"The Wilson's Disease Association funds research and facilitates and promotes the identification, education, treatment, and support of patients and other individuals affected by Wilson's Disease."

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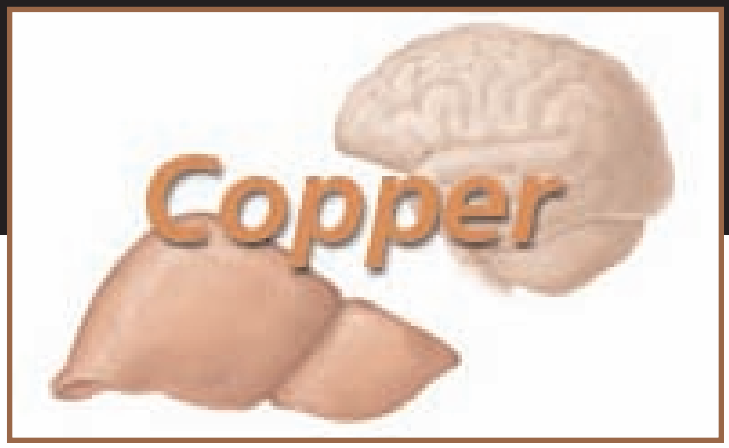

WILSON DISEASE:
MAINTAINING A SUCCESSFUL TREATMENT PLAN

WILSON'S DISEASE ASSOCIATION
INTERNATIONAL

PATIENT HANDBOOK

WILSON DISEASE:

MAINTAINING A SUCCESSFUL TREATMENT PLAN

A Patient Handbook

Authored by:

Mary L. Graper
President
Wilson's Disease Association International

First Edition
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WDA Executive Director:

Kimberly Symonds, manages the national office in Wooster, OH, and facilitates all essential program and administrative tasks. Her efforts are vital to the success of the Association.

Medical Advisory Committee:

Our Board and staff are guided by its Medical Advisory Committee (MAC) whose members are healthcare professionals with relevant professional degrees, knowledge, and demonstrated clinical and/or scientific expertise pertinent to Wilson disease. Without their volunteer assistance, the WDA would not be able to accomplish the many patient initiatives that we do. Current members of the MAC are:

Chair, Michael Schilsky, M.D.
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Our Mission
The Wilson's Disease Association funds research and facilitates and promotes the identification, education, treatment, and support of patients and other individuals affected by Wilson's Disease.

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INTRODUCTION

Much research has shown evidence that self-management tools, when used by patients with a chronic disease, substantially improve outcomes. These include reduced healthcare costs, fewer hospitalizations, emergency situations, unplanned physician office visits, and an overall better quality of life.

Self-Management is not to be confused with "Self-Care". Self-Care would be to make changes in your treatment on your own, without consulting a professional. This could be detrimental to your health and lead to undesirable outcomes. Self-Management tools are strategies employed by you the patient, your family, friends, advocates, and caregivers in partnership with your healthcare professionals. **Do not attempt to use any of the strategies or suggestions included in this guide without advice from your healthcare team.** In other words, do not try it on your own. Always consult the healthcare professionals in charge of managing your Wilson disease (WD). Your job is to be observant in monitoring and noting subtle changes in physical or emotional symptoms, laboratory values, or other difficulties you may be having, that might be important information for your physician or other health care professionals to have when determining your further course of treatment.

You are central to the success of your treatment, but you are not alone in your journey. It is a group effort (Figure 1). The Wilson's Disease Association (WDA) has written this guide to assist you and others in understanding what issues may be important in managing your care. There are also useful suggestions on ways that you can help yourself. Treatment of WD is very individualized, as are many of its symptoms. Much of this information may not pertain to you, but this guide is an attempt to address many of the issues you may encounter during the course of your disease. It is not a substitute for medical advice from your treating physician, but rather a tool to assist you and your physician in providing the best care for you, and peace of mind for yourself and your family. **The importance of adhering to your treatment plan, including regular medical exams and testing cannot be underestimated!**

Figure 1.

CHAPTER 1: MEDICAL CARE

Choosing a Physician

If you are reading this handbook, you or a family member most likely have already been diagnosed with WD. Perhaps you are happy with your current doctor, or perhaps not. Choosing the right doctor to manage your WD is one of the most important decisions you can make. You have a rare disease, one that not every physician can be adept in treating. Choose a doctor who is knowledgeable about WD or is interested in learning about it and willing to consult with experts if necessary.

Helpful Tips:

- Ask prospective doctors, "How many patients with WD have you seen or treated in your career?"
- Find out if they have read the most current, accurate literature on treatment and monitoring. If the answer is no, then ask if they would be open to reading what you would be happy to provide, and/or consult with a WD expert as necessary. If you are uncomfortable with their demeanor and find yourself questioning their capabilities…look further….
- Contact the WDA for a recommendation of a qualified physician. Ask other patients with WD who they use as a treating physician and if they are satisfied.
- Consider traveling to a Wilson Disease Center of Excellence, as listed on the WDA website, to consult with its WD team. If your insurance plan does not cover this, consider making an appeal to them for coverage.

Your Role

It is important with any disease that patients play an active role in their healthcare. When you have a rare disease like WD your active participation is absolutely essential. If you don't know the answer to something, ask! The Internet has a wealth of information and we, in the 21st century are fortunate to have this wonderful resource. But, remember all information to be found there is not necessarily good information. So, if you aren't sure about something you find, ask a professional or consult with the WDA.

"Knowledge is Power."
-Sir Francis Bacon

Helpful Tips:

You should…

- Learn as much as possible about WD, your treatment options, and possible outcomes. Consult the WDA website at www.wilsonsdisease.org and request educational literature from the WDA.
- Question treatment decisions if you don't understand them or disagree with them. Seek a second opinion if you are still dissatisfied or confused.
- Accept that this is a lifelong illness that requires your attention and adherence to your treatment plan. Be a patient patient! Improvement takes time!
- Remember that you are not alone and if need be seek out the support of family, friends and others with WD.

Advocates

Sometimes it can be difficult to advocate on your own behalf. Maybe you find it hard to be objective about, and mindful of, what is necessary for your own well being, or you have difficulty with communicating or remembering things. In this case, choose a trusted friend or family member to advocate for you. Two sets of eyes, ears, and minds can often be better than one. Remember to sign the proper release forms so that your physician can include your Advocate in discussions about your medical care.

Helpful tips:

Your Advocate should...

- Know you well, be supportive, reliable, and be willing to do whatever is in your best interest.
- Learn as much as possible about WD and how it has affected you.
- Be familiar with treatment options and monitoring tools.
- Get to know your healthcare providers and be authorized by you to discuss your case with them.

Your Advocate could...

