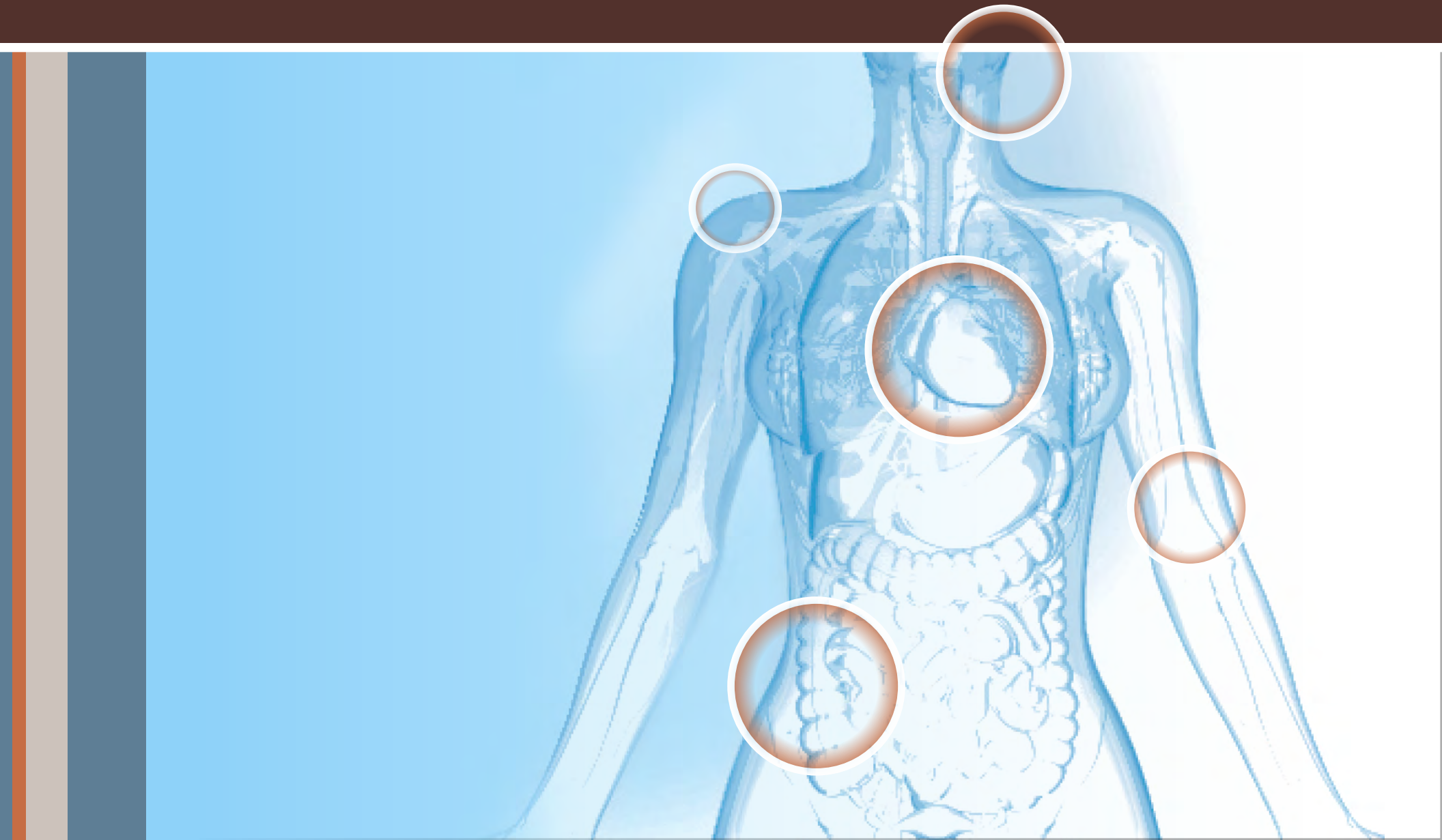
Systemic Lupus Erythematosus (SLE): Focus on Organ Damage



