



Lupus and Kidney Involvement

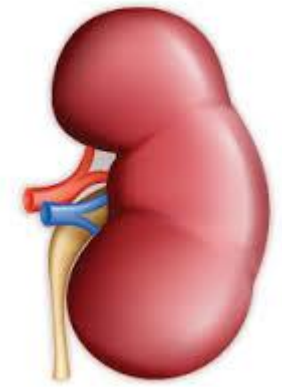
Lupus Society of Illinois 2015

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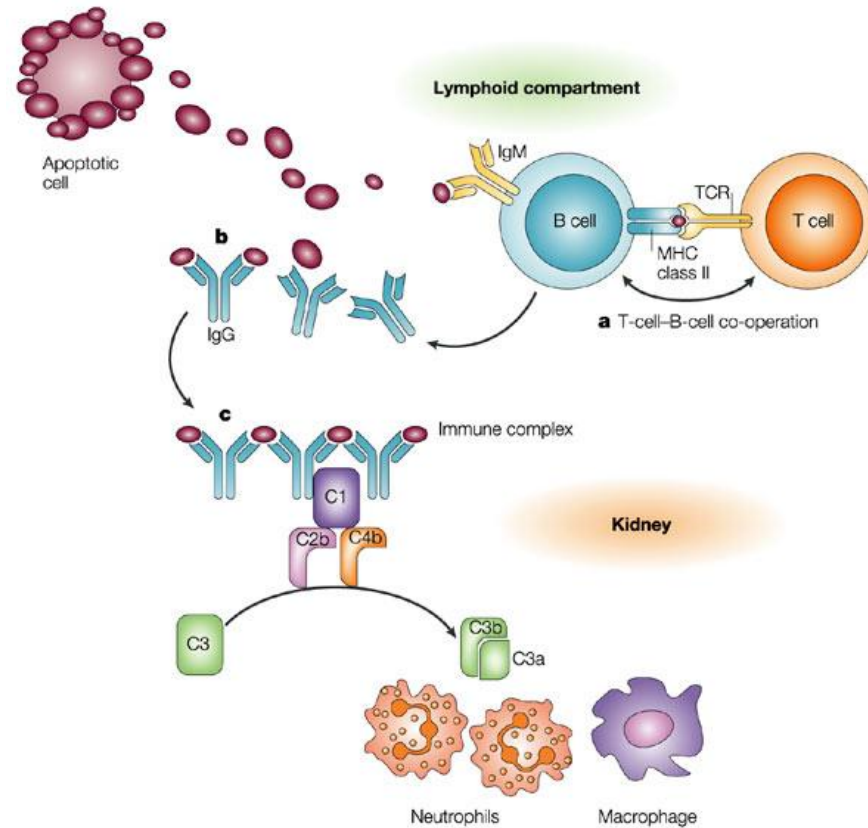
What we will cover



- What is lupus nephritis?
- What are the symptoms, how would I know I could have it?
- How do you make the diagnosis?
- What are the treatments?
- What should I expect?
- Questions

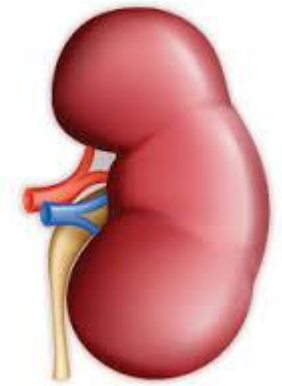
Lupus Nephritis—what is it?

- Lupus or Systemic Lupus Erythematosus (SLE) is an auto-immune condition
- Normally, the body can tell the difference between what is foreign (i.e. infections, foreign bodies, etc) and what is natural to the body
- In SLE, the body loses some of that ability and auto-antibodies are formed





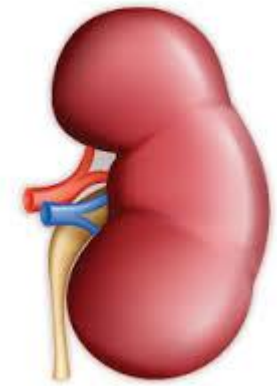
Lupus Nephritis—what is it?