- Suggest questions to ask your doctor based on your Advocate's observations and your input.
- Accompany you to your appointments, take notes during your exam, clarify information the physician is providing, or ask additional questions that may not have occurred to you.
- Help you understand and remember any instructions given by your doctor and ensure that you are following them between appointments.
- Call your physician for any laboratory results, review them with you, and help you formulate any questions about the results.
- Assist in any other way that you, your Advocate, and your healthcare providers think may be helpful.

Visiting Your Doctor

Making and keeping regular appointments, as recommended by your physician is essential to monitor your progress. Most physicians recommend biennial (twice yearly) visits and ***biochemical testing***. If there is a specific problem that needs additional monitoring, more frequent visits and testing may be recommended. In general, doctors are busy and most likely have scheduled a limited time for your examination. In order to get the most out of your visit, consider the following points.

Helpful tips:

Before you go...

- If your doctor tends to be busy or overscheduled, try to request the first appointment of the morning or afternoon. This may shorten the time you spend in the waiting room.
- Contact your doctor's nurse to inquire whether you need to have any laboratory testing done prior to your appointment.
- Make a list of all your medications and the schedule for taking them.
- If there are any specific problems you feel need to be addressed, beyond the scope of a routine exam, inquire whether you might need to schedule a longer appointment.
- Ensure that your treating physician has received any other lab results from other specialists you may have seen. If you can, bring copies of these with you to your examination.
- Be sure that your ***"Wilson Disease Patient Lab Tracker"*** is up to date and any new information has been recorded.
- Make a list of questions you may have for your physician so that you will not forget to ask them during your visit.

When you go...

- Take along your updated ***"Wilson Disease Patient Lab Tracker"*** and any other lab results your physician may not have seen.
- Be sure you bring your current list of all medications, including vitamins, herbal, homeopathic, and over-the-counter remedies and the dosages you are taking or, take the bottles along with you so that the doctor or an assistant can accurately review them.
- Arrive early if there is any new insurance, contact, or other information you wish to provide.

> ***"Nothing in life is to be feared. It is only to be understood."***
>
> *-Marie Curie*

While you are there...

- Answer all of your doctor's questions honestly. If you don't, you are only hurting yourself!
- Report any new symptoms or changes since your last visit. Ask whether they are relevant to your WD and what, if anything, you need to be aware of and report.
- Discuss any difficulties you may be having with taking your medication; timing, reactions, adherence (if you are taking the medications as prescribed), etc.
- Be aware of any trends in lab values you note, as reflected in your ***"Wilson Disease Patient Lab Tracker"***, and ask what they might mean.
- Ask the doctor or his assistant to write down any new instructions and explain them to you. If you have questions about them, this is the time to ask!

Your Healthcare Team

While your healthcare may be managed by your local ***Primary Care Physician*** (PCP), you may need to be referred to other specialists as necessary to monitor other aspects of your care. (Table 1) If you are being cared for by a WD Center of Excellence you may see one or more members of the WD interdisciplinary team. It is important to be familiar with who your healthcare team members might be, their area of expertise, and their role. (Table 2)

Table 1. LICENSED MEDICAL DOCTORS

TITLE	ROLE
Primary Care Physician	An M.D. who oversees your overall health care issues in addition to WD. Should receive periodic reports from any specialists you may see.
Academic Physician	An M.D. who practices clinical medicine, engages in scientific research, and is a faculty member at an accredited medical school.
Hepatologist	An M.D. who has undergone specialized training in the field of gastroenterology and concentrates on treating liver diseases.
Neurologist	An M.D. who has undergone specialized training and concentrates on treating disorders of the nervous system.
Movement Disorders Specialist	A neurologist with additional training in the specialty of neurological disorders that affect the speed, quality, and ease of body movements.
Psychiatrist	An M.D. with specialized training in diagnosing and treating psychiatric, behavioral, and emotional disorders.
Resident/Fellow	A "Resident" is a physician in training. A "Fellow" has completed their Residency training and is training in a subspecialty.

Table 2. OTHER LICENSED HEALTHCARE PROFESSIONALS

TITLE	ROLE
Dietician/Nutritionist	Plans diet and nutrition programs for patients with dietary restrictions
Genetic Counselor	A medical genetics expert with a master of science degree
Medical Assistant	Performs various administrative and basic clinical tasks.
Registered Nurse (RN)	Has completed a certified RN program and performs basic medical tasks as instructed by a physician. Often provides educational resources and coordinates your care.
Nurse Practitioner (NP)	An RN with advanced training who can perform physical exams and prescribe medicine and other therapies.
Physician's Assistant (PA)	Has completed a 2 year certified PA program and practice medicine under the supervision of an M.D.
Social Worker	Assists individuals and families with counseling and by providing resources for financial, employment, disability, and other issues created by a chronic illness.
Physical Therapist (PT)	Experts in evaluating and treating mobility problems and assisting caregivers on effective ways to provide assistance.
Occupational Therapist (OT)	OTs help patients improve their ability to perform tasks in living and working environments. They design treatments to develop, recover, or maintain the daily living and work skills of their patients.
Speech Pathologist	An expert trained to evaluate and treat speech, voice, swallowing, and communication problems.
Pharmacist (RPh)	A valuable resource for providing information on prescription medication and possible side effects and drug interactions.

CHAPTER 2: MEDICATIONS

Treatment to reduce excess copper…

This is THE most important medication you must take. Treatment for WD is LIFELONG. The current accepted therapies for WD are the ***chelators***, trientine (Syprine®) and d-penicillamine (Cuprimine®[USA]), and a ***metallothionein inducer***: zinc salts (zinc acetate, Galzin™[USA], Wilzin®[Europe]), zinc gluconate, zinc sulfate and others. A New Drug Application has been filed in the United States, with intent to file in Europe, for a new ***chelator***, ammonium tetrathiolmolybdate (TM) treatment for Wilson disease (Coprexa™). For more information on each, including dosing and monitoring guidelines, please refer to the WDA publication, *A Diagnosis, of Wilson's Disease, What Now? Treatment and Management.* Your physician should be familiar with the accepted treatment and monitoring guidelines and make adjustments in your regimen as necessary.

Non-Adherence is a Fatal Disease!

Pregnancy…

All women with WD who become pregnant must remain on their copper reduction therapy throughout their entire pregnancy. If you discontinue your WD treatment while you are pregnant, you risk a decline in your health and liver failure may occur. Ask your obstetrician to consult with your hepatologist concerning any adjustments in your dosages. Current recommendations indicate that if you are on zinc salts therapy no adjustment is necessary. For the chelating agents, d-penicillamine and trientine, a 25% - 50% dosage reduction is suggested. As always, continue regular monitoring to ensure adequate copper balance.

