

## Paediatrics to Geriatrics: The Continuum

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In many parts of Asia today, pediatricians are still grappling with the childhood problems of infectious diseases, diarrhoeal diseases and malnutrition. In Singapore, it was no different up to the mid 1980s. In line with the economic and urban transformation, our population has also experienced vast improvement in health care. This is reflected by the marked decrease in the infant mortality rate over the past 4 decades, from 20.5 deaths per 1000 live births in 1970 to 2.1 in 2005. Likewise, with the improvement in public health, there has been a significant decrease in the hospital mortality rate, with a change in the pattern of mortality over the last 4 decades. Where infections used to be the major killer, this is no longer true as malignancies and other chronic diseases are increasing in importance as causes of deaths in children. Therefore, what is the role of paediatricians in our modern day practice, with the decline in the incidence of serious childhood infections?

Our understanding of molecular medicine has allowed us to develop newer drugs and molecules that target specific genes or proteins which mediate disease. However, despite apparent disease control in many instances, the life expectancy of our population has not increased to the degree that we would have liked. The average life expectancy of our population today has only increased by an average of 10 years over the past 4 decades, i.e., from less than 70 years in the 1960s to 77.9 years for men and 81.6 years for women in 2005. In addition, the incidence of various adult diseases such as hypertension, type 2 diabetes, cardiovascular disease and end-stage renal disease have been increasing over the years. Should this be the concern of paediatricians?

Adult diseases often have their basis in infancy and childhood. The “Barker” hypothesis states that the quality of fetal growth and development could influence susceptibility to adult diseases.<sup>1</sup> There is epidemiologic evidence that diseases such as cardiovascular disease, hypertension, stroke, type 2 diabetes, allergy and chronic renal failure may have their origins in fetal life. Studies have convincingly shown that birth weight is inversely related to the risk of developing coronary heart disease, hypertension and type 2 diabetes. In addition, an increasing number of studies, both in humans and animals, have shown that fetal growth retardation appear to impact upon

nephron number, resulting in a decrease in renal reserve. Multivariate models suggest that various risk factors, which start in childhood, act in concert in these predisposed individuals contributing to the development of chronic kidney disease in later life.

The concept of developmental plasticity as proposed by Gluckman et al<sup>2</sup> states that the responses required to cope with environmental challenges in early life may have long-term effects on the adult organism. In studies examining early life influences on development of obesity, hypertension and dyslipidemia in children, post-natal weight gain in well-nourished infants was shown to be the dominant factor associated with hypertension and early weight gain. Moreover, childhood obesity is also an important predisposing factor of the metabolic syndrome and its consequent risk of hypertension, ischaemic heart disease and type 2 diabetes. Hence the axiom “from cradle to grave” certainly has a biological basis, and lifestyle changes are therefore just as important as our modern medical interventions!

James Joyce, one of the significant writers of the 20<sup>th</sup> century, made this famous quote: “*I am tomorrow, or some future day, what I establish today. I am today what I established yesterday or some previous day.*” Therefore how we care for the child today, will impact on his well-being tomorrow as an adult. Long-term morbidity and mortality is often seen in young adults with childhood-onset diseases. In other words, despite early intervention and treatment of chronic childhood diseases with apparent “good” medical control, there is still significant long-term adult morbidity. This is well illustrated in young adults with childhood-onset chronic kidney disease, where cardiovascular and cerebrovascular complications are the major causes of death. Several studies have demonstrated advanced coronary and carotid arteriopathy in young adults who had chronic kidney failure since childhood, and this correlated with cumulative dialysis time, as well as the cumulative serum calcium-phosphate product, a biochemical index of control of renal bone disease.<sup>3</sup> Hypertension and anaemia are other major risk factors for cardiovascular morbidity in children with end-stage renal disease. Several studies have shown that a significant proportion of children and adolescents on chronic dialysis

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have evidence of chronic heart disease. This raises the question as to how “good” control is defined, for example in the control of blood pressure in children. Are the current “gold” standards good enough?

Worldwide there is an increasing trend of chronic renal failure in the adult population, with diabetes being the major cause of this increase. In children, there is also a trend of an increase in the incidence of chronic renal insufficiency over the past decade, from 0.994 to 2.334 per 100,000 children per year, coinciding with a dramatic global increase in obesity and diabetes mellitus.<sup>4</sup> The cumulative incidence of end-stage renal failure in adults who presented with diabetes before the age of 21 years has been reported to be 21.3%. The level of glycaemic control in the first 2 decades of insulin-dependent diabetes mellitus was found to be a strong predictor of chronic kidney failure, with an incidence ranging from 9.2% in the best tertile of glycaemic control to 36.3% in the worst tertile.<sup>5</sup> This again serves to emphasise the importance of good control during childhood and adolescence if an impact is to be made on the reduction of diabetic complications in adulthood.

Many chronic diseases in childhood are treated with long-term medications, which have potential side effects. A good example of this is seen in childhood nephrotic syndrome, which is supposed to be relatively benign as minimal change disease is the most common cause. In a large unselected series of children with steroid-responsive nephrotic syndrome followed up for more than 15 years, the mortality is less than 1% with death due to sepsis or thrombosis, not renal failure. Unfortunately, not all children will go into long-term remission. In fact, about 15% to 20% will continue to be nephrotic into adulthood, and will still require steroids for treatment.<sup>6</sup> Therefore in the group of steroid-dependent children, who constitute up to 40% of childhood nephrotic syndrome, what is the long-term morbidity? Well-recognised complications of long-term steroid therapy in children include growth retardation and development of cataracts. This is related to a large extent on how often the child required daily steroids to achieve remission. Therefore one strategy to reduce the effect of corticosteroids on growth is to use an alternate day steroid therapy regimen, especially during the peripubertal period. Another example of this is the use of alkylating agents in the treatment of children with relapsing nephrotic syndrome.

Meta-analysis showed that long-term adverse effects included malignancies which were observed in 14 children after high doses of either chlorambucil or cyclophosphamide.<sup>7</sup> With regard to gonadal toxicity, no safe threshold for a cumulative amount of cyclophosphamide was found in males, but there was a marked increase in the risk of oligo- or azoospermia with higher cumulative doses.

In conclusion, if we are to improve adult health and therefore impact on life expectancy, we must address the issues of child health and disease at the earliest possible stage, which includes the fetus. In this way, modern health care is indeed a continuum from paediatrics to geriatrics. Thus, despite a decreasing birth rate in many countries and improved infant mortality rates, paediatric care is still fundamental to the long-term health of society. In a way, these principles were first expounded by the ancient Chinese physicians as recorded in the “*Medical Classics of the Yellow Emperor*” where it has been written that “*the best doctor prevents the cause of the disease, the average doctor prevents the onset of the disease, and the mediocre doctor treats the disease*”.

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