Treatment Options for Nephrotic Syndrome

Los Angeles Family Wellness Day

January 20, 2019
What Do The Kidneys Do?

Healthy, functioning kidneys are important because they:

• **Eliminate** waste products, drugs and toxins from the blood
• **Regulate:**
  • electrolyte concentrations (like salt and potassium)
  • amount of fluid within the body
  • blood pressure
• Help **maintain** acid base balance
• **Produce hormones** that affect blood and bones
What Do The Kidneys Do?

The Nephron

- Each kidney has **ONE MILLION** nephrons
- Each nephron is composed of a glomerulus and a tubule
- **The glomerulus filters** wastes and excess fluids
- **The tubules modify** the waste to form urine
Disruption of the Glomerular Structure Leads to Nephrotic Syndrome
Think of the kidney as a sieve - it keeps the good stuff in and drains the water. When you have Nephrotic Syndrome, the colander holes are too big and the good stuff gets out.
Nephrotic Syndrome

- Nephrotic Syndrome (NS) is a collection of symptoms
- This results in:
  - Higher protein in urine
  - Lower protein in the blood
- NS is a sign of kidney damage
- Damage can be from an unrelated condition
- Damage can be from a kidney disorder
  - This is called Primary, or Idiopathic
Nephrotic Syndrome – many diagnoses

“NEPHROTIC WHAT?!...”
Understanding Primary Nephrotic Syndrome

TIP: Don’t be intimidated by the disease names; they are just descriptions of how the kidney tissue looks under a microscope.

Nephrotic Syndrome (NS) is not a disease, but an umbrella term for the collection of signs and symptoms that occur when the kidney filters (glomeruli) leak protein into the urine.

Some symptoms of NS include:
- Proteinuria (‘leaking’ protein into the urine)
- Edema (swelling)
- Hypertension (increased blood pressure)
- Hypoproteinemia (low blood protein)
- Hypercholesterolemia (high cholesterol)

Someone who is experiencing these symptoms but has not had a kidney biopsy is diagnosed with Nephrotic Syndrome.

To learn more about what is causing a patient’s Nephrotic Syndrome, doctors may choose to perform a kidney biopsy. After a biopsy, a patient is usually diagnosed more specifically, based on what can be seen under the microscope. The most common diagnoses are:

Focal Segmental Glomerulosclerosis (FSGS)
Some sections of kidney filters show scarring.

Minimal Change Disease
Kidney tissue shows very little change from normal kidney tissue.

Membranous Nephropathy
Kidney tissue has a thicker than normal filtering barrier or glomerular basement membrane.
Biopsies help narrow down specific diagnosis

THE LOW-DOWN ON Kidney Biopsies

Kidney biopsies are important because they can help your doctor learn what is causing your nephrotic syndrome and how severe it is. This will help them form your treatment plan. Additional biopsies may be done later on to see how your treatment is working.

BIOPSY PROCEDURE

1. Biopsies are typically performed by a nephrologist or interventional radiologist.
2. Biopsies are often done after light sedation or local anesthesia.
3. A small piece of tissue from one kidney is taken by a specialized needle for examination under a microscope by a kidney pathologist.
4. After a biopsy, limited activity or bed rest will be recommended for a period of time.
Biopsies for Kids and Adults

**FOR KIDS**

Nephrologists will usually recommend a child have a biopsy if:

- They have certain findings when they are first diagnosed (such as abnormal kidney function or a family history of nephrotic syndrome.)
- They do not respond to their very first course of prednisone ("steroid resistant")
- They initially responded to steroids but have gradually become less responsive or have frequent relapses or cannot be weaned off steroids ("steroid dependent")
- They have unusual findings such as abnormal kidney function.

**FOR ADULTS**

Kidney doctors are more likely to recommend a biopsy for adult patients when they are first diagnosed.

The results of a biopsy will help determine what is causing a patient's Nephrotic Syndrome and can help guide treatment.
Treatment Goals

**Short Term**

- **Reduce / eliminate protein spillage** into the urine
- **Improve** clinical symptoms (swelling, edema, fatigue)
- **Correct abnormalities** of the blood levels (cholesterol, albumin)

**Long Term**

- **Prevent recurrences** of protein spillage into the urine
- **Preserve kidney** function
- **Avoid** treatment-related complications
Treatment Options: First Line

1. Usually, patients are treated with corticosteroids first.

Corticosteroids (Prednisone)
Treatment Options: Second and Third Line and Rescue Therapies

If steroids fail to cause remission (usually within 8-12 weeks), or if a patient becomes "steroid dependent," one or more of the following treatments may be tried:

- Cyclophosphamide (Cytoxan)
- ARBs
- Cyclosporine (Neoral)
- Methylprednisolone (Solu Medrol)
- Mycophenolate (MMF, Cellcept, Myortic)
- Plasmapheresis (Liposorber)
- Prograf (Tacrolimus)
- Adrenocorticotropin (ACTH Acthar Gel)
- ACE Inhibitors
- Rituxan (Rituximab)
There are a number of other potential treatments that may reduce proteinuria in Nephrotic Syndrome patients. Ask your doctor about clinical trials for these.
Treatment of Nephrotic Syndrome