SLE: Focus on Organ Damage

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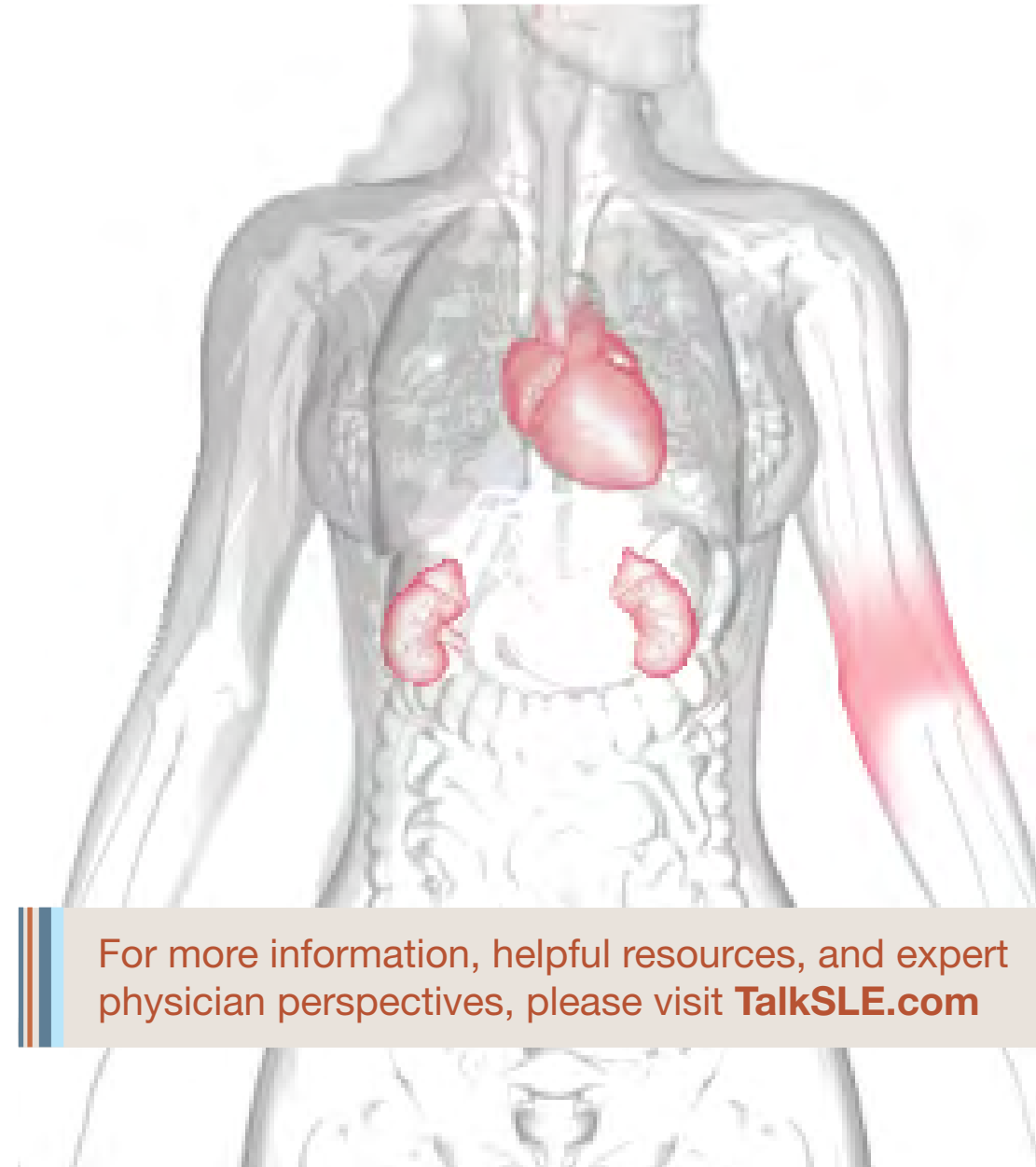

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Overview of Systemic Lupus Erythematosus (SLE)

SLE is a chronic, inflammatory, multisystem, autoimmune disease in which one's own antibodies react to normal cells.[1] The signs and symptoms of SLE vary greatly and may change over time, making accurate diagnosis of the condition challenging.[2] There are a wide range of clinical manifestations that occur; some of the most common are listed below.[3]

Extreme fatigue

Joint pain, stiffness, and swelling in 2 or more joints

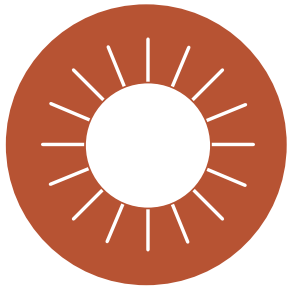
Fever over 100°F

Nephropathy

Neurologic Involvement

Malar Rash

Serositis



Skin rashes after UV light exposure

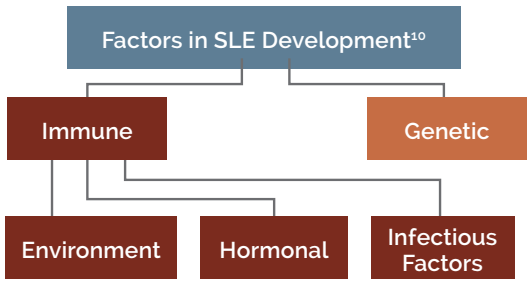
Overview of Systemic Lupus Erythematosus (SLE)

Epidemiology of SLE

In the United States, there are approximately **171,000 adults currently affected with SLE.**[4,5] **Most patients are women of childbearing age (14 to 50 years of age).**[4,5] SLE is also more common and severe among non-white populations.[6,7] Of those diagnosed with SLE, younger patients have a greater risk of poor clinical outcome. Specifically, prepubertal versus post-pubertal onset of SLE is associated with a greater risk of organ damage.[8]

