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Systemic Lupus Erythematosus

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1. WHAT IS SYSTEMIC LUPUS ERYTHEMATOSUS

1.1 What is it?

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can affect various organs of the body, especially the skin, joints, blood, kidneys and central nervous system. "Chronic" means that it can last for a long time. "Autoimmune" means that there is a disorder of the immune system, which, instead of protecting the body from bacteria and viruses, attacks the patient's own tissues.
The name "systemic lupus erythematosus" dates back to the early 20th century. "Systemic" means that it affects many organs of the body. The word "lupus" is derived from the Latin word for "wolf" and it refers to the characteristic butterfly-like rash on the face, which is similar to the white markings on a wolf's face. "Erythematosus" in Greek means "red" and it refers to the redness of the skin rash.

1.2 How common is it?

SLE is recognized worldwide. The disease appears to be more common in people of African American, Hispanic, Asian and Native American origin. In Europe about 1:2,500 persons are diagnosed with SLE and about 15% of all lupus patients are diagnosed prior to the age of 18 years. Onset of SLE is rare before the age of 5 and uncommon before adolescence. When SLE appears before the age of 18, physicians use different names: paediatric SLE, juvenile SLE and childhood-onset SLE. Females of child-bearing years (15 to 45) are most often affected and, in that particular age group, the ratio of affected females to males is 9 to 1. Before puberty, the proportion of affected males is higher and

about 1 of every 5 children with SLE is male.

1.3 What are the causes of the disease?

SLE is not contagious; it is an autoimmune disease, where the immune system loses its ability to distinguish between a foreign substance and an individual's own tissues and cells. The immune system makes a mistake and produces, amongst other substances, autoantibodies that identify the person's own normal cells as foreign and attack them. The result is an autoimmune reaction, which causes inflammation of specific organs (joints, kidneys, skin, etc). Inflamed means that affected body parts become hot, red, swollen and sometimes tender. If the signs of inflammation are long-lasting, as they may be in SLE, then damage to the tissues may occur and normal function is impaired. This is why treatment of SLE is aimed at reducing the inflammation.
Multiple inherited risk factors combined with random environmental factors are considered responsible for this abnormal immune response. It is known that SLE can be triggered by various factors, including hormonal imbalance in puberty, stress, and environmental factors such as sun exposure, viral infections and medications (e.g. isoniazid, hydralazine, procainamide, anti-seizure medications).

1.4 Is it inherited?

SLE can run in families. Children inherit some as yet unknown genetic factors from their parents that may predispose them to develop SLE. Even if they are not necessarily pre-destined to develop SLE, they may be more likely to get the disease. For example, an identical twin has no more than a 50% risk of getting SLE if the other twin is diagnosed with SLE. There is no genetic testing or a prenatal diagnosis available for SLE.

1.5 Can it be prevented?

SLE cannot be prevented; however, the affected child should avoid contact with certain situations that may trigger the onset of the disease or cause the disease to flare (e.g. sun exposure without using sunscreens, some viral infections, stress, hormones and certain medications).

1.6 Is it infectious?

SLE is not infectious. This means that it cannot be passed from person to person.

1.7 What are the main symptoms?

The disease may begin slowly with new symptoms appearing over a period of several weeks, months or even years. Non-specific complaints of fatigue and malaise are the most common initial symptoms of SLE in children. Many children with SLE have intermittent or sustained fever, loss of weight and appetite.

With time, many children develop specific symptoms that are caused by involvement of one or several organs of the body. The skin and mucosal involvement are very common and may include a variety of different skin rashes, photosensitivity (where exposure to sunlight triggers a rash) or ulcers inside the nose or mouth. The typical 'butterfly' rash across the nose and cheeks occurs in one-third to one half of affected children. Increased hair loss (alopecia) may sometimes be noticed. The hands turn red, white and blue when exposed to the cold (Raynaud’s phenomenon). The symptoms can also include swollen and stiff joints, muscle pain, anaemia, easy bruising, headaches, seizures and chest pain. Kidney involvement is present to some degree in most children with SLE and it is a major determinant of the long-term outcome of this disease.

The most common symptoms of major kidney involvement are high blood pressure, protein and blood in urine and swelling, particularly in the feet, legs and eyelids.

