] Another startling statistic is that 53% of the hypertensives detected in the survey had not been diagnosed previously. Furthermore, 70.1% of all known hypertensives had poor blood pressure control, defined as systolic blood pressure $\geq$140 mmHg or diastolic blood pressure $\geq$90 mmHg (World Health Organisation, 1996), while 66.4% of those on drug treatment had poor blood pressure control. Thus, achieving better control of hypertension and diabetes at the community level could reduce the burden of renal disease in Singapore.

Reducing renal failure in Singapore is not complicated: simple measures such as regular, opportunistic screening by primary care physicians, for hypertension and diabetes, can identify a large proportion of those at risk for renal disease. Further, screening for renal disease in at risk individuals, with a simple urine dipstix can detect the large proportion with possible renal disease. Though those patients with glomerulonephritis require further evaluation and specific treatment by a nephrologist, for the remainder, treatment is straightforward – control blood pressure to <130/80 mm Hg, use ACEI and/or ARB, treat diabetes to target HbA1c <7.0% and treat those with hyperlipidaemia and renal disease as high-risk individuals for cardiovascular disease. These therapies can all be initiated by a primary care physician.

In a community based programme in rural India, social and preventive health workers of the Kidney Help Trust examined the urine of every individual for albumin and reducing substances, and checked the blood pressure of every person aged over 5; 90% of the population cooperated.[17] Six per cent were hypertensive and 4% had diabetes. Using only the cheapest agents available and at a cost of 27 US cents for one year per person (reserpine, hydrallazine and hydrochlorothiazide for hypertension, and glibenclamide and metformin for diabetes), Mani and workers[17] were able to control the blood pressure to 140/90 mm Hg or less in 96% of cases, and to achieve a HbA1c <7.0% in 50% of the diabetics in the study. Surely we in Singapore can do as well.

The evidence is clear, preventive nephrology is necessary to halt the epidemic of renal failure. There is an urgent need for a paradigm shift with detection and prevention of CKD back to the primary care physician. The time for action is now.

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