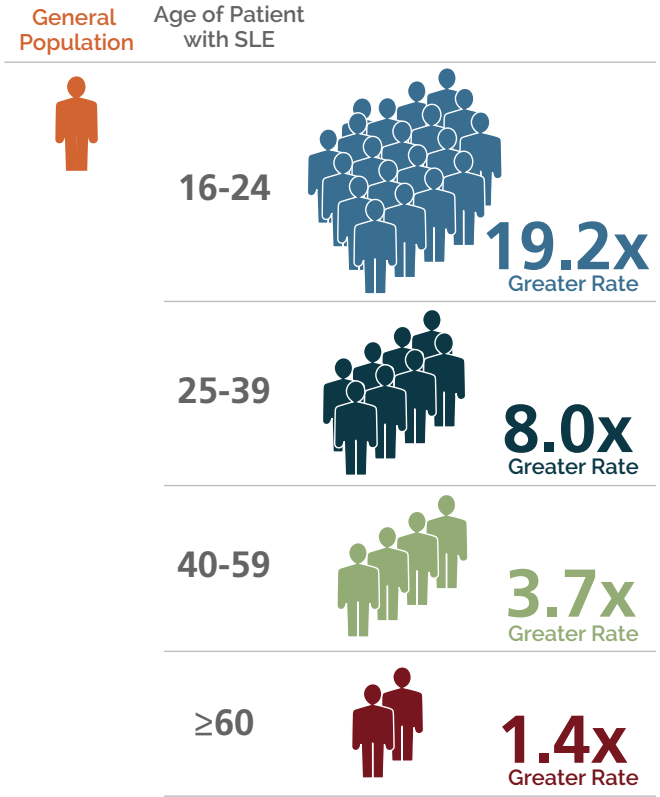
Pathogenesis of SLE

A combination of factors may play a role in the development of SLE. Studies suggest that many different genes, not just a single genetic component, contribute to the development of SLE.[9]



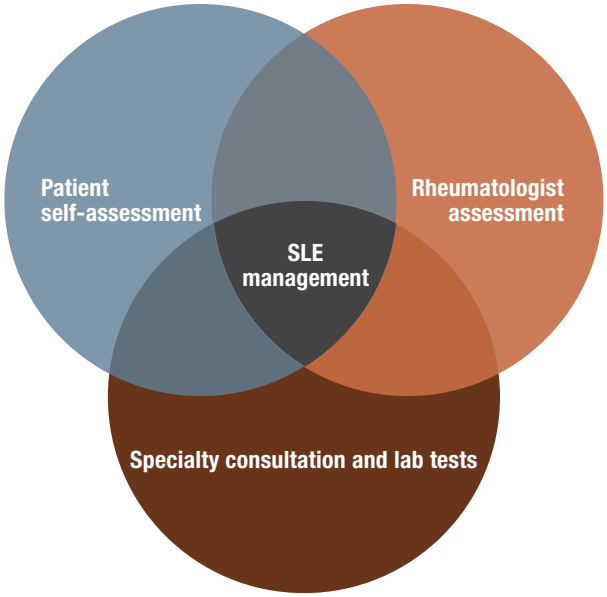
SLE is a disease of the immune system.[1] The dysfunctional immune system may result in the activation of autoreactive antibodies.[10] These B cells are abnormal cells that are autoreactive, making autoantibodies.[1] **Autoantibodies attack the body's own tissue[1] and can be present from 5 to 7 years before the clinical onset of SLE.**[11] Autoantibodies bind to intracellular molecules released upon apoptosis to form immune complexes, which are deposited in organs throughout the body.[10]

Estimated Mortality Rate Compared With Age-matched General Population[12]



2 Disease Activity and Organ Damage

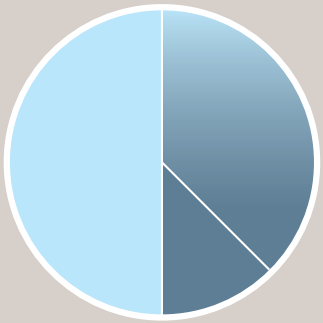
The routine monitoring of disease activity is a key component to the successful management of patients with SLE.[13] Disease activity can be assessed in several ways. Some physicians use the Physicians Global Assessment (PGA) or the SLEDAI* score to track changes in disease activity.[14,15] Additional assessments include laboratory tests and subspecialist consultations as needed.[13,16] In addition, patients self-report SLE manifestations. Here, tools such as the Lupus Checklist or the Lupus Impact Tracker may be helpful.† Further information can be compiled via the physician's assessment including a full history and physical examination and laboratory tests.



