Patient Resource

BCRenal
Provincial Health Services Authority

Lupus Nephritis

What is it? And what is the broader disease, lupus?

Lupus nephritis (sometimes referred to as LN) is one of a larger group of kidney diseases known as glomerulonephritis (GN). **"Nephritis"** means inflammation of the kidneys, and "lupus" is explained directly below.

"Lupus" is a short form for **systemic lupus erythematosus** (also known as SLE) and is an autoimmune disease in which the immune system attacks healthy tissues. When this attack targets the kidneys, specifically the glomeruli – the tiny filters of the kidneys responsible for filtering waste and excess fluid from the blood – it causes the inflammation named lupus nephritis.

Lupus/SLE can affect many organs throughout the body. Which organs it affects varies from person to person. Some people experience both widespread (systemic) symptoms and kidney problems. Others have kidney problems with few other symptoms, and another group are affected by lupus/SLE without kidney problems.

This handout will focus **only** on lupus that affects the kidneys – lupus nephritis (LN).

Here's what happens in lupus nephritis:

- In lupus/SLE, the immune system, which normally fights infections, mistakenly produces antibodies[1] that attack the body's own cells and tissues (autoantibodies), leading to inflammation and damage in different organs, including the kidneys. We don't fully understand why this happens.
- These autoantibodies form immune complexes[2] (clumps of antibodies and other proteins) that get trapped in the kidneys' filters (glomeruli).
- The immune complexes trigger an inflammatory response, causing the kidney's filters to become swollen and damaged.

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[1] Antibodies are protective proteins produced by your immune system. They attach to antigens (foreign substances) — such as bacteria, fungi, viruses and toxins — and remove them from your body. Source: https://my.clevelandclinic.org/health/body/22971-antibodies.
Autoantibodies are malfunctioning parts of your body's natural defenses. Instead of targeting germs and other invaders, they attack your body. This can lead to lots of different issues and health conditions. Source: https://my.clevelandclinic.org/health/symptoms/autoantibodies.

[2] Immune complex is an antibody bound to an antigen. Immune complexes are part of a normal immune response. However, when immune complexes accumulate in the blood, they can cause autoimmune disorders. Source: https://clinicalinfo.hiv.gov/en/glossary/immune-complex.

- This damage makes the kidneys leaky, allowing blood and protein to spill into the urine.
- Over time, repeated inflammation can lead to scarring (fibrosis) in the kidneys, reducing their ability to function properly.
- There are different classes of lupus nephritis, ranging from mild inflammation to severe scarring that can lead to kidney failure if not treated.