1.8 Is the disease the same in every child?

Symptoms of SLE vary widely between individual cases so that each child's profile or list of symptoms is different. All of the symptoms described above can occur either at the beginning of SLE or at any time during the course of the disease with different severity. Taking medications that were prescribed by your lupus doctor will help control SLE symptoms.

1.9 Is the disease in children different from the disease in adults?

SLE in children and adolescents has manifestations as SLE in adults. However, in children, SLE has a more severe course in that children more often show several features of inflammation due to SLE at any given time. Children also have kidney and brain disease with SLE more often than adults.

2. DIAGNOSIS AND THERAPY

2.1 How is it diagnosed?

The diagnosis of SLE is based on a combination of symptoms (such as pain), signs (such as fever), blood and urine tests and when other illnesses have been ruled out. Not all symptoms and signs are present at any given time and this makes it hard to diagnose SLE quickly. To help distinguish SLE from other diseases, physicians of the American College of Rheumatology have established a list of 11 criteria that, when combined, point to SLE.

These criteria represent some of the more common symptoms/abnormalities observed in patients with SLE. To make a formal diagnosis of SLE, the patient must have had at least 4 of these 11 characteristics at any time since the beginning of the disease. However, skilled doctors can make a diagnosis of SLE even if less than 4 criteria are present. The criteria are:

The ‘butterfly’ rash

This is a red rash occurring across the cheeks and over the bridge of the nose.

Photosensitivity

Photosensitivity is an excessive skin reaction to sunlight. Skin covered by clothing is usually not involved.

Discoid-lupus

This is a scaly, raised, coin-shaped rash that appears on the face, scalp, ears, chest or arms. When these lesions heal, they can leave a scar. Discoid lesions are more common in black children than in other racial

groups.

Mucosal ulcers

These are small sores that occur in the mouth or nose. They are usually painless, but nose ulcers may cause nosebleeds.

Arthritis

Arthritis affects the majority of children with SLE. It causes pain and swelling in the joints of the hands, wrists, elbows, knees or other joints in the arms and legs. The pain may be migratory, meaning that it goes from one joint to another, and it may occur in the same joint on both sides of the body. Arthritis in SLE usually does not result in permanent changes (deformities).

Pleuritis

Pleuritis is the inflammation of the pleura, the lining of the lungs, whereas pericarditis is the inflammation of the pericardium, the lining of the heart. Inflammation of these delicate tissues may cause fluid collection around the heart or lungs. Pleuritis causes a particular type of chest pain that gets worse when breathing.

Kidney involvement

Kidney involvement is present in nearly all children with SLE and ranges from very mild to very serious. At the beginning, it is usually asymptomatic and can be detected only by urine analysis and blood tests of kidney function. Children with significant kidney damage may have protein and/or blood in their urine and may experience swelling, particularly in the feet and legs.

Central nervous system

Involvement of the central nervous system includes headache, seizures and neuropsychiatric manifestations such as difficulty concentrating and remembering, mood changes, depression and psychosis (a serious mental condition where thinking and behaviour are disturbed).

Disorders of the blood cells

These disorders are caused by autoantibodies that attack the blood cells. The process of destruction of red blood cells (which carry oxygen from the lungs to other parts of the body) is called haemolysis and may

cause haemolytic anaemia. This destruction may be slow and relatively mild or may be very quick and cause an emergency.
A decrease in the number of white blood cells is called leukopoenia and is usually not dangerous in SLE.
A decrease in platelet counts is called thrombocytopenia. Children with decreased platelet counts may have easy bruising of the skin and bleeding in various parts of the body, such as the digestive tract, urinary tract, uterus or brain.

Immunologic disorders

These disorders refer to autoantibodies found in the blood which point to SLE:
a) Presence of antiphospholipid antibodies (appendix 1);
b) Anti-native DNA antibodies (autoantibodies directed against the genetic material in the cells). They are found primarily in SLE. This test is often repeated because the amount of anti-native DNA antibodies seems to increase when SLE is active and the test can help the physician measure the degree of disease activity.
c) Anti-Sm antibodies: the name refers to the first patient (Ms. Smith) in whose blood they were found. These autoantibodies are found almost exclusively in SLE and often help to confirm the diagnosis.

Antinuclear antibodies (ANA)

These are autoantibodies directed against cell nuclei. They are found in the blood of almost every patient with SLE. However, a positive ANA test on its own is not proof of SLE, since the test may also be positive in other diseases and can even be weakly positive in about 5-15 percent of healthy children.