Patients still accrue organ damage even with low/moderate disease activity.[17] Organ damage is usually assessed by using the Systemic Lupus International Collaborating Clinics(SLICC)/American College of Rheumatology Damage Index (SDI).[18] Damage must be present for at least 6 months and can result from previous disease activity, medications, or both.[18] Organ damage is considered to be permanent.[18]

*SELENA-SLEDAI = Safety of Estrogens in Lupus Erythematosus: National Assessment Version of the Systemic Lupus Erythematosus Disease Activity Index.
†To download the Lupus Checklist and the Lupus Impact Tracker, please visit the Patient Educational Materials section of TalkSLE.com

Patients Still Accrue Organ Damage Even With Low/Moderate Disease Activity[17]



33% TO 50%

of patients with SLE experience **PERMANENT ORGAN DAMAGE** within the first 5 years of diagnosis.[19,20]

RISK FACTORS ASSOCIATED WITH ORGAN DAMAGE[17]:

- Age at onset of SLE
- Male sex
- Immunosuppressant use
- Existing organ damage

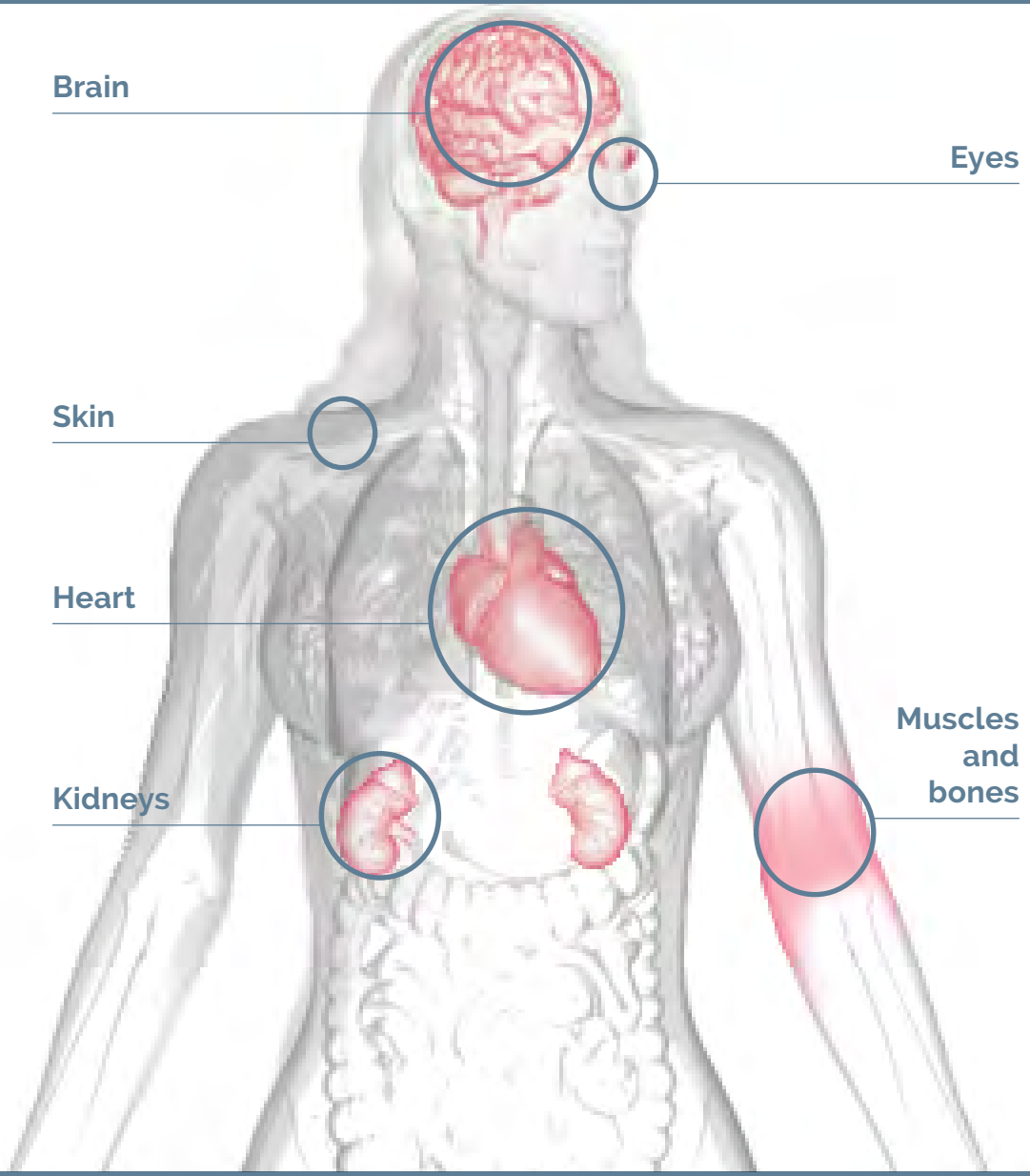
Major Organ Systems Affected by SLE

Organ damage accrues early in the course of the disease, with 33% to 50% of patients receiving SDI scores greater than 0 in the first 5 years following diagnosis.[19,20]

Organ systems commonly affected by SLE

Major organ systems are affected by SLE and require specific monitoring and management.

