CHAPTER I

Introduction

Systemic lupus erythematosus (SLE) is a fluctuating, chronic, multisystem inflammatory disease that is extremely variable in its clinical manifestations.*(1)* It ranges from a relatively mild condition characterized by a facial rash, joint pains and fatigue to a severe life-threatening illness. General systemic symptoms such as fever, weight loss, fatigue, arthralgia and general malaise are common in juvenile-onset SLE (JSLE). The fatigue may be profound, disabling, and difficult to treat. The characteristic skin rash is the facial butterfly rash crossing the bridge of the nose, sparing the nasolabial folds. Other rashes (e.g. vasculitis) may occur in JSLE, and many children with lupus exhibit marked photosensitivity. Alopecia is usually mild but can be severe with scarring. Raynaud's phenomenon is common, as is haematological involvement including leucopenia, lymphopenia, thrombocytopenia and haemolytic anaemia. Cardiopulmonary manifestations in JSLE are increasingly recognized and include pericarditis, myocarditis, diffuse interstitial lung disease and pulmonary haemorrhage. Neuropsychiatric SLE is a cause of much long-term morbidity and may manifest as seizure activity, psychosis, aseptic meningitis, headaches or altered mood. Renal involvement occurs frequently in JSLE, and when present tends to dominate the clinical picture. It may present as asymptomatic haematuria and proteinuria, hypertension, nephrotic syndrome or a rapidly progressing glomerulonephritis. Renal biopsy has an important role to play in determining the severity and therefore the likely outcome of the renal disease. Children with SLE are at particular risk from infection, now the most common cause of death. This results both from the disease process itself and from the use of immunosuppressive treatment regimens.

Approximately 15–20% of all cases of SLE have their onset before 16 years of age.*(1)* There is a paucity of data addressing the epidemiology of pediatric SLE. The incidence of SLE appears to be increased in Hispanic, Asian, and African–American pediatric populations, but large-scale, population-based studies have not been

performed. Finnish, Canadian, US, and Japanese registries and surveys suggest an incidence of pediatric SLE between 0.36–0.60 per 100,000 population per year.*(2)* Advances in our understanding of the biology, diagnosis, treatment and supportive care of SLE over the past 50 years have dramatically improved the prognosis of children and adolescents with SLE. Five and ten year survival rates have increased from less than 40% in the 1960s *(3)* to 80–90% in the 1980s and 1990s.*(4)* In the 2000s reports, the 5-year survival rate approaches 100%, and the 10-year survival rate is close to 90%.*(5)* Consequently, children and adolescents with SLE are living longer and enter adult life with a chronic disease and morbidity as well as significant responsibilities, such as hospitalizations, multiple physician visits, frequent laboratory monitoring, health-care costs and limiting activities, which significantly disrupt patients' and their families' lives and require psychosocial adaptation. Improved outcomes compel pediatricians to focus on prevention of later generally unpredictable complications of SLE and its therapy and psychosocial issues of the family, child, and adolescent.

Diagnosing and/or caring for a young person with SLE in adolescence presents major challenges to all involved in their care. The 'tasks' of adolescence have been defined as achieving physical and sexual maturity, acquiring the skills needed to carry out adult roles in society, gaining autonomy from parents, and realigning social interactions and relationships with members of the same and opposite sex.*(6)* During a time of such profound bio-psychosocial development, the impact of a chronic, complex illness is significant. Chronic illness itself may affect physical development during adolescence (e.g. delayed sexual maturation and physical growth). Uncertainty about the future, dependence upon ongoing medical support, adjustment to complex medication regimens, changes to physical appearance, and adjustment to significant lifestyle changes cannot be underestimated. Most of the drugs available for the treatment of JSLE have significant potential short-, medium- and long-term side-effects that many young people find intolerable. Both visible and invisible signs of SLE itself, and consequences of treatment, may alter deeply the self-esteem and his relationships with other adolescents. Persistent headaches, mood swings and cognitive difficulties may impair seriously their learning skills. Physical changes induced by steroid use, often