- Auto-antibodies can form against a variety of proteins in the body and form “immune complexes” that flow through the circulation
- Auto-antibodies can also form against proteins specific to parts of the body (skin, lung or heart lining, the kidneys, etc)



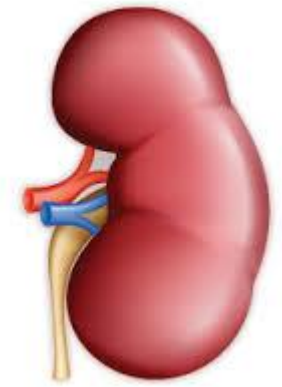
Lupus nephritis—what is it?



- Just like attacking an infection, the body's immune system is recruited and attacks where the antibodies settle
- The healthy tissue is then injured in the “cross-fire” of the immune system attacking the immune complex
- The result is inflammation leading to damage of healthy tissues



Lupus Nephritis—what is it?

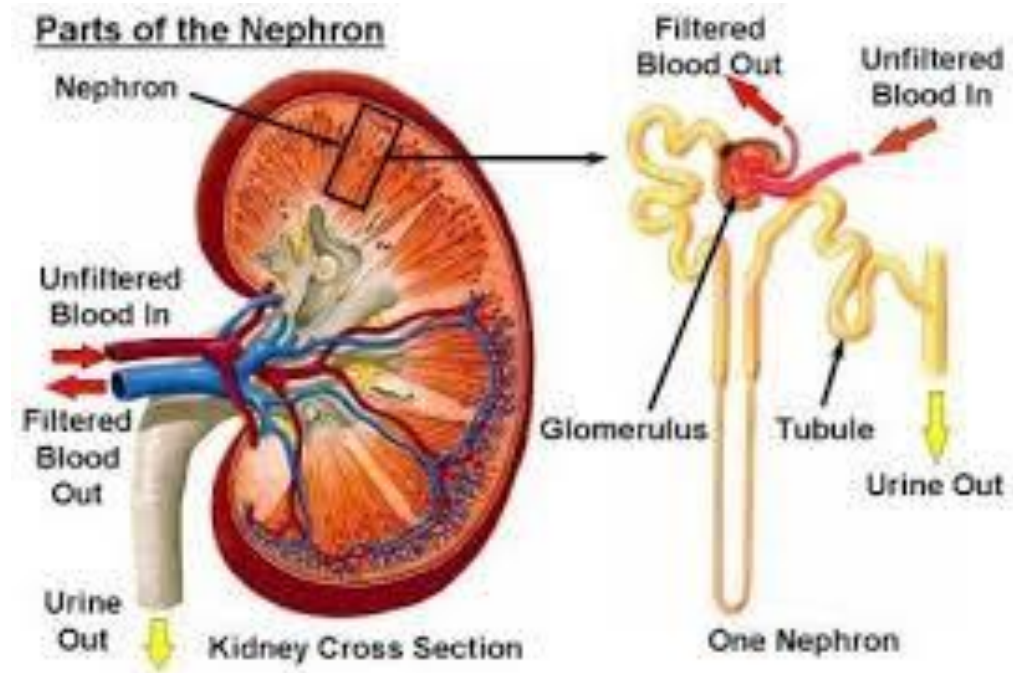


- Kidneys are the blood filter making it a common place for immune complexes to get “caught”
- About ½ of patients with lupus may develop some kidney issues
 - Mostly due to the lupus involving the kidney
 - Some due to medications used to treat the arthritis

Lupus Nephritis

What are the symptoms?

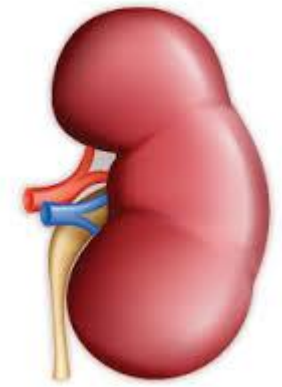
- The kidney has a few critical functions
 - Filter the toxins that the body normally produces
 - Filter medications out of the body after they have done their job
 - Remove excess salt and water from the body
 - Regulate the body chemistry including acid level and electrolytes (potassium, sodium, etc)
- Lupus involving the kidney can affect any of these functions





Lupus Nephritis

What are the symptoms?