Adherence (Compliance with taking your medications)…

Taking your medicines as prescribed is extremely critical to the success of Wilson disease treatment. One of the advantages of having WD is that it is VERY treatable with effective, safe medications leading to a normal life expectancy…IF…you faithfully take your medications, as prescribed, LIFELONG. There are varying reasons for non-adherence in patients with WD and your physician has probably heard them all. Adherence is especially difficult in patients who were asymptomatic at diagnosis. These patients often do not see a cause and effect relationship: "Now that I am on medication, I feel much better." Here we offer some possible solutions to some of the complaints you may have. (Table 3)

Table 3.

COMPLAINT	SOLUTION
"I forget"	Ask someone to remind you or purchase a Pill Box Timer, take your medications the same time every day as part of your daily routine.
"I'm not sure how to take them"	Ask your doctor to clarify the schedule for taking your medication.
"I feel fine"	You still have a life-threatening illness that will worsen without your medication. Take them diligently regardless of how you feel.
"I have unpleasant side-effects"	Ask your doctor what you can do to relieve them.
"I have too many pills to take"	Make a written daily timeline for yourself, hour by hour, to ensure proper spacing between meals and other medications.
"I have trouble swallowing"	You might need to be evaluated by a ***speech pathologist*** or have other studies to determine if there is a physical reason for your difficulty swallowing.

Vaccines…

Ask your physician if you are immune to Hepatitis A and B. If you are not, you should receive vaccinations for Hepatitis A and B. These and other forms of viral ***hepatitis***, if contracted can cause additional liver damage. The Hep A and B vaccinations will offer protection against infection of these viral diseases that afflict the liver.

Pain Medication…

You may be confused about what medication to take for occasional aches and pains. This should be discussed with your physician and you should adhere to that advice. Many of the nonsteroidal anti-inflammatory drugs (NSAIDs), e.g., ibuprofen, can cause liver and kidney damage, and too much acetaminophen, e.g., Tylenol, can cause liver injury. Many other pain medications might contain combinations of pain killers, including acetaminophen, so it is important to discuss their safety with your ***pharmacist*** and physician.

NSAIDs? **OR** **Acetaminophen?**

Other Medications...

You may have other conditions, either associated with your WD or unrelated, that require medication. Again, it is very important that your WD treating physician be aware of what you are taking to ensure that they will complement your WD treatment regimen rather than interfere with it.

CHAPTER 3: DIET AND NUTRITION

Food…

Adherence to a low copper diet is most important during the initial phase of treatment. The recommendation is to avoid the foods highest in copper content: organ meats, shellfish, chocolate, nuts, and mushrooms. Once copper levels have stabilized at normal levels, these foods are allowed occasionally. Refer to *"Copper Content of Foods"* on the WDA website. For a more comprehensive list refer to the U.S. Department of Agriculture (USDA) website at www.usda.gov and click on "Nutrient Lists". If you are a vegetarian, please consult a ***dietician***, as many of the foods and protein sources in a vegetarian diet are high in copper. **Wilson disease cannot be managed by diet alone. Proper medication is necessary lifelong!**

Water…

Copper content of the drinking water you consume should also be tested. If the water is over 0.1 ppm (parts per million) (which is 0.1 mg/L), consider an alternate water source or invest in a good filtering system that removes copper. Your local community or private water testing firms can perform the testing on your home water supply. If you have copper plumbing in your home, some of the copper content can be reduced by running the water for a while before you use it. As water sits in the pipes the copper leaches into the water. For this same reason, avoid using copper cookware for preparation of food. If you work or reside in a location where the water supply has not been tested, consider using bottled water that does not contain copper.

Vitamins…

Consult your healthcare professional before taking a multi-vitamin. If your physician approves, ask your ***pharmacist*** to find a good supplement that does not contain copper. If you are a woman who is pregnant, or wishes to become pregnant, please have your obstetrician consult with your ***hepatologist*** before prescribing prenatal vitamins. Most prenatal vitamins contain an abundance of copper and these should be avoided.

Other Dietary Supplements…

There are many over-the-counter dietary supplements and herbal preparations that claim to be beneficial for some part of your body. Be cautious about this because many can interact with other prescription medications you are taking. Some can be beneficial but others may actually be injurious to your health. Also, many supplements are processed by the liver and may cause additional liver damage or, in the case of existing liver damage, may not be properly utilized by the body. Please refer to the U.S. Food and Drug Administration (FDA) publications, *"What Dietary Supplements Are You Taking? Does Your Health Care Provider Know? It Matters, and Here's Why" and "Dietary Supplements What You Need to Know"* included with this Handbook (Insert). These contain much useful information about dietary supplements, and personal logs that you can fill in and **share with your doctor**.

CHAPTER 4: SPECIAL CIRCUMSTANCES

Some patients may experience more severe manifestations of WD. There are some self-help measures you can take to avoid an emergency situation. But, always remember that if you are having an extreme emergency, seek help **immediately**! Wear a MedicAlert® bracelet so that others will know how to help you.

Hepatic Issues

Ascites

Fluid accumulation within the abdominal cavity that occurs with portal-hypertension (increased pressure in the circulation from the intestine to the liver caused by scarring or swelling of the liver). This may be treated by restricting dietary salt and use of diuretics or "water pills" as they are commonly known.

Bleeding Tendency

Causes of "easy" bleeding include ***thrombocytopenia*** due to hypersplenism from ***portal hypertension*** or due to reduced levels of clotting factors due to the liver damage caused by WD in some patients. If you have this problem, your physician should be advising you on the likelihood that it will continue or resolve. Meanwhile, there some measures you can employ to reduce the incidence of, or guide you through, a potential bleeding episode.

Helpful Tips:

- Personal care: use a soft toothbrush to prevent bleeding gums; use an electric razor; keep your fingernails short and smooth; avoid hard, repeated scratching of itchy skin.
- Watch for increased bruising and spreading of existing bruises.
- Avoid foods that may irritate the mouth or intestinal track.
- If you are prone to nosebleeds, do not tilt your head back in an effort to stop it. Instead you should sit upright, pinch the nose shut applying pressure to the nose and breathe through your mouth. Once the nosebleed has stopped, do not pick or blow your nose, or bend over for several hours.