Widely accepted initial therapy for both children and adults:

**Prednisone**

- If there are frequent relapses, or the patient is non-responsive,
  - Talk to your doctor about adding other medications to the prednisone
  - Talk to your doctor about trying a different therapy plan
  - Be prepared for the “laundry list” of side effects that may occur
  - Talk to your doctor about clinical trials

Prednisone acts as an immunosuppressant. This will help reduce swelling, and, hopefully, help the kidneys function properly.
Personalized Treatment of Nephrotic Syndrome

Primary Nephrotic Syndrome is difficult to treat because of the **variable clinical courses**

- Steroid Responsive vs. Steroid Resistant

- An “off-label” medication is one that is approved by FDA for a disease that is not Nephrotic Syndrome, but used to treat it anyway by a doctor’s recommendation

- **Clinical trials** are always an option
  - For both children and adults

- Some patients have found **alternative therapies** useful for some of the symptoms
  - Acupuncture, vitamin therapies, diet and lifestyle changes

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**Second-Line Therapies**

- Abatacept
- Acthar
- Cyclophosphamide
- Cyclosporine
- Tacrolimus (Prograf)
- Mycophenolate (Cellcept or Myfortic)
- Rapamycin
- Rituxan
- Rituximab

*Talk to your doctor about the appropriate therapy for you-based on symptoms, age, side-effects and delivery methods.*
Current Treatment Options

• **None** of them:
  – Are **specifically designed** to treat Nephrotic Syndrome

• **Sometimes treatments:**
  – Have some short and long-term **side effects**
  – Are classified as ‘off label’ and therefore may bring **insurance headaches**
  – May become **ineffective** over time
Are there established guidelines for how to treat Nephrotic Syndrome?
Common Questions about Nephrotic Syndrome Treatments

I was labeled “steroid resistant” and my doctor still has me taking prednisone with my second line medication. Why?
Common Questions about Nephrotic Syndrome Treatments

Why do different doctors prescribe different second line medications for people with the same diagnoses?
I want to participate in a clinical trial, but my doctor said she wants to try other medications first. Does this make sense?
Should I get a genetic test? Will the results impact my treatment plan?
Common Questions about Nephrotic Syndrome Treatments

Why would I want to join a clinical trial? How do I know which clinical trial is right for me?

About the DUPLEX Study

- The aims of the study are to learn how safe the investigational medication is and to see how well it works to slow the decline of kidney function in patients with FSGS.
- Approximately 300 people will participate in about 150 study sites worldwide.
- The study will last up to 27 months.
- Participants receive either sparsentan or a comparator medication, which are taken by mouth.

You may be eligible to participate in the DUPLEX Study if you:
- Are 8–75 years of age living in the US (18–75 years of age in other countries)
- Have been diagnosed with FSGS without a known or obvious cause

Talk with your doctor and family members about joining the DUPLEX Study. Sites are open and currently recruiting.

To find a site near you, visit FSGSDUPLEX.com, clinicaltrials.gov NCT03493685, or contact medinfo@retrophin.com
The Gateway Initiative: Helping Clinical Trials Succeed, and Addressing Gaps in Treatment
Solution 1
Clinical Trials are not well publicized

Gateway to find patients & expand the clinical trial-ready community

- User friendly clinical trials.gov digital tool
  - www.kidneyhealthgateway.com

Global expansion
- NephCure Canada
- NephCure European partnerships
# KidneyHealthGateway.com Digital Tool

## Am I Eligible?

**What is your current eGFR?**

**Why are we asking this question?**
Not sure of your eGFR? Copy and paste this link into a new browser tab to calculate your estimated value:

[https://www.kidneydiseaseinfo.com/home/physicians/egfr-calculator](https://www.kidneydiseaseinfo.com/home/physicians/egfr-calculator)

- [ ] > 60
- [X] 45-60
- [ ] 30-44
- [ ] 15-29
- [ ] <15
- [ ] NOT SURE

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Patient friendly website with log-in feature for customized trial connector.
NEPHROTIC SYNDROME SPECIALISTS PROGRAM
Timely treatment and prognosis

Patients who receive expert care earlier are more likely to access appropriate treatments (including clinical trials) sooner and experience better outcomes.

Patients who experience a delay in finding expert care are at risk for irreversible kidney (podocyte) damage.

*Most nephrologists see only a handful of primary nephrotic patients throughout their career!
NEPHROTIC SYNDROME SPECIALISTS

Pilot Phase
- 100 Nominated Pediatric & Adult Clinicians
- Selection Criteria
- Continuing Medical Education Program
- List of designated specialists

2019 & Beyond
- Growing list to 300 specialists
- Expanding to countries beyond the US
- Leveraging influence around trials
SUMMARY

• Goals of Treatment:
  - **Reduce** proteinuria
  - **Lower** blood pressure
  - **Reserve** kidney function

• Each therapy has its own risks and side effects - have an **open and honest conversation** with your doctor

• **Clinical Trials** are therapeutic options too. Ask your doctor

• The importance of clinical trials and the **Gateway program** to help you find the right trial for you

• Lifestyle **changes** help reach treatment goals