2.2 What is the importance of tests?

Laboratory tests can help diagnose SLE and decide which internal organs, if any, are involved. Regular blood and urine tests are important for monitoring the activity and severity of the disease and to determine how well the medications are tolerated. There are several laboratory tests that can help to diagnose SLE and to decide which medications to prescribe, and to assess whether the currently prescribed medications are working well to control SLE inflammation.

Routine clinical tests: they indicate the presence of an active systemic disease with multiple organ involvement. Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP) are both elevated in inflammation. CRP can be normal in SLE, while ESR is elevated. Increased CRP can indicate an additional infectious complication. A full blood count may reveal anaemia and low platelet and white cell counts. Serum protein electrophoresis may reveal increased gammaglobulins (increased inflammation and autoantibody production). Albumin: low levels may indicate kidney involvement. Routine biochemistry tests may reveal kidney involvement (increases in serum blood urea nitrogen and creatinine, changes in electrolyte concentrations), abnormalities of liver function tests and increased muscle enzymes if muscle involvement is present. Liver function and muscle enzymes tests: if muscle or liver involvement is present, then levels of these enzymes will be increased. Urine tests are very important at the time of diagnosis of SLE and during the follow-up to determine kidney involvement. Urine analysis can show various signs of inflammation in the kidney such as red blood cells or the presence of an excessive amount of protein. Sometimes, children with SLE may be asked to collect urine for 24 hours. In this way, early involvement of the kidneys can be discovered. Complement levels – complement proteins are part of the inborn immune system. Certain complement proteins (C3 and C4) may be consumed in immune reactions and low levels of these proteins signal the presence of active disease, especially kidney disease. Many other tests are now available to look at the effects of SLE on different parts of the body. A biopsy (the removal of a small piece of tissue) of a kidney is often performed when the kidney is affected. A kidney biopsy provides valuable information on the type, degree and age of SLE lesions and is very helpful in choosing the right treatment. A skin biopsy of a lesion may help to make a diagnosis of skin vasculitis, discoid lupus or helps determine the nature of various skin rashes of a person with SLE. Other tests include chest X-rays (for heart and lungs), echocardiography, electrocardiogram (ECG) for the heart, pulmonary functions for the lungs, electroencephalography (EEG), magnetic resonance (MR) or other scans of the brain and possibly various tissue biopsies.

2.3 Can it be treated/cured?

At present, there is no specific medication to cure SLE. SLE treatment

will help control signs and symptoms of SLE and help prevent complications of the disease, including permanent damage to the organs and tissues. When SLE is first diagnosed, it is usually very active. At this stage, it may require high doses of medications to control the disease and prevent organ damage. In many children, the treatment brings SLE flares under control and the disease may go into remission, when little or no treatment is needed.

2.4 What are the treatments?

There are no approved medications for the treatment of SLE in children. The majority of symptoms of SLE are due to inflammation and so the treatment aims at reducing that inflammation. Five groups of medications are almost universally used to treat children with SLE:

Non-steroidal anti-inflammatory drugs (NSAIDs)

NSAIDs such as ibuprofen or naproxen are used to control the pain of arthritis. They are usually prescribed for a short time only, with instructions to decrease the dose as the arthritis improves. There are many different drugs in this family of medications, including aspirin. Today, aspirin is rarely used for its anti-inflammatory effect; however, it is widely used in children with elevated antiphospholipid antibodies to prevent unwanted blood clotting.

Antimalarial drugs

Antimalarials such as hydroxychloroquine are very useful in treating and controlling sun sensitive skin rashes such as the discoid or the sub-acute types of SLE rashes. It may take months before these drugs have a beneficial effect. When administered early, these drugs also seem to reduce the disease flares, improve control of kidney disease and protect the cardiovascular and other organ systems from damage. There is no known relationship between SLE and malaria. Rather, hydroxychloroquine helps regulate immune system abnormalities with SLE, which are also important in persons with malaria.