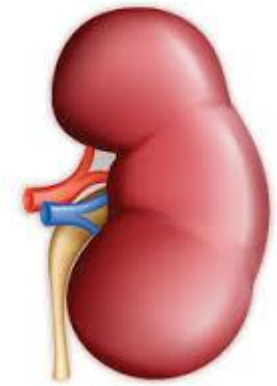


- The inflammation can be mild
 - No significant damage to the functions of the kidney
 - Slight compromise of the filter making it “leaky” leading to a small amount blood in the urine that usually cannot be seen with the naked eye (microscopic hematuria)
- The inflammation can be severe
 - Damage to the kidney’s filtering system making it harder to clear out the toxins the body normally makes, medications taken and extra salt and water
 - Damage to the filter making it very “leaky” resulting in more severe blood in the urine and loss of proteins in the urine



Lupus Nephritis

What are the symptoms?

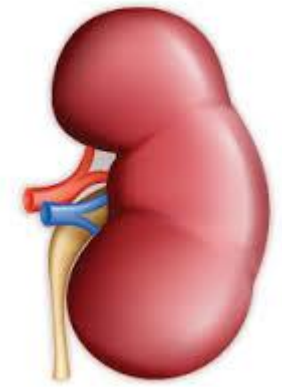


- In the mild cases, the only way to suspect this would be urine testing showing blood in the urine
- In the severe cases, the effects of the protein leakage and decreased filtering ability show up in the following ways
 - “Bubbles” in the urine
 - High blood pressure
 - Fluid retention (swelling in the feet, face, stomach area)
 - Urine tests showing protein in the urine
 - Blood tests showing decreased filtering ability of the kidney (increased blood creatinine)



Lupus Nephritis

What are the symptoms?

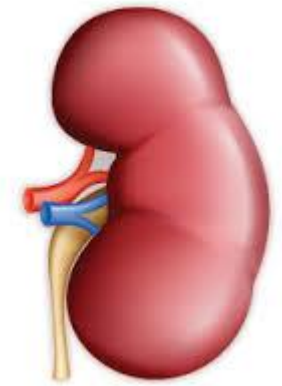


- Lupus activity in the kidney *usually* corresponds to lupus activity elsewhere (i.e. lupus in the skin, joints, etc is quiet, lupus in the kidney is usually absent or mild and, likewise, if lupus in the rest of the body is active, lupus in the kidney can develop and be more severe)
- The initial screening is usually done by a primary care physician or rheumatologist, who then will likely refer to a nephrologist (kidney doctor) for further testing



Lupus Nephritis

How is it diagnosed?

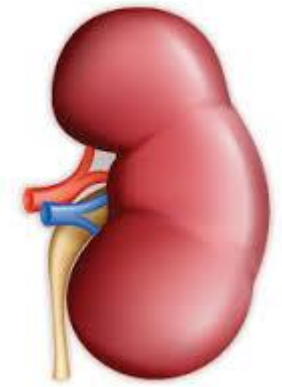


- The initial suspicion of lupus involving the kidney (lupus nephritis) is made by the abnormal blood and urine tests
- To determine the exact nature of the injury, a sample of the kidney has to be reviewed under a microscope
- Sampling of the kidney is done with a ultrasound-guided kidney biopsy



Lupus Nephritis

How is it diagnosed?



How is a kidney biopsy performed?

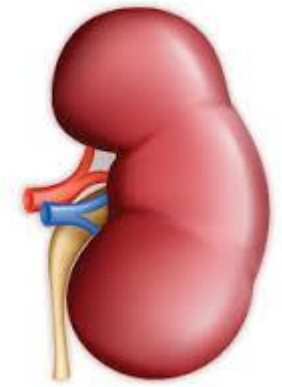
Why is a kidney biopsy necessary?

What are the risks and benefits of a kidney biopsy?

What can I expect during and after a biopsy?