The diverse clinical manifestations of SLE are the result of inflammation in affected organ systems.[13] Multiple organ systems are known to be affected, with some of the most commonly affected organs shown in the figure to the right.[13] Severity of the disease can vary from mild to potentially fatal, due to detrimental organ damage.[1]



Major Organ Systems Affected by SLE

Mucocutaneous involvement is almost universal in SLE.[21] These manifestations include rashes, photosensitivity, nasal and oral ulcers and alopecia.[21]

DIAGNOSIS & MONITORING

Physician assessment includes patient history of dermatologic issues, physical examination and serological studies.[13] The diagnosis of the cutaneous and mucocutaneous manifestations of SLE is based on **clinical observation, histopathology, and immunohistology of skin lesions.** Serum autoantibodies are considered immunologic markers for distinct clinical types of the illness.[13]

Progression of dermatologic manifestations of lupus can be monitored through 3 avenues:

- physician assessment
- additional specialist consultation
- patient self-report

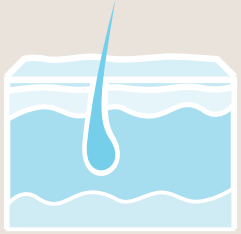
Physicians should encourage **patients to report all rashes, oral ulcers, and sensitivities.**[13]

SPECIALIST REFERRAL

A dermatologist may be used for a second opinion, further evaluation, or a possible biopsy. A dermatologist may also be considered if serologic testing indicates positive for Sjögren's syndrome A (SSA) and Sjögren's syndrome B (SSB) antibodies that can be associated with subacute cutaneous lupus.[22]

For more information from a dermatologist perspective of SLE, please watch Webcast 3 at **TalkSLE.com**

SKIN MANIFESTATIONS ARE SEEN IN NEARLY 80% OF PATIENTS WITH LUPUS.[1]



Classification of some SLE-associated Rashes[22]

Lupus—specific Rash	Lupus—nonspecific	
Malar rash	Livedo	
Discoid rash	Leukocytoclastic vasculitis	
Subacute cutaneous	Urticarial vasculitis	

Patients should report all rashes and sensitivities.[13]

Major Organ Systems Affected by SLE

Neurologic manifestations in patients with SLE vary in severity from mild to severe and affect the central, peripheral, and autonomic nervous systems.[1,23] **Cognitive impairment is the most frequent neurologic damage in SLE.**[24] Patients with SLE should be encouraged to report all neurological symptoms, even if the patient does not think they may be SLE related.[16]

DIAGNOSIS & MONITORING

The American College of Rheumatology **(ACR) has developed standardized nomenclature for neuropsychiatric syndromes** observed in SLE that may aid in the diagnosis of neurologic manifestations of SLE.[25] For patients experiencing **symptoms of cognitive impairment, they may be monitored by clinical history** because no specific instrument has been validated in clinical practice.[26]

SPECIALIST REFERRAL

If the patient is experiencing any neurologic symptoms for which no explanation can be provided, it may be beneficial to refer the patient for formal neuropsychiatric testing.[26] Cognitive testing may be performed by a neurologist or psychologist, along with lab tests and, in some cases, magnetic resonance imaging (MRI).[25] This can include attention/concentration tests, word-finding tasks, and ratings of depression on a scale such as the Center for Epidemiologic Studies Depression Scale (CES-D).[26]

For more information on assessment of neurologic manifestations of SLE, please watch Webcast 2 on **TalkSLE.com**

80%

OF PATIENTS WITH SLE **HAVE COGNITIVE IMPAIRMENT**[27]

The ACR has identified neuropsychiatric syndromes that may be observed in SLE including[13,25]**:**

- Acute confusional state
- Anxiety disorder
- Cognitive impairment
- Cranial neuropathy
- Headache
- Mood disorder
- Myelopathy
- Polyneuropathy
- Psychosis
- Seizure disorders

Major Organ Systems Affected by SLE

Posterior subcapsular cataracts are the most common ocular damage in SLE.[24] However, SLE may affect almost any part of the eye and visual pathway.[28]

DIAGNOSIS & MONITORING

Patients should report all symptoms, because they may not realize the symptoms could be a sign of complications.[28] The physician can determine if there is a history of ophthalmic issues, perform a physical examination, and assess the field of vision.[28] **Pain** (often accompanied by visible inflammation or redness) usually **indicates significant external/anterior segment disease.**[28] Problems with vision (blurring, distortion, double vision) usually indicate posterior segment/neuro-ophthalmic disease.[28] Patients' eyes should be **monitored on a regular basis**, based on the severity of their symptoms.[28]