Corticosteroids

Corticosteroids, such as prednisone or prednisolone, are used to reduce inflammation and suppress activity of the immune system. They are the main therapy for SLE. In children with mild disease, corticosteroids

associated with antimalarial drugs may be the only therapy needed. When the disease is more severe, with involvement of kidneys or other internal organs, they are used in combination with immunosuppressive drugs (see below). Initial disease control usually cannot be achieved without daily corticosteroid administration for a period of several weeks or months and most children require these drugs for many years. The initial dose of corticosteroids and the frequency of administration depend on the severity of the disease and the organ systems affected. High-dose oral or intravenous corticosteroids are usually employed for treatment of severe haemolytic anaemia, central nervous system disease and the more severe types of kidney involvement. Children experience a marked sense of well-being and increased energy after a few days on corticosteroids. After the initial manifestations of the disease are controlled, corticosteroids are reduced to the lowest possible level that will maintain the well-being of the child. Tapering of corticosteroids dose must be gradual, with frequent monitoring to make certain that clinical and laboratory measures of disease activity are suppressed.

At times, adolescents may be tempted to stop taking corticosteroids or to reduce or increase their dose; perhaps they are fed up with the side effects or perhaps they are feeling better or worse. It is important that children and their parents understand how corticosteroids work and why stopping or changing the medication without medical supervision is dangerous. Certain corticosteroids (cortisone) are normally produced by the body. When treatment is started, the body responds by stopping its own production of cortisone and the adrenal glands that produce it get sluggish and lazy.

If corticosteroids are used for a longer period of time and then suddenly stopped, the body may not be able to start producing enough cortisone for some time. The result could be a life-threatening lack of cortisone (adrenal insufficiency). Additionally, reduction of the dose of corticosteroid that is too rapid may cause the disease to flare.

Non-biological disease modifying drugs (DMARDs)

These medications include azathioprine, methotrexate, mycophenolate mofetil and cyclophosphamide. They act in a different manner from corticosteroid drugs and suppress inflammation. These medications are used when corticosteroids alone are unable to control SLE and help doctors to decrease the daily doses of corticosteroids in order to reduce

side effects while controlling SLE features.
Mycophenolate mofetil and azathioprine are given as tablets and cyclophosphamide can be given as tablets or intravenous pulses. Cyclophosphamide therapy is used in children with serious central nervous system involvement. Methotrexate is administered as tablets or injection under the skin.

Biologic DMARDs

Biologic DMARDs (often simply called biologics) include agents that block the production of autoantibodies or the effect of a specific molecule. One of these drugs is rituximab, which is primarily used when the standard treatment fails to control the disease. Belimumab is a biologic drug directed against antibody-producing types of blood B cells and it was approved for treatment of adult SLE patients. Generally, the use of biologics in children and adolescents with SLE is still experimental.
Research in the field of autoimmune diseases and particularly SLE is very intensive. The future goal is to determine the specific mechanisms of inflammation and autoimmunity, in order to better target therapies, without suppressing the entire immune system. Currently, there are many ongoing clinical studies involving SLE. They include testing new therapies and research to expand the understanding of different aspects of childhood SLE. This active ongoing research makes the future increasingly brighter for children with SLE.

2.5 What are the side effects of drug therapy?

The medications used for treating SLE are quite useful in treating its signs and symptoms. Like all medications, they can result in various side effects (for a detailed description of side effects, please see the section on Drug Therapy).

NSAIDs may cause side effects such as stomach discomfort (they should be taken after a meal), easy bruising and, rarely, changes in kidney or liver functions. Antimalarial drugs may cause changes in the retina of the eye and therefore patients must have regular checks by an eye specialist (ophthalmologist).

Corticosteroids can cause a wide variety of side effects in both the short

and the long term. The risks of these side effects are increased when high doses of corticosteroids are required and when they are used for an extended period. Their main side effects include: Changes in physical appearance (e.g. weight gain, puffy cheeks, excessive growth of body hair, skin changes with purple striae, acne and easy bruising). Weight gain can be controlled by a low calorie diet and by exercise. Increased risk of infections, particularly tuberculosis and chickenpox. A child who is taking corticosteroids and has been exposed to chickenpox should see a doctor as soon as possible. Immediate protection against chickenpox may be accomplished by administering preformed antibodies (passive immunization). Stomach problems such as dyspepsia (indigestion) or heartburn. This problem may require anti-ulcer medication. Growth suppression Less frequent side effects include: High blood pressure Weakness of the muscles (children may have difficulty in climbing stairs or getting up from a chair). Disturbances in glucose metabolism, particularly if there is genetic predisposition to diabetes. Changes in mood including depression and mood swings. Eye problems such as cloudiness of the lens of the eyes (cataract) and glaucoma. Thinning of bone (osteoporosis). This side effect may be decreased by exercise, by eating foods rich in calcium and by taking extra calcium and vitamin D. These preventive measures should be started as soon as a high corticosteroid dose is begun. It is important to note that most of the corticosteroid side effects are reversible and will disappear when the dose is decreased or stopped. DMARDs (biologic or non-biologic) also have side effects that can become serious.