Esophageal Varices

If you are thought to have cirrhosis with ***portal hypertension***, you are at risk for developing distended veins in the esophagus or stomach (or other places in the gastrointestinal tract). These distended veins or **varices** can bleed at times. You might need to undergo an endoscopic evaluation to look for these varices, and may require medication to lower pressure or even direct banding of the varices to eradicate them. **If you experience severe gastrointestinal bleeding as evidenced by vomiting blood or dark tarry stools, this may indicate a variceal bleed and is a life-threatening emergency. Call emergency services (911) and get transported to the nearest emergency room immediately!**

Hepatic Encephalopathy

An occasional complication of liver impairment due to WD is ***encephalopathy*** or altered mental function. ***Encephalopathy*** may be very subtle with minor lapses in concentration and sleep disturbance, or more severe with disturbance of speech, gait and other motor functions or an alteration of the level of consciousness that can progress from lethargy to coma. Factors that may worsen ***encephalopathy*** include medications that alter consciousness (e.g. many sleep aids and sedatives), constipation, kidney failure, infections and worsening liver function.

If symptoms of ***encephalopathy*** are noticed either by you or someone else, please seek intervention from your ***hepatologist.*** Your ***hepatologist*** can evaluate the cause of the episode and its severity and may recommend changes in diet or additional medication until the condition has reversed.

Neurological Issues

If your case of WD has caused neurological symptoms, these symptoms may vary depending on the extent to which your brain has been affected and location of the injury due to deposition of copper before you were diagnosed. ***Dystonia*** (increased muscle tone) and ***dysphagia*** (difficulty swallowing) may cause significant disabilities or lead to risk of further injury. Ask your physician to what extent these symptoms are present, and whether they may resolve or improve over time. In certain circumstances, other adjunct therapies or even surgical intervention are available to improve your quality of life.

Swallowing Problems (Dysphagia)

Helpful Tips:

- Seek help from a speech therapist or other expert. You may benefit from thickeners for liquids or other measures designed to help with swallowing.
- Do not eat alone. Make sure your dining companions are familiar with the Heimlich maneuver.
- Cut your food into small pieces and eat slowly, chewing thoroughly before swallowing. Do not talk with food in your mouth.
- If something gets stuck in your throat, try to clear your throat and try to swallow it again, or spit it out before taking a breath, to avoid aspiration.
- Sit upright, with your head tilted slightly forward, while eating and remain upright for awhile after finishing. Drink plenty of fluids with meals. Using a straw for fluids may be helpful.
- Drooling can occur if you are not swallowing as frequently. Try taking small sips of water throughout the day to encourage more frequent swallowing. Chewing gum may also help to control drooling. *Note: Botox injections applied to the salivary glands by a* ***Movement Disorder Specialist*** *may also help to reduce saliva production.*
- Consult with a dietician about the types of foods that may be more easy to swallow

Difficulty Speaking (Dysarthria or Dysphonia)

Helpful tips:

- Ask your physician about an evaluation by a ***speech pathologist*** and possible speech therapy.
- Carry written identification and an explanation of your problem.
- Carry writing material, prewritten words, or another assistive speaking device.
- Have an audible means of attracting the attention of those to whom you wish to speak, such as a bell, whistle, etc.
- Inquire about the possibility of using an assistive speaking device such as a voice amplifier or portable electronic communicator.

Difficulty with Balance/Walking (Segmental or Generalized Dystonia, Dyscoordination)

Helpful tips:

- Ask your physician about an evaluation by a ***Physical*** or ***Occupational Therapist***.
- Walk slowly and rest frequently if you are having difficulty or tire easily.
- Use a cane, walker, wall, or companion's arm for support if necessary.
- Remove household obstacles such as throw rugs, high thresholds, children's or pets' toys or anything else that you might stumble on. Avoid slippery floors, especially in stocking feet.
- If you have difficulty going up or down stairs, sit down and raise or lower yourself step by step.
- Install rubber safety treads and a rail in your shower. Sit on a shower chair while bathing or showering.

Seizure Disorders

About 6% of patients with WD may experience epileptic seizures from the copper deposition and related damage in certain areas of the brain. This incidence is about 60% higher than in the general population. Occasionally, some patients may experience seizures after starting penicillamine treatment. If you have experienced seizures you will need to continue to undergo evaluation and monitoring by your doctor and you may need medication specifically to prevent recurrent seizures, but there are some things you can do to keep yourself safe.

Helpful Tips:

- If you feel a seizure coming on, and you are at home alone, call your emergency number (e.g., in the United States, 911). If you are in public, call out for help.
- Lie down on your side in a safe area; if you have anything in your mouth, spit it out.
- If you are driving, put on your hazard lights, pull out of traffic, and turn off the engine. Call 911 or use the horn to summon help.
- Remove hazards in your home that might cause a fall, or injury during a fall; keep your bed low to the floor; avoid activities that may trigger a seizure.

Tremors

Tremors are caused by lesions deep inside the brain that can cause your arms, head, hands, trunk or legs to shake. They are not life-threatening but may be embarrassing or make some tasks difficult to perform. Ask your physician or Movement Disorders Specialist if there is any medication, physical therapy, or surgery that may help to alleviate some of effects of your tremors. There are also many adaptive devices commercially available to make some of your daily activities easier.

> ***"Wendy (a WD patient with tremors), are you cold?"***
>
> *-Elliot, Age 11*

Action Tremor → Tremor that occurs during intentional movements such as eating, drinking, writing.

Postural Tremor → Tremor that may be absent in a certain body position but are triggered by a particular movement or change in position.

Intention Tremor → Tremor that is triggered by reaching out to grasp an object.

Rest Tremor → Tremor that occurs in the affected part of the body when the body is relaxed.

Psychiatric Symptoms

Psychiatric manifestations, including behavioral abnormalities, unstable mood, depression, personality changes, delusions, hallucinations, cognitive impairment, and suicidal thoughts, are more prevalent in patients presenting with neurological Wilson disease than with the hepatic presentation. Frequently psychiatric symptoms are the initial presentation, noted by the physician, and patients are often referred to a ***psychiatrist*** for treatment before the underlying cause is discovered.

Some of these symptoms may abate with successful treatment of the WD. Others may be permanent depending on the degree of severity of the neurological involvement. Moreover, some mood disorders may simply be reactive to the challenges of living with a chronic disease. Nonetheless, your mental health is critical to your overall sense of well-being and should be taken seriously.

Helpful tips:

- Make your treating physician aware of any of these issues and ask whether you might benefit from seeing a mental health professional.
- If you are being treated by a mental health professional, make sure that your diagnosis of WD is known.
- Identify and avoid anything, as much as possible, that may trigger or worsen the symptoms.
- Develop a coping strategy. Utilize relaxation techniques: deep breathing exercises, listening to soothing music, meditating, practicing yoga, self-hypnosis, or whatever seems to help.
- Be sure that your family and friends are aware of, and understand your problems and how best to support you. They should know what to do for you if you are engaging in more unusual, dangerous, risky, or harmful behavior.
- Try to listen to their feedback. If they say that you are scaring them, please listen and ask for additional help. If you are scaring yourself, please seek medical help immediately.