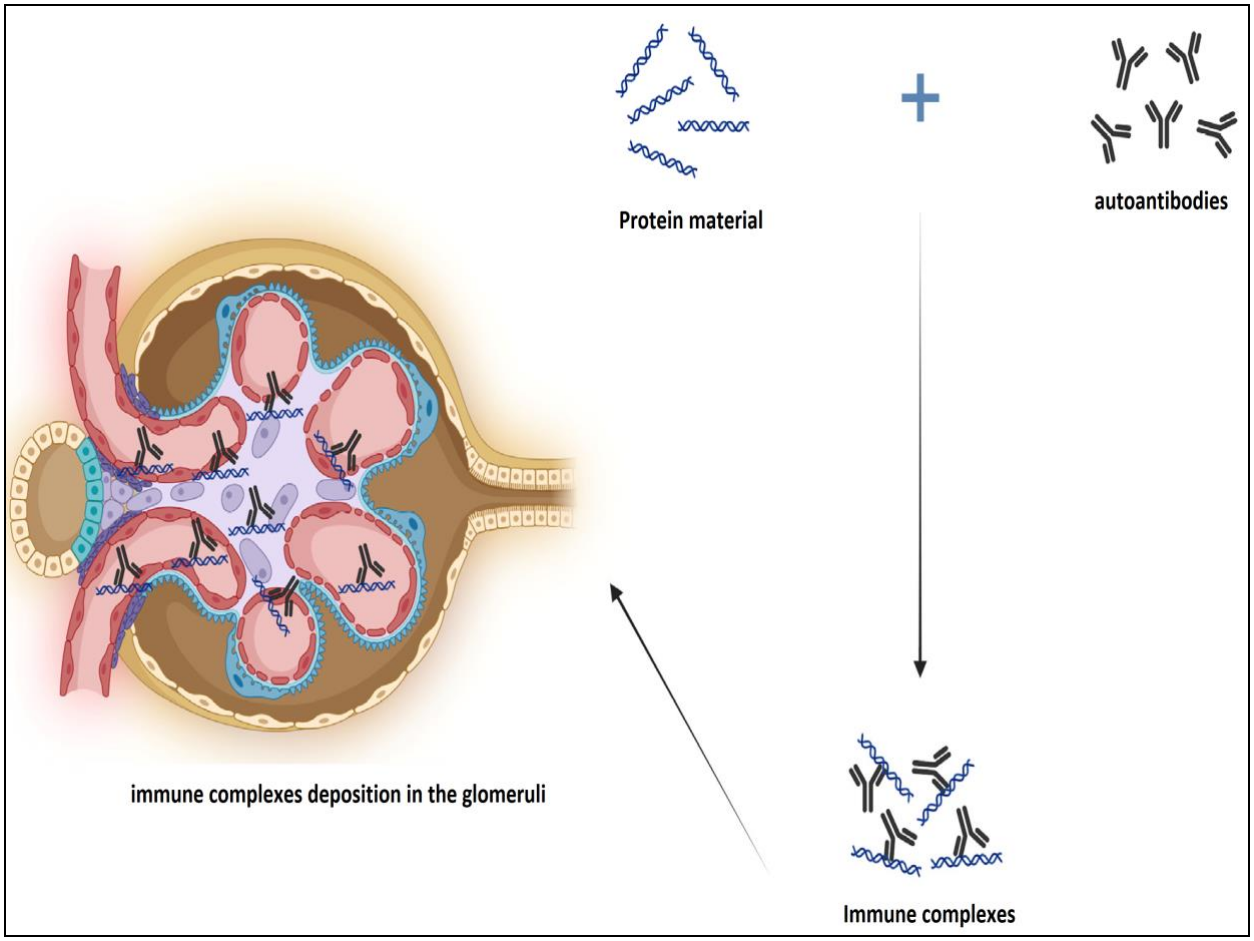

Figure source (modified): https://www.mdpi.com/1422-0067/25/16/8981

The symptoms of lupus nephritis may include:

- Swelling (edema) – puffiness in the legs, ankles, feet, and/or around the eyes.
- Foamy or bubbly urine – due to excess protein leaking into it from the kidneys.
- Blood in the urine – may look pink, red, or brown.
- Weight gain – caused by fluid retention, not actual fat gain.
- Symptoms common for lupus/SLE and lupus nephritis:
    - Fatigue and feeling weak.
    - Joint pain or swelling.
    - Skin rash, often on the face (butterfly-shaped rash).
    - Fever without an infection.

Effects of lupus/SLE on various areas of the body:

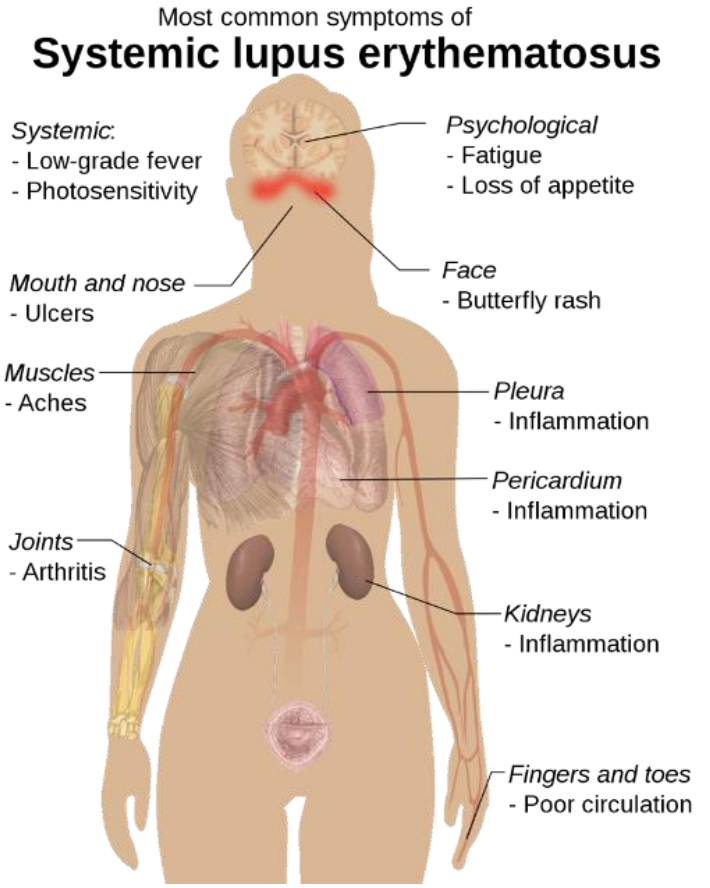

Figure source: https://storymd.com/journal/lw233xdf8m-lupus/page/4q35qu77q8-symptoms-of-systemic-lupus-erythematosus-lupus

The complications of lupus nephritis may include:

- Declining kidney function, which may lead to kidney failure over time requiring dialysis or transplant.
- More frequent infections – the immune system may not work as well due to protein loss.
- Blood clots – the clotting system may not work as well due to protein loss.
- High blood pressure – the kidneys help regulate blood pressure, so damage to the kidneys can cause it to rise.

What happens after you have been diagnosed with kidney disease due to lupus nephritis?

- After your kidney biopsy is reported and a final diagnosis of lupus nephritis is made, your kidney doctor (nephrologist) and/or kidney care team may order further tests or scans and will discuss appropriate treatment with you.
- If multiple organs are involved, your kidney care team may refer you to other specialists for assessment of damage in other organs in order to come up with a treatment plan that covers all affected organs. For example, you may be referred to a rheumatologist or a respirologist.

How is lupus nephritis treated?

Note: This section will **only** discuss the treatment of lupus nephritis (LN) - lupus that affects the kidneys.

The aim of treatment is to lower the production of autoantibodies and stop the immune system from causing further damage. The treatment for people with affected kidneys is usually conducted in two phases:

1. **The initial (induction) phase** of treatment may include steroid drugs known as corticosteroids to reduce inflammation, in addition to one or more of the medications below to suppress the immune system and/or reduce inflammation:
    - Mycophenolate mofetil (MMF)
    - Cyclophosphamide
    - Tacrolimus/cyclosporine
    - Rituximab
    - Belimumab

- During this phase of treatment, you are at a higher risk of bacterial and viral

2. **The subsequent (maintenance) phase** of treatment will start after remission[3]. Medications in this phase are used to prevent relapses and may include:
    - Mycophenolate mofetil (MMF)
    - Corticosteroids
    - Azathioprine
    - Tacrolimus/cyclosporine
    - Rituximab
    - Belimumab

- Treatment with these medications will continue for at least 2 years and may be extended for a longer period.

[3] Remission, by definition, is when symptoms of a disease [like kidney disease] lessen or go away for a period of time. You can have partial or full remission. It can last for months, years or the rest of your life. Remission isn't the same thing as a cure. But if you stay in remission for a long time, some health-care providers might say that you're cured. Source: https://my.clevelandclinic.org/health/articles/24673-cancer-remission.

infection. If you develop a fever, please seek medical attention immediately.

- The length of treatment is individualized based on disease severity, response to treatment, and previous relapses.

- New medications may become available for controlling lupus nephritis in the coming years as more research is being done in this area.

