Systemic Lupus Erythematosus in Children: An Update

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Introduction
Systemic lupus erythematosus (SLE, or lupus), a rheumatic disease of unknown cause, is characterized by the presence of autoantibodies directed against antigens, leading to inflammatory damage of many target organs including the joints, kidneys, blood cells, and the central nervous system. SLE in children and adolescents (pSLE) may have a great variability in disease presentation and course. Childhood lupus frequently presents with systemic and constitutional symptoms like fever, fatigue, malaise etc. On the other hand they have a higher rate and severity of organ involvement. So, disease damage develops more quickly than adults.

Historical Review
The word lupus, derived from the Latin word for wolf, was originally used in medicine from the 13th to the 19th centuries to describe a dermatitis characterized by recurrent, florid facial ulcerations. In 1872 Kaposi first clarified the acute and chronic types of the skin disease. In 1895, Osler recognized the systemic nature of this disease, its characteristic exacerbations and remissions, and suggested that “erythema exudativum” was a form of vasculitis. The clinical features of SLE as recognised today, however were first described by Baehr, Kemperer, and Schirlin in 1935. They emphasized that characteristic visceral involvement could occur even in the absence of typical skin lesions. Description of LE cells in 1948 made it possible to recognize a wider spectrum of SLE patients.

Epidemiology
The incidence of SLE varies significantly in different populations and races. In United States, annual incidence rate in adults ranges from 1.9 to 5.6 per 100,000 population. Approximately 15-20% of all SLE cases are diagnosed in childhood. Disease onset before 5 years of age is unusual, although lupus has been diagnosed even in the 1st year of life. Most paediatric patients are diagnosed during adolescence.

SLE is considered as a predominantly female disease. Although most affected patients are female, the ratio changes with age. Prior to puberty, the female to male ratio is 3:1, after puberty, the ratio becomes 9:1. The median age at pSLE diagnosis is 12 years. One study found that female preponderance was significant only in post-pubertal patients.

Aetiopathogenesis
Except for drug-induced lupus, the aetiology of SLE is unknown. But it is evident that SLE results from the interactions of many factors: some genetic, some acquired, some possibly environmental. Its precise pathogenesis is unclear. There is a growing evidence in favour of a clearance deficiency of apoptotic cells as the core mechanism in the pathogenesis of SLE. Defective clearance of apoptotic cells causes secondary necrosis with release of intracellular contents and inflammatory mediators. Macrophages respond and present self antigens to T and B cells.

The central immunological disturbance in patients with SLE is autoantibody production. These antibodies are directed at several self molecules found in the nucleus, cytoplasm, and cell surface, in addition to soluble molecules such as IgG and coagulation factors. The production of antibodies result from complex mechanisms involving every key facet of the immune system. It appears that excessive and uncontrolled T cell help in the differentiation and activation of auto antibody forming B cells is probably a final common pathway. The abnormal cellular and humoral response to the formation of auto antibodies is modulated by genetic, environmental, and hormonal factors.

Genetic factors
- Genes of the MHC HLA-Al, B8 and DR3 have been linked to lupus.
- Genetic deficiency of complement factors C1q, C2, C4 have also been linked to lupus.
Environmental factors

- Occupational exposure - Silica, pesticides, mercury etc.
- Drugs
- Sunlight
- Epstein – Bar Virus (EBV) has also been identified as a possible factor in the development of lupus.

Hormones

Steroids have many effects on both the innate and adaptive immune systems and are therefore of importance in disease pathogenesis. Although sex hormones do not cause SLE, they probably play a role in disease predisposition, severity and activity. The basic pathological features of SLE are that of inflammation and blood vessel abnormalities, which include band or occlusive vasculopathy, vasculities, and immune complex deposition. The best characterized organ pathology is in the kidney. By light and immuno-fluorescence microscopy, renal biopsies in SLE patients display mesangial cell proliferation, inflammation, basement membrane abnormalities, and immune complex deposition.