Sleep Disorders (*Insomnia or Hypersomnia*)

Keep in mind that often times sleep problems can be related to mood disorders, stress, tension, anxiety, and some medications. Discuss this possibility with your doctor. Report sleepwalking, sleeptalking, strange dreams, or other unusual behavior. Insomnia at bedtime can cause daytime sleepiness (hypersomnia), irritability, and lack of concentration or memory.

> ***Always laugh when you can. It is cheap medicine.***
> *-Lord Byron*

Helpful tips:

- If you have insomnia try to go to sleep at the same time each night, avoid stimulants such as caffeine and heavy meals late in the day, get regular exercise but not too close to bedtime, do something relaxing prior to attempting sleep.
- If you are sleepy during the day do not operate a vehicle or machinery, be the sole person in charge of young children, or perform activities requiring concentration. Change your position, get up and move around, or attempt some light exercise if possible.

Other

Traveling

If you are planning to travel, ask your treating physician for a letter describing your medical history. Carry the letter and your ***"Wilson Disease Patient Lab Tracker"*** with you in case you require medical attention while away from home.

CHAPTER 5: FAMILY CONCERNS AND GENETICS

Most likely when you were diagnosed your physician encouraged you to have your close family members tested for WD also. Because WD is transmitted as an ***autosomal recessive disease***, if you have WD, each of your parents carries a gene change, called a ***mutation***,that when passed on to you together, led to your WD. If you have siblings, who have the same mother and father, it is possible that some of them may also have inherited both of these ***mutations*** and have Wilson disease. Each of your family members has a chance of carrying one of these ***mutations*** and therefore the chance of having WD. (Figure 2) There are biochemical and genetic testing methods to have your family members tested. Please ask your physician which method of testing is most suitable for your family members and ask if a consultation with a ***genetic counselor*** is advisable.

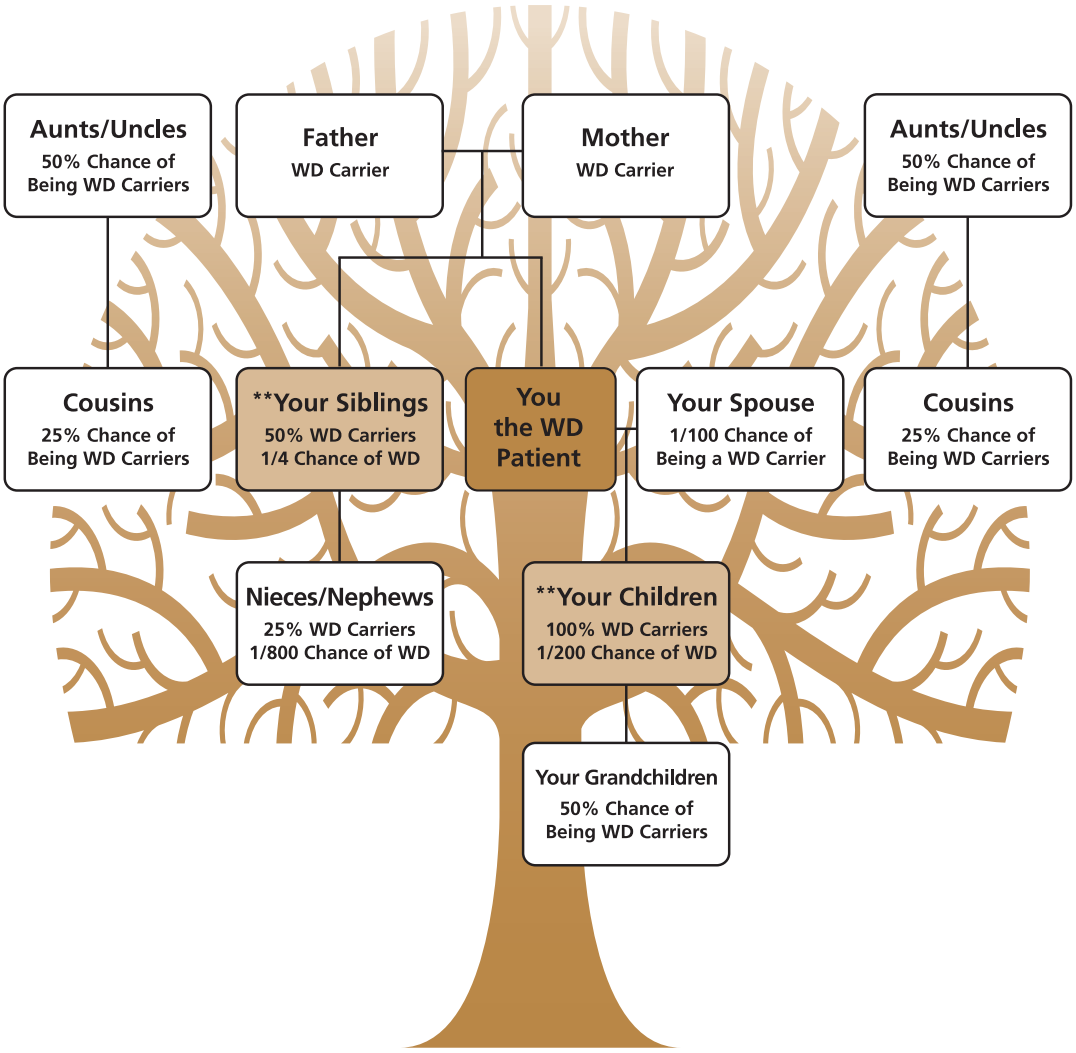

Figure 2. RISK OF FAMILY INHERITANCE OF WILSON'S DISEASE

***Highest risk of having WD and should be tested*

This ***pedigree*** is a basic risk profile for family members. A ***genetic counselor*** can provide a more detailed ***pedigree*** of specific family relationships for your family.

APPENDIX A: GLOSSARY OF MEDICAL TERMS

This section is intended to help you understand some of the medical "jargon" that you may hear or see in print during the course of your treatment. The terms are explained, as much as possible, in layman's language to make it easy for those who are not well versed in medical terminology.

Ageusia - Loss of taste.

Agranulocytosis - An acute condition marked by severe decrease in white blood cells and by fever, exhaustion, chills, swollen neck, and sore throat sometimes with local ulceration; believed to be basically a response to the side effects of certain drugs.

Alopecia - Sudden loss of hair in defined patches with little or no inflammation.

Anaphylaxis - Extreme sensitivity to a foreign protein or drug; can be severe and sometimes fatal; causes a drop in blood pressure, difficulty breathing, fainting, itching, and hives.

Anemia - A condition caused by too few red blood cells in the bloodstream, resulting in insufficient oxygen to tissues and organs.