devastating to teenage girls, such as obesity, hypertrichosis, striae constitute intolerable stigmata often more stressful than the disease itself. Others restrictions in terms of diet, oral contraception, sun avoidance and alcohol and tobacco use may accelerate their social exclusion. The adolescent will search progressively to manage his health care by his or her own. As they strive to become independent from their parents, issues of self-advocacy and decision-making about treatment options, adherence to medication, 'risky' health behaviours, disease education, and generic health concerns become important factors that need to be addressed. To satisfy this goal, he will expect his physician to involve him directly in decision-making regarding his treatment, whatever is the parents' point of view. Questions regarding intimacy, confidentiality and role distribution in treatment execution may be potential source of difficulties. These characteristics of the disease impact the quality of life (QOL) in unique ways, thus measuring the objective outcomes of morbidity and mortality only does not fully reflect the burden of disease borne by the sufferers. Appropriate QOL evaluation in children with chronic diseases such as SLE will lead to formulation of important therapeutic interventions, improve understanding between pediatricians and parents, and enhance overall compliance and treatment effects that will result in better QOL for the patients.*(7)*

QOL is an expansive, multidimensional, dynamic, and personal concept defined differently by various researchers.*(8-10)* For patients with chronic diseases, health-related QOL (HRQOL) is a relevant construct, defined as 'optimum levels of mental, physical, role and social functioning, including relationships, and perceptions of health, fitness, life satisfaction and well-being'.*(8)* Generic QOL, physical function, and health status scales may not adequately capture the extent of specific impact that a particular disease may have upon the patient's QOL.*(11)*

The assessment of QOL has become an important facet of management of chronic diseases such as this and is considered to be very relevant for clinical practice, interventional trials and outcome monitoring.*(12,13)* Studies in adults with SLE have shown that QOL and health status are significantly affected.*(14-21)* Evaluation of QOL in adolescents with SLE is complicated by disease heterogeneity, instruments without

appropriate focus, and lack of measurement tools specifically for adolescents and their unique needs.

Generic instruments developed for use within a general population such as Pediatric QOL Inventory (PedsQL), child health questionnaire (CHQ), childhood health assessment questionnaire (CHAQ), TNO AZL children's quality of life questionnaire (TACQOL) may be limited to assessing the overall aspects of all diseases and may lack responsiveness to clinical changes. As such, these instruments may not adequately capture and measure the extent of the impact on a particular organ system especially in a case of central nervous or renal involvement, where cognitive function, psychiatric, financial and logistic effects require consideration. Self-esteem and body image may be affected particularly in adolescents with widespread skin rash, cushinoid features, alopecia and/or fatigue affecting their peer relationships. Adolescent's changing needs and expectations, as they grow, limited availability of age-specific questionnaires during the transition from childhood to adulthood, and the use of proxy-respondents compound difficulties of QOL measurement. Although adult studies have shown that SLE significantly affects QOL and health status, literature addressing the QOL in adolescents with SLE is lacking.*(14-27)*

Qualitative research has yielded as many as 12 concepts: uncertainty/unpredictability of SLE, fatigue, pain/symptoms, social support, misunderstood by others, fear, dependence/feelings of inadequacy/loss of self, limited/ restricted activities, personal self-management, medical treatment, emotional stress and financial issues.*(28)* The unpredictability of SLE in terms of the course of disease, extent of organ involvement and response to treatment is a significant component of the patient's QOL that is not well represented by general health instruments even though it may be indirectly assessed with a helplessness index.*(29, 30)*

There are many instruments measuring QOL, physical function and health status in children, but the existing measures largely focus on impact of physical function, which are more applicable in diseases such as juvenile arthritis causing impairment of physical function.*(31-37)* Most of them were not developed specifically for SLE and therefore present different limiting features when considered in the overall aspects of pediatric

SLE and the responsiveness to clinical changes. Recently, a novel pediatric SLE-specific QOL tool titled, Simple Measure of the Impact of Lupus Erythematosus in Youngsters© (SMILEY©) was developed to reflect QOL issues in children with SLE in pediatric practice.*(38)* However, multi-center studies needs to be conducted to assess responsiveness of SMILEY© to change in disease activity. Cross-cultural validation of SMILEY© is also needed.

The objective of this study is to employ analytic techniques to identify the indices and domains that are critical in determining QOL in Thai adolescents with SLE. This will enable the development of a comprehensive QOL instrument for adolescent SLE. Then we can formulate appropriate interventions targeted at improving QOL, and, in the long term, optimize care and improve their self-efficacy and disease management.