Other organ systems affected by SLE usually display non-specific inflammation or vascular abnormalities, although pathological findings are sometimes minimal. Occlusive vasculopathy is a common histological feature associated with presence of antiphospholipid antibodies. Atherosclerosis and tissue damage caused by hypertension, corticosteroids, and other drugs can be found in patients with long standing SLE.

Clinical Presentation:

Children with lupus present with diverse and often severe manifestations (Table-I). Most frequently they present with systemic, constitutional symptoms such as fever, diffuse hair loss, fatigue, weight loss, and evidence of diffuse inflammation as demonstrated by lymphadenopathy and hepatosplenomegaly. These manifestations may be seen throughout the course of the disease or intermittently. Skin, musculoskeletal, and renal systems are the most common organ involved in childhood SLE. Carreno et al in their study found a higher frequency of cutaneous vasculitis, seizures, nephropathy and discoid lupus erythematosus in childhood SLE. On the other hand adults had more incidence of articular manifestations. Some other studies also observed a higher frequency of renal disease, chorea, central nervous system involvement or hematological findings among childhood SLE. In a recent meta analysis significant differences were found in clinical manifestations between childhood-onset lupus and adult-onset lupus. Malar rash, ulcers/mucocutaneous involvement, renal involvement, seizures, thrombocytopenia, hemolytic anemia, fever and lymphadenopathy were common in childhood-

<table>
<thead>
<tr>
<th>Table-I</th>
<th>Clinical Features of Systemic Lupus Erythematosus</th>
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<tbody>
<tr>
<td>Constitutional</td>
<td>Fever, malaise, weight loss</td>
</tr>
<tr>
<td>Cutaneous</td>
<td>Butterfly rash, discoid lupus, periungual erythema, photosensitivity, alopecia, mucosal ulcerations.</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Polyarthralgia and arthritis, tenosynovitis, myopathy, aseptic necrosis</td>
</tr>
<tr>
<td>Vascular</td>
<td>Raynaud’s phenomenon, livido reticularis, thrombosis, erythromelalgia</td>
</tr>
<tr>
<td>Cardiac</td>
<td>Pericarditis and effusion, myocarditis</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Pleuritis, basilar pneumonia, atelectasis, hemorrhage.</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Peritonitis, oesophageal dysfunction, colitis</td>
</tr>
<tr>
<td>Liver, spleen</td>
<td>Hepatomegaly, splenomegaly</td>
</tr>
<tr>
<td>Nodes</td>
<td>Lymphadenopathy</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Organic brain syndrome, seizures, psychosis, chorea, cerebrovascular accident, polyneuritis and peripheral neuropathy, cranial nerve palsies, pseudo tumour cerebri.</td>
</tr>
<tr>
<td>Occular</td>
<td>Exudates, papilledema, retinopathy.</td>
</tr>
<tr>
<td>Renal</td>
<td>Glomerulonephritis, nephrotic syndrome, uremia, hypertension.</td>
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</tbody>
</table>
onset SLE with ORs ranging from 1.3 to 3.7. However, Raynauds, pleuritis, and sicca were more common in adult-onset SLE.

Overall 60-80% of children with SLE have abnormalities of the urinary tests or of renal function early in the course of the disease. In 90% of patients, renal disease occurs within two years from disease onset\(^\text{18}\). Some children may present solely with renal disease, with a picture of nephrotic syndrome; rarely a child or teen may present with renal failure at the onset\(^\text{19}\).

Another study comparing childhood SLE with adult onset SLE done in a multicenter, multiethnic disease cohort showed that juvenile onset patients had significantly more renal and neurologic involvement at the time of entry into the study\(^\text{20}\). These patients also had more active disease at diagnosis, as measured by valid disease activity measure.