2.6 How long should treatment last?

The treatment should last as long as the disease persists. It is generally agreed that most children with SLE are withdrawn completely from corticosteroid drugs only with great difficulty. Even a long-term maintenance therapy with very low dose of corticosteroid can minimize the tendency toward flares and keep the disease under control. For many patients, this may be the best solution to prevent the risk of flare. Such low doses of corticosteroids have very few and generally mild side effects.

2.7 What about unconventional/complementary therapies?

There are many complementary and alternative therapies available and this can be confusing for patients and their families. Think carefully about the risks and benefits of trying these therapies as there is little proven benefit and they can be costly both in terms of time, burden to the child and money. If you want to consider complementary and alternative therapies, please discuss these options with your paediatric rheumatologist. Some therapies can interact with conventional medications. Most doctors will not be opposed, provided you follow medical advice. It is very important not to stop taking your prescribed medications. When medications are needed to keep the disease under control, it can be very dangerous to stop taking them if the disease is still active. Please discuss medication concerns with your child’s doctor.

2.8 What kind of periodic check-ups are necessary?

Frequent visits are important because many conditions that may occur in SLE can be prevented or treated more easily if detected early. Generally, children with SLE need to be seen at least every 3 months by a rheumatologist. As needed, consultation with other specialists is sought: paediatric dermatologists (skin care), paediatric haematologists (blood diseases) or paediatric nephrologists (kidney diseases). Social workers, psychologists, nutritionists and other health care professionals are also involved in the care of children with SLE.
Children with SLE should have regular blood pressure checks, urinalyses, complete blood counts, blood sugar analyses, coagulation tests and checks on complement and anti-native DNA antibodies levels. Periodic blood tests are also mandatory throughout the course of therapy with immunosuppressive agents to make certain that levels of blood cells produced by the bone marrow do not become too low.

2.9 How long will the disease last?

As mentioned above, there is no cure for SLE. Signs and symptoms of SLE can be minimal or even absent if medications are taken regularly and as prescribed by the paediatric rheumatologist. Among others factors, failure to take medications regularly, infections, stress and sunlight can lead to worsening of SLE; this worsening is also known as a "lupus flare". It is often very difficult to predict what the disease course

will be.

2.10 What is the long-term evolution (prognosis) of the disease?

The outcome of SLE improves dramatically with the early and prolonged disease control as can be achieved with the use of hydroxychloroquine, corticosteroids and DMARDs. Many patients with childhood onset of SLE will do very well. Nonetheless, the disease can be severe and life-threatening and may remain active throughout adolescence and into adulthood.

The prognosis of SLE in childhood depends on the severity of the internal organ involvement. Children with significant kidney or central nervous system disease require aggressive treatment. In contrast, mild rash and arthritis may be easily controlled. The prognosis for an individual child, however, is relatively unpredictable.

2.11 Is it possible to recover completely?

The disease, if diagnosed early and treated appropriately at an early stage, most commonly settles and can go into remission (absence of all signs and symptoms of SLE). However, as already mentioned, SLE is an unpredictable chronic disease and children diagnosed with SLE normally remain under medical care with continuing medication. Often, an adult specialist must follow the SLE when the patient reaches adulthood.

3. EVERYDAY LIFE

3.1 How might the disease affect the child and the family's daily life?

Once children with SLE are treated, they can lead a quite normal lifestyle. One exception is exposure to excessive sunlight/UV-light in discos, which may trigger or make SLE worse. A child with SLE should not go to the beach all day or sit out in the sun by the pool. Regular sunscreen with SPF 40 or higher is mandatory. It is important that children by the age of 10 start assuming a progressively greater role in taking their medication and making choices about personal care. Children and their parents should be aware of the symptoms of SLE in

order to identify a possible flare. Certain symptoms such as chronic fatigue and the lack of drive may persist for several months after a flare is over. Regular exercise is important to maintain a healthy weight, maintain good bone health and stay conditioned.