Lupus Nephritis

How is it diagnosed?



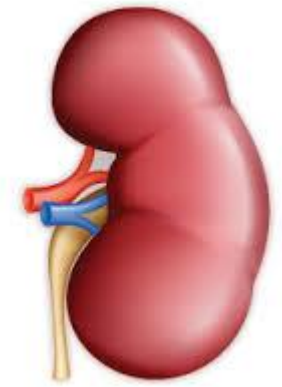
How is a kidney biopsy performed?

- Kidney biopsies are done under “ultrasound guidance”
 - Sonogram of the kidney is taken
 - The pictures guide a small needle used to sample the kidney
- Kidney biopsies are done with local anesthetic and, sometimes, “twilight”
 - You should feel “pressure,” but not significant pain
 - The procedure itself takes about 10 minutes
 - 2-3 samples of the kidney are taken (about 30 glomeruli out of 1 million)
 - It is an outpatient procedure and you should be able to go home the same day
- Kidney biopsies are overall very safe with some precautions
 - Blood pressure needs to be fairly well controlled
 - No use of blood thinners of any kind
 - Monitoring for signs of bleeding, etc



Lupus Nephritis

How is it diagnosed?



The biopsy is reviewed under the microscope by a pathologist to determine the extent and the nature of the injury

The pattern is classified according to a universally accepted classification system (ISN/WHO Lupus Nephritis classification)

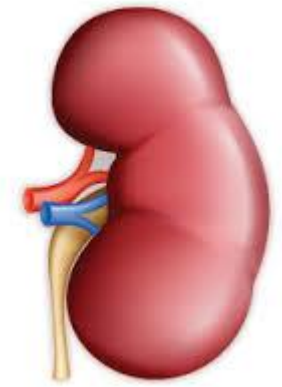
The classification mostly indicates severity

- Class I minimal findings
- Class II mesangial proliferative
- Class III focal proliferative
- Class IV diffuse proliferative
- Class V membranous



Lupus Nephritis

How is it diagnosed?



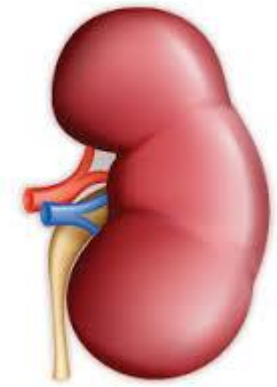
The biopsy provides the following information that blood and urine testing cannot

- The pattern of injury (what part of the kidney is involved, i.e. blood vessels, tubules, the filter itself)
- The severity of injury (is a small percentage of the kidney injured or is it most of the kidney—focal vs. diffuse)
- The extent of “active” injury (inflammation) or “injury” (scarring)—the more active injury there is, the more likely it will respond to treatment and the more scarring, the more likely the injury is irreversible



Lupus Nephritis

What are the treatments?

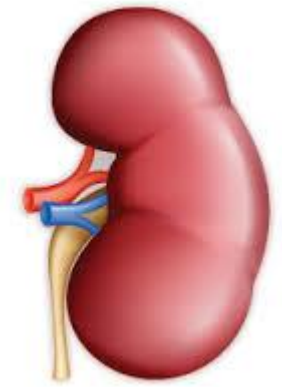


- Treatments for lupus nephritis are directed at quieting the immune system
- Treatment is considered in two “parts”
 - Induction—immediately after diagnosis and until disease is quiet (in remission) 3-6 months
 - Maintenance—after the disease level has quieted down (in remission) to prevent recurrence/relapse—usually 12-18 months
 - Medications can overlap between utility in induction and/or maintenance



Lupus Nephritis

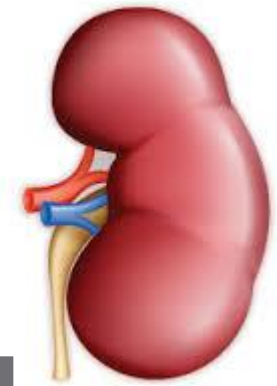
What are the treatments?