Neurologic manifestations of SLE are difficult to diagnose because they may be vague and varied\(^\text{10}\). After renal disease, neurologic problem is the second leading cause of serious morbidity and mortality. Psychiatric manifestations including psychosis, seizures and headaches are the most common CNS symptoms. Headaches, difficulty with concentration or memory, depression or a decline in school performance, all may be due to lupus cerebritis but also may result from coping difficulties with a chronic illness or an effect of steroid treatment\(^\text{10}\).

The World Health Organization (WHO) has defined a morphologic classification of kidney biopsies in SLE, and this classification was revised in 2003 by the International Society of Nephrology and the Renal Pathology Society\(^\text{2}\). The histologic classes range from normal by light microscopy (class I) to advanced sclerotic nephritis (class VI). It is well recognised that patients with class IV nephritis can present with a normal serum creatinine level, blood pressure and with minimally active urine sediment. Because treatment differs, a renal biopsy is warranted at the time of initial presentation in patients with an active urine sediment or abnormal renal function\(^\text{2}\). At disease onset, more severe proteinuria, more haematuria, a lower serum albumin and the need for antihypertensive drugs are all associated with a higher class of lupus nephritis\(^\text{18}\).

Hematologic Involvement
Anemia, thrombocytopenia, and leukopenia are seen in 50% to 75% of patients. The coombs’ test is positive in approximately 30% to 40% of patients, but less than 10% of patients have overt hemolysis\(^\text{2, 21}\). Thrombocytopenia may be the initial presentation in up to 15% of pediatric cases. Patients with chronic autoimmune idiopathic thrombocytopenic purpura should be assessed for the presence of antinuclear antibodies, as they are at high risk of developing SLE.

Cardiovascular involvement
Any layer of the heart may be involved in SLE, although the pericardium in affected most commonly\(^\text{10}\). Less commonly, endo-or myocarditis or vulvular disease is found, and rarely, ischaemic heart disease may result secondary to coronary artery vasculitis\(^\text{22}\). Vulvular abnormalities are frequent in patients with SLE among which mitral valve lesions being most common\(^\text{23}\). Other cardiovascular abnormalities include raised pulmonary artery pressure, pericardial effusion, hypokinesis and aortic insufficiency.

The major cardiovascular morbidity associated with SLE is premature atherosclerosis. A number of atherosclerotic risk factors, including lipid abnormalities, altered endothelial function, nephritis, and proteinuria have been implicated in the development of premature atherosclerosis in patients with childhood SLE.

Pulmonary involvement
Pulmonary involvement is common in childhood SLE and occurs in 25% to 75% of cases\(^\text{2}\). The clinical spectrum includes pleuritis, pneumonitis, pulmonary haemorrhage, pulmonary hypertension, and pneumothorax. Patients with SLE receiving immunosuppressive therapy are at high risk for infection with opportunistic organisms including Herpes viruses, Pneumo—cystis carini and fungal infections. These infections must be ruled out before the introduction of significant immunosuppressive therapy.

Gastrointestinal involvement
Gastrointestinal involvement occurs in 20% to 40% of patients\(^\text{2}\). Abdominal pain can result from peritoneal inflammation (serositis), vasculitis, pancreatitis, malabsorption, pseudo-obstruction, paralytic ileus, or direct bowel wall involvement (enteritis).

Diagnosis of childhood SLE:
Early diagnosis is the key to getting the best possible outcome for children with SLE. With early diagnosis and treatment, much of the long-term organ damage
can be prevented and the prognosis is greatly improved\textsuperscript{24}. The most important cause for delay in the diagnosis is the failure of the initial physician/paediatrician to consider the possibility of a lupus diagnosis.

The diagnosis of lupus is confirmed by the combination of clinical and laboratory manifestations revealing a multisystem disease\textsuperscript{1}. The revised ACR classification criteria are commonly used by the rheumatologistis to diagnose SLE, although these criteria were not specifically developed as diagnostic criteria\textsuperscript{24}. The criteria were created to allow physicians to exclude patients who most definitely did not have SLE.