Anorexia - Prolonged loss of appetite and distaste for food.

Aplastic anemia - Anemia that is characterized by defective function of the blood-forming organs (as the bone marrow) and is caused by toxic agents or is idiopathic in origin. Also called ***hypoplastic anemia***.

Ascites - The accumulation of fluid in the abdominal cavity, most commonly caused by cirrhosis of the liver.

Basal ganglia - Group of cells deep in the brain that initiate and control movement.

Bile - A yellowish green digestive fluid produced in the liver necessary for the digestion and absorption of fat.

Biochemical testing - Measuring the amount of a substance in the body through blood or urine analysis.

Ceruloplasmin - A blood glycoprotein to which copper is bound during transport and storage.

Chelator - binds the excess copper in the body and increases the excretion of copper in the urine.

Cholestasis - A reduction or stoppage of **bile** flow between the liver and the upper part of the small intestine.

Cirrhosis - A chronic progressive disease of the liver characterized by the replacement of healthy cells with scar tissue (**fibrosis**).

Cupriuria - The presence of excess copper in the urine.

Cutaneous macular atrophy - Spotted skin rash.

Diplopia - A disorder of vision in which two images of a single object are seen because of unequal action of the eye muscles (***double vision***).

Dysarthria - Difficulty in speaking words due to poor coordination of the speech muscles. Speech is slurred and there are uncontrolled fluctuations in volume.

Dysphagia - Slow movement of the tongue, lips, throat and jaws that causes drooling and difficulties in swallowing, caused by dystonia of the vocal chords. The voice may be hoarse, tone and volume may be diminished causing the speech to have a soft whisper-like quality

Dystonia - The condition of a sustained increase in muscle tone, sometimes with contractions or spasms of muscles of the shoulders, neck, and trunk. It frequently causes twisting and repetitive movements or abnormal postures, due to disease involving the basal ganglia of the brain.

Edema - The swelling of soft tissues as a result of excess water accumulation.

Elastosis perforans serpiginosum (EPS lesions) - Ring-shaped small, localized, superficial, solid elevations of skin, possibly occurring in groups. They may be discolored in varying hues of red, brown, or black. The outer layer of skin is thickened around a central plug of the skin's elastic tissue which is extruded through the outer layer of skin. EPS lesions have been identified as a possible side effect of long-term use of penicillamine.

Encephalopathy - A condition used to describe the harmful effects of liver failure on the central nervous system. Features include confusion ranging from confusion to unresponsiveness (coma). Symptoms generally related to the liver's inability to properly detoxify the blood and is associated with elevated blood ammonia levels. Treatment includes different methods to eliminate the production of ammonia from the gastrointestinal tract and to trap substrate for ammonia production so that it will not be absorbed by the gastrointestinal (GI) tract.

Endoscopy - A procedure using an endoscope , a small, flexible instrument that is a tube with a light and a lens on the end used to look into the esophagus, stomach, small and large intestine etc.

Esophageal varices - Stretched veins in the walls of the lower part of the esophagus and sometimes the upper part of the stomach and rarely in the small intestine and rectum. A complication of portal hypertension (increased blood pressure in the portal vein caused by liver disease). May cause massive bleeding.

Fatty liver (steatosis) - The build-up of fat in the liver cells.

Fibrosis - An abnormal thickening and scarring of the liver tissue.

Goodpasture's syndrome - A condition characterized by rapid destruction of the kidneys and hemorrhaging of the lungs. It is an autoimmune disease produced when the patient's immune system attacks cells presenting the Goodpasture antigen, which are found in the kidney and lung, causing damage to these organs; caused by a possible toxicity of penicillamine treatment.

Hematemesis - Vomiting of blood; may be red, appear as coffee grounds, brown or black.

Hematuria - The presence of blood or blood cells in the urine.

Hemolysis - Breakdown of red blood cells, causing fewer than normal red cells to be available in the circulation to transport oxygen.

Hepatitis - Inflammation of the liver.

Hepatomegaly - Enlargement of the liver.

Hepatosplenomegaly - Enlargement of the liver and spleen.

Hyperkeratosis - Thickening of the outer layer of the skin.

Hypogeusia - Decreased sensitivity to taste.

Jaundice - Yellow or greenish hue to the skin and/or whites of the eyes caused by elevated bilirubin (formed when red blood cells are broken down; bilirubin taken up and transported by the liver into bile that is excreted into the intestine.

Kayser-Fleisher ring - A brown or greenish brown ring of copper deposits around the cornea; can only be seen with a slit-lamp by an ophthalmologist or optometrist early on, but may be visible to the naked eye when very large.

Leukopenia - An abnormal reduction in the number of white blood cells (leukocytes) circulating in the blood, most commonly caused by a reaction to various drugs.

Lichen planus - Shiny, flat-topped bumps that often have an angular shape. These bumps have a reddish-purplish color with a shiny cast due to a very fine scale. The disease can occur anywhere on the skin, but often favors the inside of the wrists and ankles, the lower legs, back, and neck.

Lupus erythematosus - A disorder characterized by skin inflammation, especially over the nose and cheeks - "butterfly rash"; or red scaly patches.

Lupus nephritis - Inflammation of the kidney associated with systemic **lupus erythematosus** that is typically characterized by **proteinuria** and **hematuria**, and that often leads to renal failure.

Lymphadenopathy - Abnormal enlargement of the lymph nodes.

Melena - Passing of dark blackish stools, indicating a bleeding disorder in the upper gastrointestinal track.

Myasthenic syndrome - Progressive weakness and exhaustibility of voluntary muscles without atrophy or sensory disturbance.

Nephrolithiasis - A condition marked by the presence of renal calculi (kidney stones).

Metallothionein Inducer - Removes copper from the body by increasing the amount of metallothionein in the cells of the intestines. Copper is bound within these cells and excreted through the stool.

Nephrotic syndrome - A collection of symptoms that affect the kidneys, resulting in a severe, prolonged loss of protein into the urine, decreased blood levels of protein (especially albumin), retention of excess salt and water in the body, and increased levels of fats (lipids) in the blood.

Obliterative bronchitis - Acute or chronic inflammation in the lung, causing closure of the bronchial tubes.

Optical axial neuritis - Inflammation of the nerve of the eye.

Portal hypertension - an increase in the pressure within the portal vein (the vein that carries blood from the digestive organs to the liver). The increase in pressure is caused by an increase in resistance to the blood flow through the liver due to swelling or scarring of the liver.

Proteinuria - The presence of excess protein in the urine.

Pseudobulbar palsy - A set of clinical signs including slowed slurred speech; difficulty with swallowing; weakness of face, tongue, and swallowing muscles; a tendency for uncontrollable laughter or crying; and brisk jaw and gag reflexes.

