LUPUS (SYSTEMATIC LUPUS ERYTHEMATOUS – SLE)

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Abstract: Systemic lupus erythematosus (SLE) is a multifaceted autoimmune disorder characterised by a chronic relapsing–remitting course, marked by the formation of autoantibodies and immune complex-mediated tissue damage across multiple organ systems. Genetic predisposition, hormonal influences, epigenetic alterations and environmental triggers collectively breach immune tolerance and initiate aberrant activation of both innate and adaptive immune pathways. Clinical manifestations range from mucocutaneous lesions, arthralgia and serositis to life-threatening complications such as lupus nephritis, central nervous system involvement and cardiovascular disease. Diagnosis remains challenging given the heterogeneity of presentation, and incorporates serologic markers (notably antinuclear antibodies) and validated classification criteria. Therapeutic strategies focus on induction and maintenance of remission, utilising corticosteroids, antimalarials, immunosuppressants and targeted biologic agents, with the aim of minimising organ damage and improving long-term outcomes. Continued advances in pathophysiology, biomarker development and personalised treatment approaches hold promise for altering the disease trajectory and enhancing quality of life for affected individuals.

Keywords: systemic lupus erythematosus, autoimmune disease, immune complex, antinuclear antibodies, biologic therapy.

Introduction

While we do not know all the causes of lupus, our understanding does take into ac-count many factors, including genetics, the environment, epigenetics, aspects of im-mune system regulation, and sex hormones. For lupus to develop, you must be born with genes that increase the risk of developing lupus. We will call these “lupus-related genes” in this chapter. Yet, being born with those genes does not mean you’ll develop lupus. Most people born with the genes never do. It’s the combination of factors that makes the difference: the more there are, the higher the chances of developing lupus (figure3.1). For example, if you are a male born with just one lupus-causing gene from one parent, have never smoked cigarettes, and have not had excessive sun ex-posure, you have a lower chance of developing lupus. However, if you are a female who has inherited multiple lupus genes from your father and mother, smoked ciga-rettes, had a stressful life, and suntanned regularly, you have a much higher chance of developing SLE.Genetic PredispositionGenes are a set of biological instructions for much of what makes us who we are as in-dividuals. Genes from our mothers and fathers decide if we are born with blue eyes or a big nose. Collections of genes are strung together in a twisted string (or strand) called DNA. DNA exists inside the nucleus (package found toward the middle of cells) and mi-tochondria of most cells in our body. Mitochondria are structures in cells that pro-duce energ y. They contain small amounts of DNA that are handed down from the mother’s side of the family. However, the vast majority of DNA is located in the nuclei (plural of nucleus). The DNA contains the genetic code that tells each cell what sub-stances to produce and how the cell should function.Lupus tends to be more common in some ethnic and racial groups. According to the Lupus Foundation of America, lupus occurs in 1 out of 700 Caucasian American women between 15 and 64years old, while it appears in 1 out of 250 to 350 African American women of the same age. Other countries have similar findings about racial differences. Certain ethnic groups,

such as those of African, Indigenous (such as Native American and Aboriginal Australians), and non-white Hispanic descent, have a higher number of people affected by lupus than others. The best explanation for this is the genes passed down from each generation

Lupus is a disease in which the immune system attacks the body's tissues and organs. Lupus causes widespread inflammation and tissue damage in the organs it affects. There are four types of lupus.

Types of lupus

All four lupus types involve damage to the body's organs. But they may have different causes, affect different organs, cause different symptoms, and have different treatments.

Systemic lupus erythematosus (SLE)

SLE is the most common and serious type of lupus. It is a long-term (chronic) disease that can range from mild to life-threatening. It can affect a person's:

Joints.

Skin.

Brain.

Lungs.

Kidneys.

Blood vessels.

There is no cure for this type of lupus, but medical treatments and lifestyle changes can help control it.

Cutaneous lupus

Cutaneous lupus is a long-term disease in which the immune system attacks the skin, causing a rash or swelling (lesions). This type of lupus usually appears where the skin is exposed to sun. There is no cure. However, there are medicines and lifestyle changes—like limiting sun exposure—that can help control it.

Drug-induced lupus

Drug-induced lupus is similar to SLE but the cause of the disease is an overreaction to certain medications. Symptoms usually occur 3 to 6 months after starting a medication. This condition disappears once the medicine is stopped.

Neonatal lupus

Neonatal lupus occurs when a developing baby is exposed to lupus in the womb, during pregnancy. It can cause skin, liver, or blood problems, which can be treated at—or even before—birth. This kind of lupus usually goes away by age 6 months.

However, it can cause serious health problems. The most serious problem—congenital heart block—can be fatal. Infants with the condition may need a pacemaker, which is a battery-operated device to prevent the heart from beating too slowly.

Main part

What causes lupus?