The presence of 4 of 11 criteria (Table-2) serially or simultaneously strongly suggests the diagnosis\textsuperscript{25}. Unfortunately, they don’t include the most common initial symptoms of SLE, which are fever, malaise (not feeling well), and aches and pains. Children with SLE

<table>
<thead>
<tr>
<th>Item</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Malar rash</td>
<td>Fixed erythema, flat or raised, over the malar eminences, sparing nasolabial folds.</td>
</tr>
<tr>
<td>Discoid rash</td>
<td>Erythematous, raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions.</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>Skin rash as a result of unusual reaction to sunlight by history or on physical exam.</td>
</tr>
<tr>
<td>Oral ulcers</td>
<td>Oral or nasopharyngeal ulceration, usually painless, observed by physician</td>
</tr>
<tr>
<td>Non-erosive arthritis</td>
<td>Involving 2 or more peripheral joints, characterized by tenderness, swelling or effusion</td>
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</tbody>
</table>
| Pleuritis/Pericarditis | a. Pleuritis- convincing history of pleuritic pain or rub or pleural effusion on physical examination.  
b. Pericarditis - documented by ECG, rub or evidence of effusion. |
| Renal disorder | a. Persistent proteinuria >0.5 gm/day or >+++ ORb. Cellular casts – may be RBC, Hb, granular, tubular or mixed |
| Neurological disorder | a. Seizures – in the absence of offending drugs, or known metabolic derangement, e.g. uraemia, Ketoacidosis or electrolyte imbalance, or  
b. Psychosis – in the absence of offending drugs, or known metabolic derangement, e.g. uraemia, ketoacidosis or electrolyte imbalance |
| Haematological disorder | a. Haemolytic anaemia with reticulocytosis, OR  
b. Leukopaenia <400c/cu.mm on 2 or more occasions OR  
c. Lymphocytopenia <1500 on 2 or more occasions, OR  
d. Thrombocytopenia <100,000/cmm in the absence of offending drugs |
| Immunological disorder | a. Anti-DNA : antibody to native DNA in abnormal titre OR  
b. Anti-Sm: presence of antibody to Sm nuclear antigen, OR  
c. Positive findings of aPL antibodies based on 1) -serum level of Ig G or Igm aCL or 2) a positive test result for lupus anticoagulant, using a standard method, or 3) a false-positive test for syphilis for at least 6 months and confirmed by TPI or FTA- abs test |
| Positive ANA | An abnormal titre of ANA by immuno- fluorescence or an equivalent assay at any point in time in the absence of drug |
will often describe a feeling of tiredness and aches for several months before the diagnosis of SLE. Many times they begin to do poorly in school, lose interests in their friends and become withdrawn. In several cases, SLE was recognized only because the primary care physician completed a SLE work up prior to the start of psychotherapy. Some SLE children have a long history of being evaluated always “without explanation” — for anemia, easy bruising, or fatigue, fever and weight loss. There is a wide variety of other “unexplained” findings. At the same time, all of these findings may be caused by many different diseases. So, how to proceed? If physicians remember that lupus is one of the possibilities in children who becomes ill, they should include Anti-nuclear antibodies (ANA) in the laboratory test. But ANA should be done by Immuno-fluorescence Assay method using Hep2 cell line. It has been shown that sensitivity of this method is much higher than that of ELISA method.

A positive ANA test should prompt further consideration of SLE, and more complete testing is needed to seek evidences of SLE (Figure 1). This is where it becomes important to consider the presence or absence of ACR criteria for a “definite diagnosis of SLE.”