General therapies:

- Lab tests: Your kidney doctor and/or kidney care team will follow you closely with frequent urine and blood tests to monitor your response to treatment and help you manage any symptoms.
- Antibiotics during immunosuppressive therapy: If you are receiving immunosuppressive therapy, depending on its type, you may be started on a combination of trimethoprim and sulfamethoxazole. These antibiotics are used to reduce the risk of very serious infection that can occur in patients on medications that reduce the immune response.
- Other medications while undergoing treatment for lupus nephritis:
    - While on high doses of corticosteroids, your kidney care team may recommend calcium, vitamin D, and medication to maintain bone health.
    - Also, while on immunosuppression, your kidney care team may offer you medication to prevent stomach upsets.
    - Medications to control swelling (diuretics) and/or blood pressure may be initiated depending on your symptoms.
- Medication options: Your kidney doctor and/or kidney care team will support you in learning about the medication options that would be best for you.
- Medication cost: BC Renal covers the cost of a wide range of medications used for lupus nephritis treatment.

- **Important:** Patients need to check with their kidney doctor and/or kidney care team before taking any over-the-counter (OTC) medications and natural health products.
- **Important:** Patients with chronic kidney disease like lupus nephritis need to keep their vaccinations updated. Some treatments may reduce the effectiveness of vaccination. You are encouraged to discuss with your kidney doctor and/or kidney care team what vaccinations may be appropriate for you.

- **Important:** Pregnancy may impact kidney function. If you are planning a pregnancy, please consult your kidney doctor. In addition, some of the medications used to treat lupus nephritis may not be compatible with pregnancy.
- **Important:** Women of childbearing age undergoing treatment for lupus nephritis should discuss a contraception plan with their kidney care team.
- **Important:** Smoking cessation is important – it can help slow down the worsening of kidney disease. Your family doctor can provide resources to help quit smoking.

Living with lupus nephritis

- Support of kidney care team: BC kidney patients registered with BC Renal have access to a comprehensive kidney care clinic (KCC) team that includes nurses, dietitians, and social workers. In most cases, patients will also have access to a pharmacist.
- Support for your wellbeing: It will be important for you to stay active and healthy. The Kidney Foundation's online Kidney Wellness Hub (https://kidneywellnesshub.ca/) has a lot of useful information. It covers staying active, eating well, mental wellbeing, and socially connecting, including peer support groups. It also provides online classes, webinar recordings, and activity suggestions for patients of all ability levels.
- Ongoing follow-up: Though most patients treated for lupus nephritis with immunosuppression medication improve, the disease course is unpredictable. Relapses are common, even many years after lupus nephritis is diagnosed. You will need ongoing follow-up with your kidney doctor and/or kidney care team.
- Risk of kidney failure: There is a portion of lupus nephritis patients who will end up with kidney failure, despite treatment. If your kidneys fail, your treatment options may include transplant, dialysis, and conservative care[4]. However, a very small portion of lupus nephritis patients may experience recurrences of the disease even after transplantation. Your kidney doctor and/or kidney care team will be there to educate and support you throughout your journey.

[4] Conservative care, sometimes called conservative kidney management (CKM) or supportive kidney care, focuses on treating the symptoms of kidney failure to make you feel as well as possible. It does not treat the causes or attempt to cure kidney failure. Although conservative care does not include dialysis or transplant, it does include all of the other parts of kidney care and support from your team. For more information see this BC Renal's handout: http://www.bcrenal.ca/resource-gallery/Documents/Patient_Guide-Transitioning_to_Conservative_Care-Kidney_Care_Clinics.pdf.

- Participation in clinical trials: Sometimes, people living with lupus nephritis may be invited to participate in a clinical trial for new therapies and medications. If you choose to volunteer in a trial, your kidney doctor and/or kidney care team will help you navigate the process.

Further information

- There may be a lot of confusing information about lupus nephritis and other kidney diseases on the Internet. The following websites are good sources of information for people living with this disease:
    - The Kidney Foundation of Canada - https://kidney.ca/
    - Kidney Wellness Hub - https://kidneywellnesshub.ca/
    - BC Renal GN web page - http://www.bcrenal.ca/health-info/kidney-care/glomerulonephritis
    - Lupus nephritis webpage – by Glomcone - https://www.glomcon.org/kidney-diseases/lupus-nephritis
- If you continue to have questions about your condition or treatment, please keep track of these questions and ask your kidney doctor and/or your kidney care team.