Experts don't know for certain what causes lupus. Studies have found that certain factors about your health or where you live may trigger lupus:

- ✓ Genetic factors: Having certain genetic mutations may make you more likely to have lupus.
- ✓ Hormones: Reactions to certain hormones in your body (especially estrogen) may make you more likely to develop lupus.
- ✓ Environmental factors: Aspects about where you live — including how much sunlight or how many toxins you're exposed to — might affect your lupus risk.

Your health history: Smoking, your stress level and having certain other health conditions (like other autoimmune diseases) might trigger lupus.

Risk factors

Anyone can develop lupus, but some groups of people have a higher risk:

Women, especially women between the ages of 15 and 44.

Black people.

Hispanic people.

Asian people.

Native Americans, Alaska Natives and First Nations people.

Pacific Islanders.

People with a biological parent who has lupus.

Fact:

On average, Black people with lupus die earlier ages—more than 10 years younger—than White people with lupus.

Symptoms:

Lupus is a long-term disease that can affect any part of the body.

People with lupus can have many different symptoms.

They may experience periods of increased symptoms (flares) or no symptoms at all (remission).

Young woman at desk with hand to bridge of nose and eyes closed.

Signs and symptoms

People with systemic lupus erythematosus (SLE)—often referred to just as lupus—can have many different symptoms.

Fatigue or extreme tiredness

The most common symptom of lupus is fatigue, which means feeling extremely tired.

Fatigue can affect a person's physical and mental health and quality of life. It can also make it hard for people with lupus to socially connect with others.

Other common symptoms

Other common symptoms include:

Pain or swelling in the muscles and joints.

Skin rashes (in particular, a butterfly-shaped face rash).

Fever.

Hair loss.

Frequent mouth sores.

Less common symptoms or related conditions

Other symptoms or conditions can include:

Sensitivity to the sun.

Heart, kidney, or lung problems.

Chest pain when deep breathing.

Fingers or toes turning blue or white or feeling numb.

Blood clotting problems (anemia).

Mental health conditions and memory changes.

Eye damage.

Flares and remission

Some adults with lupus have periods of increased symptoms, called flares.

These flares usually come and go in waves, sometimes years apart.

Some people with lupus may have flares more often throughout their life.

People with lupus might also have periods of remission when symptoms temporarily go away.

The effects of **Cigarette Smoking**

In 1980, a report described a 25-year-old lab technician who came into regular contact with a chemical called hydrazine. She developed an illness like SLE, with sun sensitiv-ity, fatigue, joint pain, and a red rash on the face. Tobacco contains hydrazine. Many studies have shown that smoking tobacco increases the risk of developing systemic lu-pus, cutaneous lupus, and other autoimmune diseases (such as rheumatoid arthritis). Tobacco also has many other dangerous chemicals, such as cadmium, polycyclic aro-matic hydrocarbons, and insecticides, which may increase the risk of developing SLE.

Management and Treatment

What is lupus treatment?

Your healthcare provider will suggest treatments for lupus that manage your symptoms. The goal is minimizing damage to your organs and how much lupus affects your day-to-day life. Most people with lupus need a combination of medications to help them prevent flare-ups and lessen their symptom severity during one. You might need:

✓ Hydroxychloroquine: Hydroxychloroquine is a disease-modifying antirheumatic drug (DMARD) that can relieve lupus symptoms and slow down how they progress (change or get worse).

✓ Nonsteroidal anti-inflammatory drugs (NSAIDs): Over-the-counter (OTC) NSAIDs relieve pain and reduce inflammation. Your provider will tell you which type of NSAID will work best for you, and how often you should take it. Don't take NSAIDs for more than 10 days in a row without talking to your provider.

✓ Corticosteroids: Corticosteroids are prescription medications that reduce inflammation. Prednisone is a common corticosteroid providers use to manage lupus. Your provider might prescribe you pills you take by mouth or inject a corticosteroid directly into one of your joints.

✓ Immunosuppressants: Immunosuppressants are medications that hold back your immune system and stop it from being as active. They can help prevent tissue damage and inflammation.

Lupus Treatment News

Dapirolizumab pegol (DZP) – In a Phase III trial, LFA Medical-Scientific Advisor Dr. Joan Merrill and Medical-Scientific Advisory Council (MSAC) member Dr. Zahi Touma presented findings that show DZP significantly improved fatigue, musculoskeletal pain and morning stiffness, offering encouraging progress toward better quality of life for people with lupus.

Obinutuzumab – In a secondary analysis of the Phase III REGENCY trial co-authored by the collaborators Dr. Richard Furie and LFA MSAC Chair Dr. Brad Rovin, as well as Dr. Amit Saxena, obinutuzumab improved kidney outcomes and demonstrated steroid-sparing benefits for people with lupus nephritis. On October 20 the drug received FDA approval for the treatment of adults with lupus nephritis.