SPECIALIST REFERRAL

The field of vision is often only assessed at a basic level in the examination room of the rheumatologist or general practitioner.[28] If it is determined that the patient has ophthalmic issues, the patient should be referred to an ophthalmologist.[28]

For more information on assessment of ophthalmic manifestations of SLE, please watch Webcast 2 on **TalkSLE.com.**

EYE DISEASE **OCCURS IN APPROXIMATELY**

20%

of patients with SLE.[1]

Encourage patients to report the following symptoms, which may be a sign of potential complications[28]**:**

- Blurriness
- Dry eyes
- Loss of vision
- Pain

Major Organ Systems Affected by SLE

There is an increased risk of coronary artery disease in patients with SLE that cannot be explained by traditional Framingham risk factors.[29] Patients **35 to 44 years of age have the greatest risk** for cardiovascular manifestations and, compared with age-matched controls, are **50 times more likely to experience myocardial infarction.**[24*] Although pericarditis is the most common cardiac condition experienced by patients with SLE,[1] **hospitalization rates for acute myocardial infarction are 2.3 times higher** than that of the general population.[30]

DIAGNOSIS & MONITORING

The physician should pay close attention to traditional Framingham risk factors[6] and any lupus-associated risk factors that the patient with SLE may exhibit, such as the duration and level of disease activity and the homocysteine level.[31] In patients with SLE, **chest pain could be a warning sign of ischemic heart disease.**[30] It is recommended that patients be **evaluated at least once yearly.**[32]

SPECIALIST REFERRAL

If needed, a cardiologist can perform additional assessments, including an electrocardiogram, an echocardiogram, functional studies, and cardiac catheterization.[30] It is important that the rheumatologist enlist a cardiologist who has experience treating patients with SLE.[31]

For more information on assessment of cardiac manifestations of SLE, please watch Webcast 2 on **TalkSLE.com**.

*An increased risk of other cardiac events including thrombotic stroke, angina, percutaneous coronary intervention, and claudication were also noted.

THE RISK OF A CARDIOVASCULAR EVENT IS **INCREASED** ABOUT

2.7-fold

in patients with SLE[33]

Important factors for diagnosing and monitoring cardiac involvement are:

FRAMINGHAM RISK FACTORS[34]:

- Age
- Smoking habits
- Diabetes
- Blood cholesterol
- Blood glucose
- Elevated blood pressure
- Prior vascular events
- Physical activity
- Family history of cardiovascular diseases
- Body mass index

LUPUS-RELATED RISK FACTORS[31]:

- Disease activity
- Duration of disease
- Renal disease
- Glucocorticoid therapy

Renal damage is one of the most serious complications of SLE, affecting the majority of patients at some point during the course of the disease.[1] Urinalysis abnormalities or renal dysfunction exists in 40% of patients with SLE early in the course of their disease.[3,35,36,37] However, up to 60% of adults develop renal abnormalities later during the course of the disease.[35,37] Lupus nephritis has a higher prevalence in African-Americans and Hispanics than in Caucasians.[36,38] The incidence of lupus nephritis is also higher in men than in women.[39] Patients should be encouraged to report all symptoms.[13]

DIAGNOSIS & MONITORING

The physician should assess the patient's history of renal disease, evaluate associated risk factors, and perform diagnostic assessments.[37] Because renal damage is a serious and prevalent complication in lupus patients, **urinalysis should be routinely performed**, even in the absence of previously diagnosed nephritis.[13] Regular monitoring should be done in patients with established lupus nephritis.[37]

SPECIALIST REFERRAL

If the patient has an abnormal urinalysis or any signs of lupus nephritis, the patient should be referred to a nephrologist.[13]

For more information on assessment of renal manifestations of SLE, please watch our Webcast 2 and 3 at **TalkSLE.com**.

RENAL DAMAGE

is one of the most serious complications of SLE.[1]

Up to 60% of adults

develop renal damage during the course of the disease.[37]

SYMPTOMS[1]:

- Edema
- Foamy urine
- Nocturia
- Tea-colored urine

RISK FACTORS[38]:

- Disease duration
- SLAM score at diagnosis
- Hispanic and African American ethnicities
- Anti-ds DNA antibodies
- Anti-RNP antibodies

ASSESSMENTS FOR DIAGNOSING & MONITORING KIDNEY INVOLVEMENT[37]:

- Immunologic tests
  - C3 and C4 levels
  - Anti-ds DNA
- Kidney biopsy
- Serum creatinine levels
- Urinalysis
  - Proteinuria (protein-to-creatinine ratio)

Osteonecrosis occurs in 5% to 12% of patients with SLE.[21] **The relative risk of osteoporotic fractures is increased 1.9-fold for every 36.5 gm of corticosteroid** that a patient takes.[40]