Psychosis - A serious mental disorder (as schizophrenia) characterized by defective of lost contact with reality, often with hallucinations or delusions.

Ptosis - A sagging or prolapse of an organ or part (renal *ptosis*); the drooping of the upper eyelid from paralysis of the third nerve.

Serous retinitis - Inflammation of the retina of the eye.

Serum free copper (Non-ceruloplasmin bound copper) - The amount of serum free copper is the amount of copper circulating in the blood which is not bound by ceruloplasmin. This is the copper which is "free" to accumulate in the liver and other organs. To calculate serum free copper, use the following formula:
(Total Serum Copper in µg/dL) - (Ceruloplasmin in mg/dL _3) = Free Copper
(Normal range is 5 to 15 µg/dL)

Sideroblastic anemia - Large numbers of iron-containing red blood cells in the bone marrow.

Splenomegaly - Enlargement of the spleen.

Thrombocytopenia - Persistent decrease in the number of blood platelets.

Toxic hepatitis - Drug-induced inflammation of the liver.

Tremor - Involuntary, somewhat rhythmic movements of the muscles that cause various parts of the body to move uncontrollably.

µg - Microgram.

µMoles - Micromoles.

Varices - (*See Esophageal varices*).

APPENDIX B: GLOSSARY OF GENETIC TERMS

Allele - One version of a **gene** at a given location (**locus**) along a chromosome.

ATP7B gene - The WD gene, encodes a copper transporting ATPase mainly expressed in the liver that is mutated and rendered absent or dysfunctional in Wilson disease.

Autosomal recessive - Describes a trait or disorder that requires the presence of two copies of a **gene mutation** at a particular **locus** in order to express observable phenotype; specifically refers to genes on one of the 22 pairs of autosomes (non-sex chromosomes).

Carrier (Heterozygote) - A person who carries one normal and one abnormal copy of a gene and therefore does not have the disease. [assuming autosomal recessive]

Chromosome - A circular strand of **DNA** that contains the **genes** and carries hereditary information.

DNA - Genetic material of all living organisms.

First-degree relative - Any relative who is one meiosis away from a particular individual in a **pedigree**; a relative with whom one-half of an individual's genes is shared (i.e., parent, sibling, offspring).

Gene - The basic unit of heredity, consisting of a segment of **DNA** arranged in a linear manner along a chromosome. A gene codes for a specific protein or segment of protein, leading to a particular characteristic or function.

Genotype - The genetic constitution of an organism or cell; also refers to the specific set of alleles inherited at a locus.

Gene sequencing (mutation screening of the entire ATP7B gene - Analysis of the entire ATP7B gene to detect and identify disease-causing mutations. An individual with confirmed Wilson disease needs to be tested first. If both mutations are identified, other family members can then be offered testing. Gene sequencing will identify both mutations in most but not all cases of Wilson disease. Useful for family members to learn if they could be affected but do not yet have symptoms, to learn they are carriers, or to allow for prenatal testing for confirmed carriers.

Haplotype analysis (Linkage analysis) - Molecular genetic testing to identify a set of closely linked segments of **DNA** (a **marker** or set of markers), comparing the markers of family members to those of an affected patient. Useful for screening siblings of an identified patient.

Heterozygote - An individual who has two different alleles at a particular **locus**, one on each chromosome of a pair; one **allele** is usually normal and the other abnormal.

Homozygote - An individual who has two identical alleles at a particular **locus** one on each **chromosome** of a pair; a disease-affected individual.

Locus - The physical site or location of a specific **gene** on a chromosome.

Marker - An identifiable segment of **DNA**.

Molecular genetic testing - (synonyms: DNA testing, DNA-based testing, molecular testing) Testing that involves the analysis of **DNA** either through **linkage analysis** or sequencing, or one of several methods of detecting a **mutation**.

Mutation - A **gene** alteration that causes or predisposes an individual to a specific disease.

Phenotype - The observable physical and/or biochemical characteristics of the expression of a gene; the clinical presentation of an individual with a particular genotype.

Proband - The family member who is affected with a genetic disease (**homozygote**) whose **markers** are used to determine if other family members have the disease **(haplotype analysis) or same mutation (mutation analysis by sequencing)**.

Pedigree - A diagram of the genetic relationships and medical history of a family using standard symbols and terminology.

Second-degree relative - Any relative who is two meioses away from a particular individual in a pedigree; a relative with whom one-quarter of an individual's genes is shared (i.e., grandparent, grandchild, uncle, aunt, nephew, niece, half-sibling).

Targeted mutation analysis - Analysis of a specific location in the ATP7B gene for a known particular mutation. Useful for specific populations of patients where the common mutations are known; for screening siblings of patients with two identified mutations.

APPENDIX C: WILSON DISEASE PATIENT LAB TRACKER

Treatment and Monitoring of Wilson Disease

The following spreadsheet is designed to help you track your most important laboratory values and tests related to your Wilson disease. Included are some tests that should be done at regular intervals, as well as some that may be done only at the start of your evaluation. Those that are done only during the initial evaluation are included separately. The tracking sheet may contain tests that your physician may feel are not required at each visit, and we recommend that you discuss this with them.

These are basic labs that will be helpful to follow your copper status and the status of liver disease but will not be able to help you follow the neurological or psychiatric symptoms if these are present. These will require continued follow-up care with your physician or specialists.

Current recommendations for the frequency of laboratory testing for many of the tests included on the Patient Care Sheet are 2-4 times annually if you are further on in the course of your disease, and more frequently if there are specific problems that your physician is addressing (see reference). Included in the tracker are categories for common neurological and psychiatric symptoms for some affected patients. The responses to these are subjective, and you may wish to enter them as present, then improved (I), not improved (NI), or worsened (W). Please consult your physician or specialist as to how they would like to follow these with you.

Initial Evaluation

It is important to try to obtain copies of your original documents for any biopsy reports or molecular genetic studies since these will help you if you require care by other physicians. The Histology section, under Liver Biopsy, should contain discussion of any fibrosis, inflammation, or steatosis found on analysis. This "Tracker" is not meant as a substitute for your routine maintenance health care that may include such testing as immunity to Hepatitis A and B, bone density studies, ECG, fecal testing for occult blood, PAP smears and mammograms, screening and surveillance for liver cancer and other studies that your doctor would like to have you perform.

Copper Tracker

The copper calculators are provided as a separate spreadsheet. These will help you calculate your "free" or non-ceruloplasmin copper. Values typically should be between 5 and 15, however there is a wide range that may be seen due to the differences in technique and range for normal between laboratories, and the fact that this is a derived and not directly measured number. Therefore this value should not be interpreted in the absence of the other test results.