Cenerimod – MSAC member Dr. Anca Askanase co-authored a Phase 2bstudy that found that cenerimod 4 mg improved alopecia and mucosal ulcers over six months, signaling potential for meaningful relief of symptoms often overlooked in lupus care.

Deucravacitinib – In a Phase II study, deucravacitinib reduced biomarkers linked to kidney dysfunction, suggesting the therapy may help protect renal health in lupus and support long-term disease management. Results were presented by the LFA's MSAC Chair Dr. Brad Rovin and MSAC member Dr. Zahi Touma, as well as Dr. Amit Saxena.

CAR T-Cell Therapy

CAR-T cell therapy continues to be one of the most promising areas of lupus research. Findings presented at ACR 2025 show growing evidence that CAR T-cell therapy may lead to deep, sustained remission and may represent a future transformative approach for people with severe lupus who do not respond to standard treatment

BMS-986353 (CC-97540) – The LFA's MSAC member Dr. Anca Askanase with Dr. Amit Saxena collaborated on the the Phase I Breakfree-1 trial which showed that this next-generation CD19 CAR T-cell therapy achieved major reductions in disease activity with a manageable safety profile in people with severe lupus.

YTB323 (Rapcabtagene Autoleucel) – In research presented by 2022 LFA Evelyn V. Hess Award recipient Dr. Eric Morand, interim results from an open-label

Phase 1/2 study, revealed complete B-cell depletion and repopulation with healthy naïve B Cells, supporting the concept of an immune "reset" for people with severe refractory lupus.

Prevention

Can I prevent lupus?

You can't prevent lupus because experts aren't sure what causes it. Talk to a healthcare provider about your risk if one of your biological parents has lupus.

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Annotatsiya

Sistemali qizil volchanka (Sistemic lupus erythematosus, SLE) — bu surunkali, qaytalanib turuvchi autoimmun kasallik bo‘lib, organizmning immun tizimi o‘z to‘qimalariga qarshi antitanachalar ishlab chiqishi va immun komplekslar to‘planishi natijasida ko‘plab organlarning zararlanishi bilan kechadi. Genetik moyillik, gormonal o‘zgarishlar, epigenetik omillar va tashqi muhit ta’sirlari immun tolerantlikning buzilishiga va tug‘ma hamda orttirilgan immun javoblarning noto‘g‘ri faollashuviga olib keladi. Klinik belgilar xilma-xil bo‘lib, teri toshmalari, bo‘g‘im og‘riqlari, serozitlardan tortib, buyrak, yurak, markaziy asab tizimi zararlanishi kabi og‘ir asoratlargacha bo‘lishi mumkin. Tashxis qo‘yish murakkab, chunki kasallik klinik jihatdan turlicha namoyon bo‘ladi; shu sababli serologik testlar (ayniqsa antinuklear antitanachalar) va maxsus tasniflash mezonlari qo‘llaniladi. Davolashning asosiy maqsadi yallig‘lanishni kamaytirish, autoimmun jarayonni bostirish va remissiyani saqlashdan iborat. Buning uchun kortikosteroidlar, immunosupressiv vositalar, antimalariy preparatlar hamda maqsadli biologik dori vositalari qo‘llaniladi. Kasallikning patogenezini chuqur o‘rganish, biomarkerlar ishlab chiqish va shaxsga yo‘naltirilgan terapiyani rivojlantirish bemorlarning uzoq muddatli natijalarini yaxshilash imkonini beradi.

Kalit so‘zlar: sistemali qizil volchanka, autoimmun kasallik, immun kompleks, antinuklear antitanachalar, biologik terapiya.

Аннотация

Системная красная волчанка (Systemic Lupus Erythematosus, SLE) — это хроническое, рецидивирующее аутоиммунное заболевание, характеризующееся выработкой аутоантител и повреждением тканей вследствие отложения иммунных комплексов в различных органах. Генетическая предрасположенность, гормональные и эпигенетические факторы, а также влияние окружающей среды нарушают иммунологическую толерантность и вызывают патологическую активацию врождённого и адаптивного иммунитета. Клинические проявления чрезвычайно разнообразны — от кожных высыпаний и артралгий до тяжёлых поражений почек, сердца, лёгких и центральной нервной системы. Диагностика затруднена из-за полиморфизма симптомов и основывается на серологических тестах (особенно на выявлении антинуклеарных антител) и международных классификационных критериях. Терапия направлена на контроль воспаления, подавление аутоиммунной активности и достижение ремиссии. Применяются кортикостероиды, иммунодепрессанты, антималярийные препараты и таргетные биологические агенты. Современные исследования патогенеза, поиск надёжных биомаркеров и развитие персонализированных подходов к лечению способствуют улучшению прогноза и качества жизни пациентов.

Ключевые слова: системная красная волчанка, аутоиммунное заболевание, иммунные комплексы, антинуклеарные антитела, биологическая терапия