- Aggressive treatment is meant to prevent progressive kidney damage to lower the risk of needing dialysis in the future
- Treatments should also be tailored to many patient clinical features
 - Is a pill easier to remember vs. an injection?
 - What side effects are acceptable?
 - How willing are people to try something new?

Lupus Nephritis

What are the treatments?

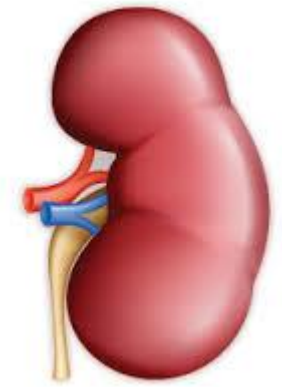


Medication	Route	Frequency	Duration	Proven track record	Induction vs. maintenance
Prednisone	Pill by mouth	Daily	Indefinite	****	Induction and maintenance
Cyclophosphamide	IV	Every 2 weeks or Every 4 weeks	3-6 months	****	Induction
Cyclophosphamide	Pill by mouth	Daily	3-6 months	****	Induction
Mycophenolate mofetil	Pill by mouth	Twice daily	18 months	****	Induction and maintenance
Azathioprine	Pill by mouth	Daily	18 months	***	Maintenance
Rituximab	IV	Every week	1 month	**	Induction and Maintenance
ACTH	Skin injection	Twice weekly	6-12 months	**	Induction and maintenance



Lupus Nephritis

What are the treatments?



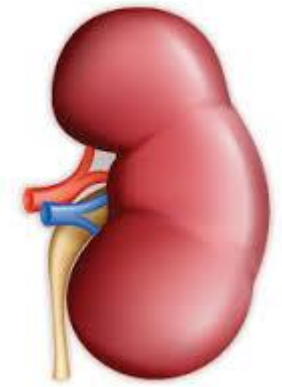
Prednisone

- A “steroid” pill that is similar to the natural hormone in the body cortisol
- Used in all forms of lupus and other auto-immune conditions (rheumatoid arthritis, gout, sarcoidosis, etc)
- Dose is adjusted based on level of inflammation and other medications
 - Usually is higher doses initially with lowering of the dose based on the response
 - Usually continued at low dose for extended period of time
 - Has to be tapered slowly to prevent shock to the body



Lupus Nephritis

What are the treatments?



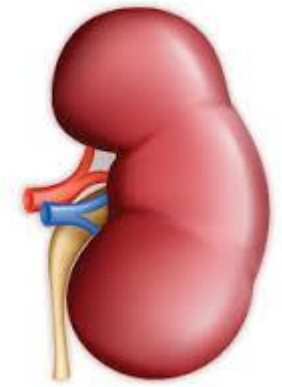
Prednisone

- Side effects can be significant, but depend on dose and duration of use. Nevertheless, use is as sparing as possible
 - Short term side effects: anxiety, sleeplessness, hyperactivity, acne, increased appetite, weight gain, suppressed immune system
 - Long term side effects: weakening of bones (osteoporosis), diabetes, high blood pressure, weight gain, fragile skin
- Should be used with another medication to limit the amount and duration used



Lupus Nephritis

What are the treatments?



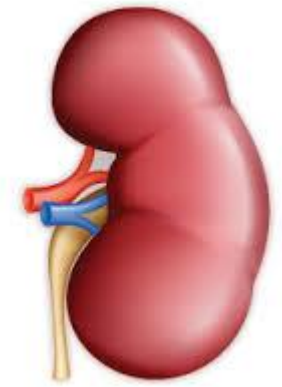
Cyclophosphamide

- “Chemotherapy” that prevents the body from making a certain part of the immune system (lymphocytes)
- Used in doses much lower than used in cancer patients
- Should be used only with close observation of body’s response (blood counts, side effect symptoms)
- Usually given in the IV form every 2 weeks or every 4 weeks for 3-6 months based on the body’s response



Lupus Nephritis

What are the treatments?