Auto antibodies are typically present years before the diagnosis of SLE. Furthermore, the appearance of autoantibodies in patients with SLE tends to follow a predictable course, with a progressive accumulation

### Table: Steroid sparing agents currently in use

<table>
<thead>
<tr>
<th>General</th>
<th>Steroid sparing agents currently in use</th>
<th>Potential treatments</th>
<th>Auto-complement therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sunscreen</td>
<td>IV glucocorticoids</td>
<td>B-cell directed therapies</td>
<td>Anti-complement therapies</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>Cyclophosphamide</td>
<td>humanized anti-CD20</td>
<td>anti-C5b monoclonal antibody</td>
</tr>
<tr>
<td>Oral glucocorticoids</td>
<td>Mycophenolate mofetil</td>
<td>anti-CD22</td>
<td>Anti-cytokine therapy</td>
</tr>
<tr>
<td>NSAID’s</td>
<td>Rituximab</td>
<td>Abetimus sodium</td>
<td>IFN-alpha</td>
</tr>
<tr>
<td>Vitamins</td>
<td>Azathioprine</td>
<td>Nucleoside analogs</td>
<td>anti-TNF therapy</td>
</tr>
<tr>
<td></td>
<td>Cyclosporine</td>
<td>Fludarabine</td>
<td>anti-Blys/APRIL Therapies</td>
</tr>
<tr>
<td>May Need:</td>
<td></td>
<td>Cladribine</td>
<td>Interleukins (anti-IL 10, anti-IL6)</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td></td>
<td>T-cell directed therapies</td>
<td>Peptide manipulation</td>
</tr>
<tr>
<td>Angiotenin-III receptor blocker</td>
<td></td>
<td>CD40 ligand</td>
<td>Autologous stem cell transplantation</td>
</tr>
<tr>
<td>Aspirin</td>
<td></td>
<td>CITA4-lg</td>
<td>High dose immunoablative</td>
</tr>
<tr>
<td>Anti-coagulation</td>
<td></td>
<td></td>
<td>therapy</td>
</tr>
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</table>

**Fig-1:** Suggested Diagnostic Protocol for Investigation of Suspected SLE

**Fig-2:** Current and Future Treatments for Lupus
of specific antibodies before the onset of SLE, while patients are still asymptomatic\textsuperscript{29}.

**Investigations in a suspected case of SLE**

Any antibody to nuclear components is an ANA\textsuperscript{27}. Most patients with positive ANAs do not have SLE, but most people with SLE have positive ANAs. Today’s ANA test is very sensitive (it detects almost every case of SLE), but it is not very specific\textsuperscript{24}. According to a guideline from College of American Pathologists (CAP), no further laboratory tests are necessary for diagnosing SLE in patients who meet ACR diagnostic criteria and also have positive ANA\textsuperscript{31}.

Testing for antibody to double-stranded DNA antigen (anti-ds DNA) and antibody to sm nuclear antigen (anti-sm) may be helpful in patients who have a positive ANA test but do not meet full criteria for the diagnosis of SLE\textsuperscript{32}. Anti-ds DNA antibodies are associated with systemic lupus and nephritis, but not subacute cutaneous lupus or discoid lupus. Antibodies to ENAs (Anti-RO/La antibodies) are very useful when anti-ds DNA or anti-sm are absent\textsuperscript{27}.

**Indicators of Inflammation**

Most acute phase indices of inflammation are increased in children in proportion to the activity of the systemic disease\textsuperscript{6}. These include an increased erythrocyte sedimentation rate (ESR), polyclonal hyper gammaglobulinaemia and increased level of \( \mu \)-2-globulins\textsuperscript{27}. C-reactive protein (CRP), an important acute phase protein that is elevated in most inflammatory conditions, is often normal. However, it is increased in patients with SLE and systemic infection and in those with serositis or arthritis\textsuperscript{33,34}.

**Haematologic abnormalities**

Aneamia

Mild or moderate anaemia occurs in approximately one half of children with SLE and is usually typical of chronic disease. In other patients, it reflects auto-immune haemolysis caused by IgG complement fixing antibodies to erythrocytes that are detected by an antiglobulin test (coomb’s test)\textsuperscript{6}.

Leukocytes and platelets

Although leukocytosis may occur, lymphocytopenia is common in patients with active disease and neutropenia often along with thrombocytopenia is found in upto 50\% of these patients\textsuperscript{35,36}. Patients with immune thrombocytopenic purpura and haemolytic anemia may progress to SLE.