DIAGNOSIS & MONITORING

The physician should perform a physical assessment[13] and perform additional tests as needed.[24] It is also important to **monitor the patient for the presence of osteoporosis** in SLE.[24,41] This can be done using dual-energy x-ray absorptiometry (DEXA), which should be conducted early in the disease course because the contribution of the disease activity is independent of the risks associated with corticosteroid use and menopausal status.[24]

Routine monitoring, such as **DEXA**, is recommended **every 2 years** in patients taking prednisone to assess the development of osteoporosis.[24] Patients may be assessed more frequently if they have additional risk factors, such as menopause.[41]

SPECIALIST REFERRAL

Patient description of joint or bone issues may require follow-up with referral to a specialist.[13] Bone mineral density assessment should be done in patients taking prednisone for greater than or equal to 3 months.[24]

For more information on assessment of musculoskeletal manifestations of SLE, please watch Webcast 1 and 2 on **TalkSLE.com**.

5% to 12%

of patients with SLE experience **SYMPTOMATIC AVASCULAR BONE NECROSIS.**[21]

SYMPTOMS OF MUSCULOSKELETAL MANIFESTATIONS[1]:

- Morning stiffness
- Painful joints
- Swollen joints

RECOMMENDED ASSESSMENT FACTORS[13]:

- History of fracture
- Number of joints involved
- Range of motion

ASSESSMENT EVERY 2 YEARS IF THE PATIENT IS TAKING PREDNISONE[24]:

- DEXA
- MRI
- Vitamin D levels

Management of SLE

For the physician to achieve the key goal of identifying and managing SLE disease activity, there is a definite need for continuous monitoring and ongoing physician–patient dialogue.[16] It is critical that the patient's partnership with the healthcare team be a strong and robust one to ensure that disease activity is identified and managed throughout their treatment.

"The management of SLE should be based on shared decisions between the informed patient and her or his physician(s)."[16]

Patients should feel empowered to be their own advocates.[16] Patients with SLE should be encouraged to report all symptoms, even if the patient does not think they may be SLE related.[16]

Consider using tools to help patients share their lupus symptoms and the impact of the disease in a systematic fashion.

Some example of useful tools available to download are:

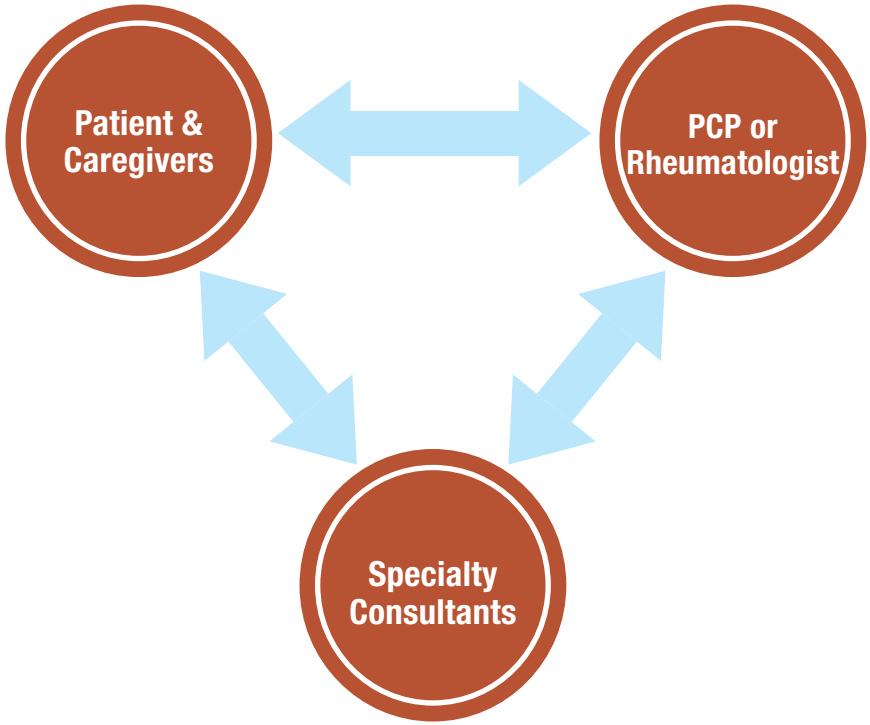
- **Lupus Checklist:** a simple checklist to help your patients recognize the symptoms and risk factors for lupus.
- **Lupus Impact Tracker:** a patient-completed tool for clinical practice to assess and monitor the impact of SLE.

To download the tools above, please visit the Patient Educational Materials section of **TalkSLE.com**. Patients can also download these tools themselves at **UsInLupus.com**

- **My Lupus Log:** an Android app to help your patients track and manage their SLE symptoms.