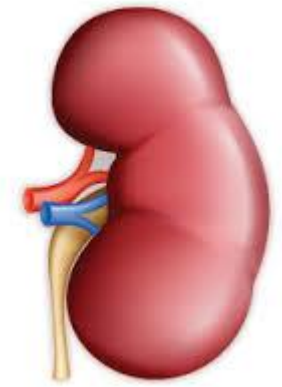
Cyclophosphamide

- Significant pros and cons for its use
- Pros
 - Effective; long track record of being effective for treatment
 - Limited course
 - IV administration only has to be done every 2 or 4 weeks
- Cons
 - Side effects of nausea, hair loss, upset stomach
 - Risk of bladder or blood cancers with extended or repeated use
 - Requires close monitoring



Lupus Nephritis

What are the treatments?



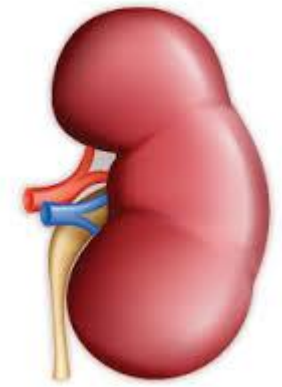
Mycophenolate mofetil

- Initially used for kidney transplants
- Interferes with part of the immune system growing (lymphocyte proliferation)
- Given in pill form twice daily
- Slightly more targeted way of suppressing immune system
- Likely works better in non-whites than whites



Lupus Nephritis

What are the treatments?



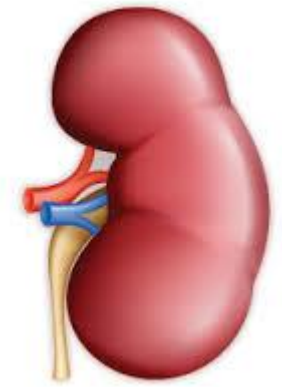
Mycophenolate Mofetil

- Pros
 - Strong evidence to support use
 - Well tolerated
 - Long track record with kidney transplant patients
- Cons
 - May not be as effective in non-African/American or non-Hispanic patients
 - Shorter “track record” in long-term efficacy



Lupus Nephritis

What are the treatments?



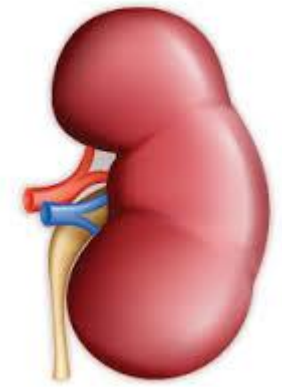
Rituximab

- Lab-generated antibody against part of the immune system
- Recruits body to targeted destruction of the immune system
- IV infusion that runs in over 4-6 hours
- Usual course is weekly for 4 weeks with at least 6 month activity



Lupus Nephritis

What are the treatments?



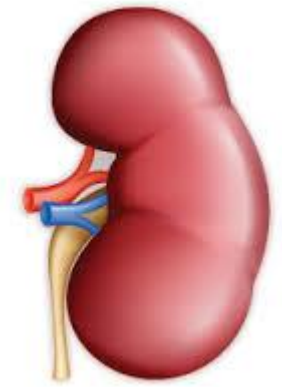
Rituximab

- Pros
 - Well tolerated
 - Limited course and ease of administration
- Cons
 - Limited data on its effectiveness
 - No “turn-off” switch, once the IV infusion is complete, it is in the body system



Lupus Nephritis

What are the treatments?



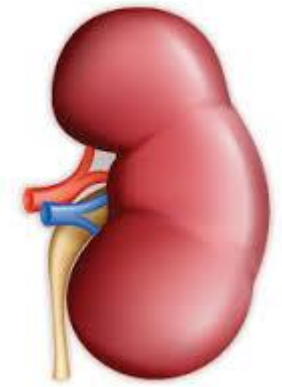
ACTH

- Lab-made form of naturally occurring hormone
- Given as skin injection twice weekly
- Can replace the need for separate prednisone use and help with non-renal symptoms (arthritis, swelling, etc)



Lupus Nephritis

What are the treatments?