**Complement**

Estimation of the serum complement level is one of the most important laboratory measures of active SLE\textsuperscript{27}. Specific components of the complement sequences (e.g. C\textsubscript{3}, C\textsubscript{4}) may be assayed, or the total haemolytic complement (CH\textsubscript{50}) may be titrated. The C\textsubscript{3} concentration is depressed less often than CH\textsubscript{50} or C\textsubscript{4}. A low C\textsubscript{4} concentration is a consistent and reliable indicator of active nephritis. Persistently low C\textsubscript{3} is associated with chronic renal disease.

For monitoring, a precise, quantitative assay is required. A combination of anti-ds DNA titre, C\textsubscript{3}, C\textsubscript{4}, CRP, and ESR provides the most useful clinical information.

**Urine analysis**

Most childhood lupus nephritis have abnormalities of the urinary sediment. Proteinuria is probably the most common abnormality, but haematuria and red blood cell casts are more important hall marks of active glomerulonephritis\textsuperscript{18}.

**Antiphospholipid antibodies**

Anticardiolipin antibodies (ACAs) of all iso-types are found in 16-60\% patients with SLE\textsuperscript{27}. IgG ACAs are a risk factor for thrombosis and the antiphospholipid syndrome.

**Management of SLE**

SLE is a chronic disease, characterized by remissions and relapses and associated with considerable morbidity and mortality. Treatment of SLE itself is associated with morbidity, the effects of which may be short term or permanent. So, counseling the child and the family is the first and foremost important aspect of management. In order to obtain optimal outcome from drug therapy, patient/family education plays a vital role and must be paid due attention.

**General measures**

Incorporation of the child and parents into the planning of the overall treatment program is best accomplished by informing them about the character, treatment and outcome of the disease\textsuperscript{6}. As with other illness in childhood, rigorous restrictions on general activity are usually unnecessary and undesirable. Except during periods of severe active disease, school attendance should be encouraged.

Although no foods are directly helpful or detrimental to the patient with SLE, a well-balanced diet with appropriate calorie intake is important. Avoidance of
“junc food” and food high in sodium helps to minimize excessive weight gain.

Sunlight is frequently responsible for exacerbations of lupus activity. Photosensitive patients must be advised to wear protective clothings with long sleeves. Use of suncreams with sun protection factor (spf) of more than 15 is necessary. Umbrella should be used for protection from sunlight if going outside during daytime is essential.

Infections are common in SLE and they are very important cause of hospitalization and death. All types of infections have been reported: bacterial, viral and opportunistic. Therefore patients must get any unexplained fever evaluated promptly. This is particularly important when lupus child is on long-term steroid/cytotoxic therapy. In order to prevent infections, it is important to optimize treatment by using the minimal effective dose of the drug to control the disease.

Specific Drug therapy
Specific treatment should be individualized and based on the extent and severity of the disease.

Non-steroidal Anti-inflammatory Drugs (NSAIDS)
Myalgia, arthralgia or arthritis response well to anti-inflammatory doses of NSAIDS. Low dose aspirin in indicated if the child has high titers of antiphospholipid antibodies.

Hydroxychloroquine
The role of hydroxychloroquine in the treatment of SLE is given much more importance than it was used to give in the past since the publication of the studies by the Canadian Hydroxychloroquine study group. These studies reported that hydroxychloroquine reduces the frequency and severity of flares in SLE patients. It also may have a role in reversing glucocorticoid-induced changes in plasma lipids.