To download this Android app, please visit the Play Store on your Android device.

Monitoring of SLE Should be a Team Effort[13]



Key Takeaways

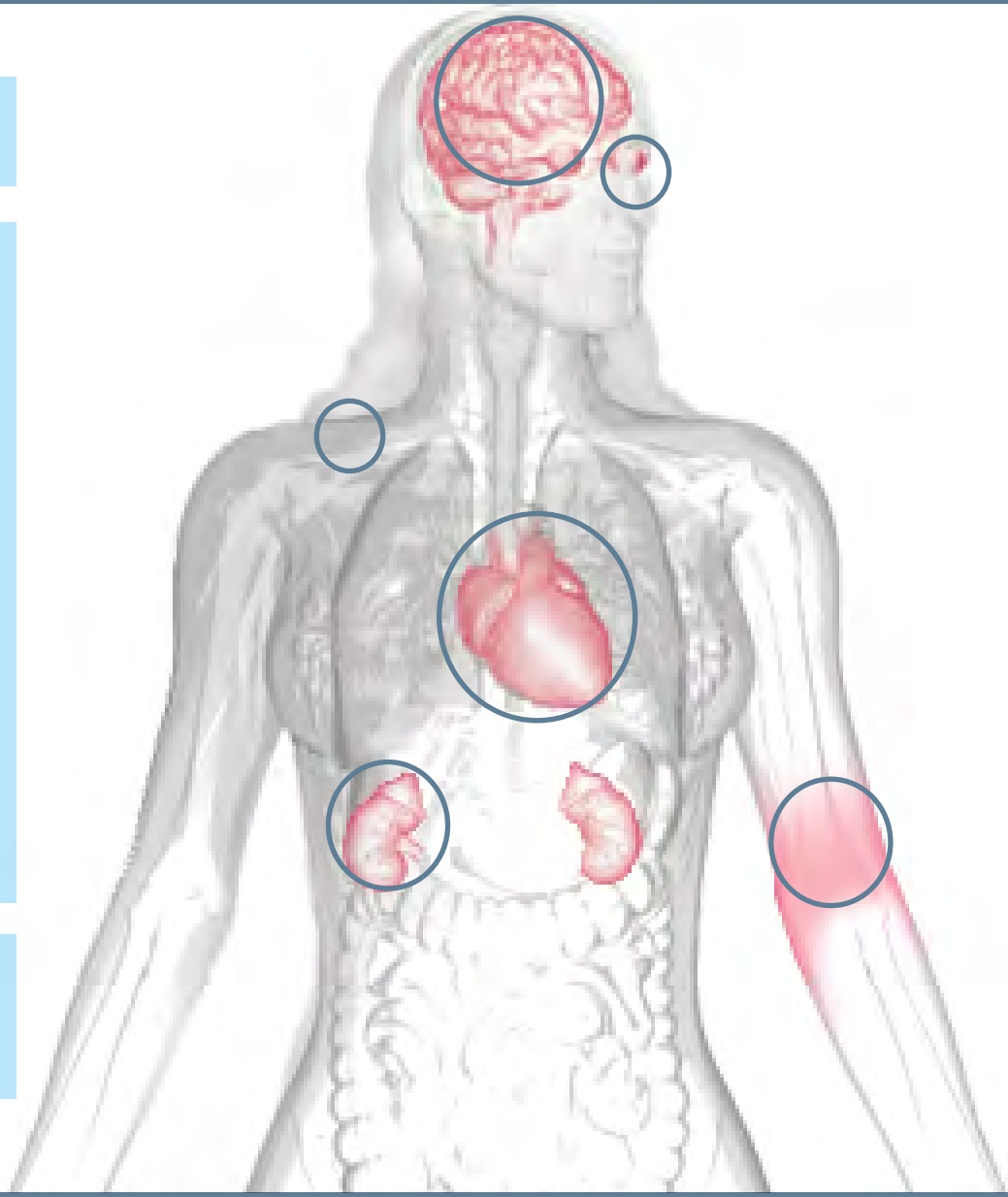
SLE presents with a variety of clinical manifestations involving different organs and organ systems.[24]

Patients with SLE should be encouraged to report all symptoms, even if the patient does not think they may be SLE related.[16]

Some of the possible symptoms for each organ include:

- **SKIN** - rashes, skin lesions, and sensitivities[13]
- **BRAIN** - cognitive impairment, depression, headache, seizures, memory loss, and difficulty thinking[13]
- **EYES** - pain, loss of vision, blurriness, and dry eyes[28]
- **HEART** - chest pain[30]
- **KIDNEY** - foamy urine, tea-colored urine, nocturia, and edema[1]
- **MUSCLES AND BONES** - painful and swollen joint, and morning stiffness[13]

To avoid progression to organ damage, all of the aspects of SLE should be addressed and specialists should be engaged as needed.[13]



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