3.2 What about school?

Children with SLE can and should attend school except during periods of severe active disease. If there is no central nervous system involvement, SLE in general does not affect the ability of the child to learn and think. With central nervous system involvement, problems such as difficulty concentrating and remembering, headaches and moods changes may occur. In these cases, education plans need to be discussed. Overall, the child should be encouraged to participate in compatible extracurricular activities as much as the disease permits. However, teachers should be made aware of the child's diagnosis with SLE so that changes can be made during times when there are SLE-related problems, including joint and other body pains that may affect learning.

3.3 What about sports?

Restraints on general activity are usually unnecessary and undesirable. Regular exercise is to be encouraged in children during disease remission. Walking, swimming, cycling and other aerobic or outdoor activities are recommended. Appropriate sun protection clothing, sunscreens with high spectrum protection and avoiding sun exposure during peak hours is advised for outdoor activities. Avoid exercising to the point of exhaustion. During a disease flare, exercise should be restrained.

3.4 What about diet?

There is no special diet that can cure SLE. Children with SLE should observe a healthy, balanced diet. If they take corticosteroids, they should be eating foods low in salt to help prevent high blood pressure and low in sugar to help prevent diabetes and weight gain. Additionally, they should have calcium and vitamin D supplements to help prevent osteoporosis. No other vitamin supplement is scientifically proven to be

helpful in SLE.

3.5 Can climate influence the course of the disease?

It is well known that exposure to sunlight may cause the development of new skin lesions and lead to flares of disease activity in SLE. To prevent this problem, use of highly protective topical sunscreens is recommended for all the exposed parts of the body whenever the child is outside. Remember to apply the sunscreen at least 30 minutes before going out to allow it to penetrate the skin and dry. During a sunny day, sunscreen must be applied every 3 hours. Some sunscreens are water resistant, but reapplication after bathing or swimming is advisable. It is also important to wear sun protective clothing such as wide-brimmed hats and long sleeves when out in the sun, even on cloudy days, as UV rays can penetrate clouds easily. Some children experience problems after they have been exposed to UV light from fluorescent lights, halogen lights or computer monitors. UV filter screens are useful for children who have problems when using a monitor.

3.6 Can the child be vaccinated?

The risk of infection is increased in a child with SLE; therefore prevention of infection by immunization is particularly important. If possible, the child should keep the regular schedule of immunizations. However, there are a few exceptions: children with severe, active disease should not receive any immunization and children on immunosuppressive therapy, high-dose corticosteroids and biologic agents should in general not receive any live virus vaccine (e.g. measles, mumps and rubella vaccine, oral poliovirus vaccine and varicella vaccine). Oral polio vaccine is also contraindicated in family members living in homes with a child on immunosuppressive therapy. Pneumococcal, meningococcal and annual influenza vaccines are recommended in children with SLE receiving high dose corticosteroids and/or immunosuppressive drugs. Vaccination with HPV of adolescent girls and boys with SLE is recommended.
Note that children with SLE may need vaccinations more often than their peers because the protection provided by the vaccinations seems last shorter with SLE.

3.7 What about sexual life, pregnancy and birth control?

Adolescents may enjoy a healthy sex life. However, sexually active adolescents treated with certain DMARDs or with active disease must use safe pregnancy prevention methods. Ideally, pregnancies should always be planned. Notably, some blood pressure medicines and DMARDs can harm the development of the foetus. Most women with SLE can have a safe pregnancy and a healthy baby. The ideal time for pregnancy would be when the disease, especially kidney involvement, has been well controlled for a prolonged time. Women with SLE may have trouble staying pregnant either because of the disease activity or the medication. SLE is also associated with a higher risk of miscarriage, premature delivery and a congenital abnormality in the baby known as neonatal lupus (appendix 2). Women with elevated antiphospholipid antibodies (appendix 1) are considered at high risk of problematic pregnancy.

Pregnancy itself can worsen symptoms or trigger a flare of SLE. Therefore, an obstetrician who is familiar with high-risk pregnancies and who works closely with the rheumatologist must monitor all pregnant women with SLE.