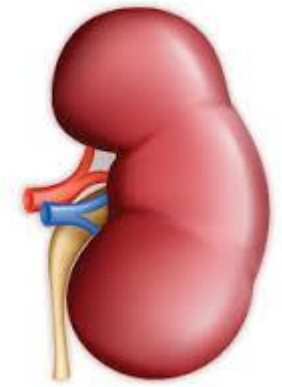
ACTH

- Pros
 - Well tolerated
 - Helpful in non-renal symptoms
- Cons
 - Limited data on its effectiveness



Lupus Nephritis

What to expect?

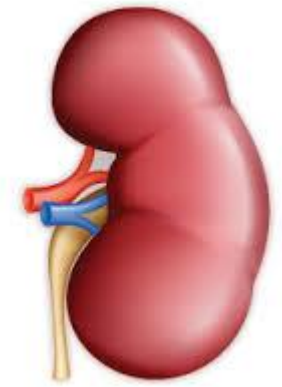


- Lupus tends to be a life-long condition, it requires consistent monitoring and follow-up to guide therapy
- Lupus nephritis can come and go—it can respond to treatment and be quiet. It may be gone forever in some, but it can come back in others
- Lupus nephritis remains the most well studied glomerulonephritis (inflammation of the kidney) and has the most current and future treatment options available



Lupus Nephritis

What to expect?

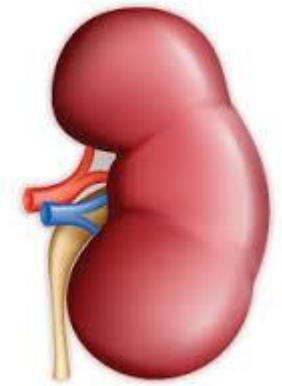


- Collaborating with your physician and sharing with them concerns you have regarding both diagnosis and treatment is the best way to develop a well-tolerated treatment plan
- As with all medicines, the treatments can have significant side effects, but they are warranted when the inflammation gets severe
- The goal is always to maximize the positive effects of the medications with the least number of side effects



Lupus Nephritis

What to expect?

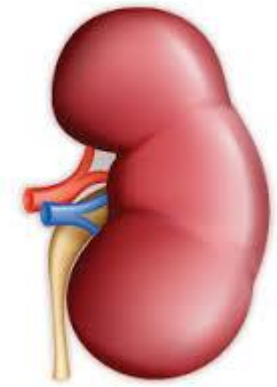


- Future medications in development are along the lines of rituximab—very targeted to maximize efficacy and limit side effects
- New blood and urine tests are in process to replace the need for biopsy to guide treatment



Lupus Nephritis

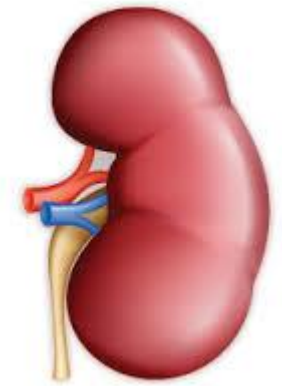
What to expect?



- Individuals that respond to treatment can live a “normal” life with kidney function recovering back to various ranges, even back the condition before they were ill
- Even after the inflammation dies down, residual damage can remain and other medications may be necessary—such as blood pressure medications and water pills
- In a small percentage of people, the inflammation and scarring do not get better and they require dialysis and eventual transplantation
- The medications used for transplants also tend to treat lupus, so the risk of recurrent kidney disease after transplantation is low (< 5% of individuals)



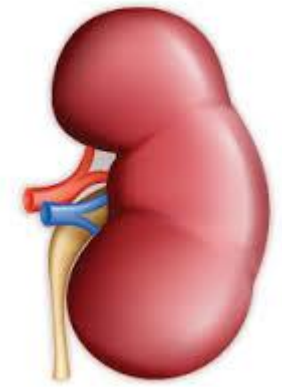
Lupus Nephritis Summary



- Lupus is an autoimmune condition caused by the production of “auto-antibodies”
- Lupus nephritis is inflammation in the kidney caused by the immune system “dysregulation”
- Lupus nephritis is common, but ranges in severity from mild to more severe
- There are current and future treatments available for lupus nephritis to help people maintain normal kidney function and optimal quality of life



Lupus Nephritis



Questions?