Corticosteroid therapy
Corticosteroids remain the back bone of treatment for SLE and are generally the first agent used. Almost all children with SLE need oral prednisolone or intravenous methyl prednisolone at somestage of the disease. Prednisolone should be given in a dose sufficient to achieve disease control, often 1 to 2 mg/kg/day. At the initiation of therapy, oral steroid should be prescribed in a divided doses to maximize the anti-inflammatory and immuno-suppressive effects. Low-dose prednisolone (<0.5mg/kg/day) is usually sufficient to control fever, dermatitis, arthritis and serositis. High dose prednisolone (1 to 2 mg/kg/day) is needed for treatment of severe type of lupus nephritis, CNS disease, acute haemolytic anaemia and parenchymal pulmonary disease. In addition I/V methyprednisolone (upto 30 mg/kg/day) in consecutive days may also be needed to manage the problems, particularly if a rapid response is needed.

Immunosuppressive Drugs
Immunosuppressive drugs like azothiarpine, cyclophosphamide (CYC), cyclosporine and mycophenolate mofetils are often required to control SLE and to improve the quality of life. A meta analysis done in adults with SLE cases found the superiority of immuno-suppressive drugs and prednisolone over prednisolone alone in lupus nephritis. The choice immunosuppressive agents should be made depending to a large extent on the severity of the disease and specific organ involvement. Figure 2 shows current and future treatments of SLE.

Rituximab
The role of B-cells in the pathogenesis of auto-immune disease is becoming increasingly clear. Rituximab (RTX) is a chimeric mouse/human monoclonal antibody. Treatment with RTX eliminates CD 20 positive B-cells both directly and by inducing apoptosis without inciting on inflammatory response in neighbouring cells.

It is demonstrated that children with SLE respond well to the combination of RTX and CYC. Twelve patients aged 11-28 years (median 14 years) with active childhood onset SLE was treated with combination of RTX and CYC. SLEDAI scores improved significantly. Therapy was well tolerated and there was no serous adverse events.

Belimumab
Recently FDA approved Belimumab (Benlysta), a new lupus drug which is designed to interfere with a protein critical to B cell activity, thus suppressing its auto-immunity. In approving the drug, the FDA analyzed two trials involving 1,684 patients with lupus, some of whom were given the medication along with their current therapy, and others were given a placebo infusion. The treated patients recorded fewer episodes of disease activity than those on placebo, and some were able to lower the dose of steroids they needed to control their disease. These patients however, showed slightly higher rates of infections and mortality than the group that didn’t receive Benlysta.
Autologous stem cell transplantation
In case of severe SLE, autologous stem cell transplantation after myeloablation with high dose cyclophosphamide had been performed with good short term effect. But it was associated with significant morbidity and mortality. Significant relapse rate was also reported in paediatric SLE.41

Prognosis
Survival of patients with systemic lupus erythematosus has increased remarkably in the last few decades, from 50% at 2 years in 1950 to more than 90% at 10 years in the 1990 and onwards.45 While lupus can be a severe and life threatening disease, many children with lupus will do very well. The prognosis of lupus in childhood depends on the severity of the internal organ involvement. However, lupus is unpredictable and no one will be able to predict with certainty the long-term outcome for a specific child. The long term prognosis of these patients remains poor mainly due to complications of the disease and/or its treatment.

Recurrent infections contribute significantly to the morbidity and mortality of children with SLE. Infections are important cause of hospitalization and death in SLE. All types of infections are reported: bacterial, viral and opportunistic.38 Osteonecrosis occurs in 10% to 12% of patients and probably reflects the effects of disease and prolonged use of corticosteroids.46 Although it is not associated with mortality, avascular necrosis contributes to significant morbidity and quality of life.

It has been clearly demonstrated that atherosclerosis is accelerated in patients with SLE.47 Atherosclerosis usually become clinically apparent only after a decade or more of active disease. It is true that medical science has not yet developed a method for curing lupus. And some patients do die from the disease. However children with non-organ threatening aspects of lupus can look forward to a normal live-span if they:

- follow the instructions of their physician
- take their medications as prescribed, and
- know when to seek help for unexpected side effects of a medication or a new manifestations of their lupus.

So, every effort must be made to assure compliance with medications and follow up, since compliance is the single best predictor of disease outcome in children with SLE.

References