The safest forms of contraception in SLE patients are barrier methods (condoms or diaphragms) and spermicidal agents. Progesterone-only systemic contraceptives are also acceptable, as are some types of intrauterine devices (IUDs). Birth control pills containing oestrogen may increase the risk of flares in women with SLE, although there are new options that minimize this risk.

4. APPENDIX 1. Antiphospholipid antibodies

Antiphospholipid antibodies are autoantibodies made against a body’s own phospholipids (part of a cell's membrane) or proteins that bind to phospholipids. The three best known antiphospholipid antibodies are anticardiolipin antibodies, antibodies against β2 glycoprotein I and lupus anticoagulants. Antiphospholipid antibodies can be found in 50% of children with SLE, but they are also seen in some other autoimmune diseases, various infections, as well as in a small percentage of children without any known illness.

These antibodies increase clotting tendency in blood vessels and have been associated with a number of illnesses, including thrombosis of the

arteries and/or veins, abnormally low blood platelet counts (thrombocytopenia), migraine headaches, epilepsy and purplish mottled discolouration of the skin (livedo reticularis). A common site of clotting is the brain, which can lead to a stroke. Other common sites of clots include the leg veins and kidneys. Antiphospholipid syndrome is the name given to a disease when thrombosis has occurred along with a positive antiphospholipid antibody test.

Antiphospholipid antibodies are especially important in pregnant women, because they interfere with the function of the placenta. Blood clots that develop in the placental vessels can cause premature miscarriage (spontaneous abortion), poor foetal growth, preeclampsia (high blood pressure during pregnancy) and stillbirth. Some women with antiphospholipid antibodies may also have trouble getting pregnant.

Most children with positive antiphospholipid antibody tests have never had a thrombosis. Research into the best preventive treatment for such children is currently being carried out. At present, children with positive antiphospholipid antibodies and underlying autoimmune disease are often given low dose aspirin. Aspirin acts on platelets to reduce their stickiness, and hence reduces the ability of the blood to clot. Optimal management of adolescents with antiphospholipid antibodies also includes the avoidance of risk factors such as smoking and oral contraception.

When the diagnosis of antiphospholipid syndrome is established (in children after thrombosis), the primary treatment is to thin the blood. Thinning is usually achieved with a tablet called warfarin, an anticoagulant. The drug is taken daily and regular blood tests are required to ensure that the warfarin is thinning the blood to the required degree. There is also heparin injected under the skin and aspirin. The length of anticoagulation therapy is highly dependent on the severity of the disorder and the type of blood clotting.

Women with antiphospholipid antibodies who have recurrent miscarriages can also be treated, but not with warfarin as it has the potential to cause foetal abnormalities if given during pregnancy. Aspirin and heparin are used to treat pregnant women with antiphospholipid antibodies. During pregnancy, heparin needs to be given daily by injection under the skin. With the use of such medications and careful supervision by obstetricians, about 80% of women will have successful pregnancies.

5. APPENDIX 2. Neonatal lupus

Neonatal lupus is a rare disease of the foetus and neonate acquired from the transplacental passage of specific maternal autoantibodies. The specific autoantibodies associated with neonatal lupus are known as the anti-Ro and anti-La antibodies. These antibodies are present in about one third of patients with SLE, but many mothers with these antibodies do not deliver children with neonatal lupus. On the other hand, neonatal lupus could be seen in the offspring of mothers who do not have SLE.

Neonatal lupus is different from SLE. In most cases, the symptoms of neonatal lupus disappear spontaneously by 3 to 6 months of age, leaving no after-effects. The most common symptom is rash, which shows up a few days or weeks after birth, particularly after sun exposure. The rash of neonatal lupus is transient and usually resolves without scarring. The second most common symptom is an abnormal blood count, which is seldom serious and tends to resolve over several weeks with no treatment.

Very rarely, a special type of heart beat abnormality known as congenital heart block occurs. In congenital heart block, the baby has an abnormally slow pulse. This abnormality is permanent and can often be diagnosed between the 15th and 25th week of pregnancy using foetal cardiac ultrasound. In some cases, it is possible to treat the disease in the unborn baby. After birth, many children with congenital heart block require the insertion of a pacemaker. If a mother already has one child with congenital heart block, there is approximately 10 to 15% risk of having another child with the same problem.

Children with neonatal lupus grow and develop normally. They have only a small chance of developing SLE later in life.