The other calculators are for determining the results of your 24 hour urine copper. Please pay careful attention to the way that the units the results are reported to you. In Canada and the European Union, values will be in micromoles while in the US it will be reported in micrograms. The volumes are often different as well – in Canada and the EU the concentrations are often reported as per liter, while in the US it is frequently reported as per deciliter (one tenth of a liter, abbreviated dl)

Reference:

Roberts E, Schilsky ML. *A practice guideline on Wilson disease*. Hepatology 37:1475-1492, 2003.
This reference is available through a link on the WDA website, www.wilsonsdisease.org, at: "About Wilson's Disease", Additional Reading.

Note: For a downloadable version of the Lab Tracker and Copper Tracker, with built-in formulas, to use in your Microsoft Excel program, please go to the Wilson's Disease Association website at: "About Wilson's Disease, Lab Tracker and Copper Calculator. If you do not have Microsoft Excel, you will also find a printable pdf. version of the Lab Tracker and an online Copper Tracker for your use. These pages are reproducible to enable you to record lab values for as long as you need them. There is no copyright protection on them.

TREATMENT AND MONITORING OF WILSON DISEASE

Name: Samuel K. Wilson		Reference	Date:	Date:	Date:	Date:	Date:
Medications	**Units**	**Range**	6/18/1998	7/13/1998			
d-Penicillamine	(mg/day)			250 tid**	** qd = once a day		
Pyroxidine (B6)	(mg/day)			50 qd**	bid = twice a day		
Trientine	(mg/day)				tid = 3 x day		
Zinc acetate	(mg/day)				qid = 4 x day		
Zinc (other)	(mg/day)						
Other medications:							
CBC/Platelets							
WBC	K/UL	4.8-10.8	6.4	7.1			
HgB	GM/DL	14.0-18.0	14.1	14.3			
HCT	%	42.0-52.0	41.2	40.9			
Platelets	K/UL	150-400	199				
Liver Function Panel							
Albumin	*Report the units and						
Total bilirubin	normal reference						
Direct bilirubin	values as your own						
Alkaline phosphatase	lab reports them.						
ALT	U/L	8.0-36	166				
AST	IU/L	13-38	67				
Alpha fetoprotein (AFP)							
Coagulation							
INR		0.0-1.1	1				
Prothrombin time	SEC.	22-33	33				
Copper and Zinc Parameters							
Serum copper							
Serum ceruloplasmin	MG/DL	20-40	23				
24 hour urine (copper/volume)	mcg/day	15-50	150	1950			
24 hour urine zinc							
Non-ceruloplasmin copper							
Urinalysis							
Protein							
WBC							
RBC							
Other							
BUN							
Creatinine							
Neurological Symptoms							
Absent	X		X				
Present	X						
Tremors	I NI W						
Speech (dysarthria)	I NI W						
Coordination	I NI W						
Swallowing	I NI W						
Insomnia	I NI W						
Other:							
Psychiatric Symptoms							
Absent	X		X				
Present	X						
Anxiety	I NI W						
Depression	I NI W						
Mood swings	I NI W						
Other:							

INITIAL EVALUATION		Date	Normal	Result
Liver Biopsy				
Hepatic copper content (mcg/g dry weight)		7/1/1998	10.1-35	1417
Histology				
Narrative: Fibrotic liver with marked		7/1/1998		
macrovesicular and microvesicular steatosis				
and scattered glycogen nuclei.				
Molecular Studies				
Mutation Analysis				
Haplotype Analysis (Affected, Unaffected, Carrier)				Affected
Narrative: Markers: D13S155, D13S169,D13S137,				
D13S228				
Immunology				
Hepatitis A immune status:	HEP A Ab		Negative	Neg.
	HAV IGM AB		Negative	Neg.
Hepatitis B immune status:	HB s Ag		Negative	Neg.
	HB s Ab		Negative	Pos.
	HB c Ab		Negative	Pos.
	HBc AB Igm		Negative	Neg.
Hepatitis C immune status:	HEP C VIRUS AB		Negative	Neg.
Liver Imaging				
CT scan				
MRI				
Sonogram				
Neurological Imaging				
CT Scan				
MRI				
PET				
Other				

TREATMENT AND MONITORING OF WILSON DISEASE							
Name:		**Reference**	**Date:**	**Date:**	**Date:**	**Date:**	**Date:**
Medications	**Units**	**Range**					
d-Penicillamine	(mg/day)						
Pyroxidine (B6)	(mg/day)						
Trientine	(mg/day)						
Zinc	(mg/day)						
Zinc (other)	(mg/day)						
Other medications:							
CBC/Platelets							
WBC							
HgB							
HCT							
Platelets							
Liver Function Panel							
Albumin							
Total bilirubin							
Direct bilirubin							
Alkaline phosphatase							
ALT							
AST							
Alpha fetoprotein (AFP)							
Coagulation							
INR							
Prothrombin time							
Copper and Zinc Parameters							
Serum copper							
Serum ceruloplasmin							
24 hour urine (copper/volume)							
24 hour urine zinc							
Non-ceruloplasmin copper							
Urinalysis							
Protein							
WBC							
RBC							
Other							
BUN							
Creatinine							
Neurological Symptoms							
Absent	X						
Present	X						
Tremors	I NI W						
Speech (dysarthria)	I NI W						
Coordination	I NI W						
Swallowing	I NI W						
Insomnia	I NI W						
Other:							
Psychiatric Symptoms							
Absent	X						
Present	X						
Anxiety	I NI W						
Depression	I NI W						
Mood swings	I NI W						
Other:							

TREATMENT AND MONITORING OF WILSON DISEASE							
Name:		Reference	Date:	Date:	Date:	Date:	Date:
Medications	**Units**	**Range**					
d-Penicillamine	(mg/day)						
Pyroxidine (B6)	(mg/day)						
Trientine	(mg/day)						
Zinc	(mg/day)						
Zinc (other)	(mg/day)						
Other medications:							
CBC/Platelets							
WBC							
HgB							
HCT							
Platelets							
Liver Function Panel							
Albumin							
Total bilirubin							
Direct bilirubin							
Alkaline phosphatase							
ALT							
AST							
Alpha fetoprotein (AFP)							
Coagulation							
INR							
Prothrombin time							
Copper and Zinc Parameters							
Serum copper							
Serum ceruloplasmin							
24 hour urine (copper/volume)							
24 hour urine zinc							
Non-ceruloplasmin copper							
Urinalysis							
Protein							
WBC							
RBC							
Other							
BUN							
Creatinine							
Neurological Symptoms							
Absent	X						
Present	X						
Tremors	I NI W						
Speech (dysarthria)	I NI W						
Coordination	I NI W						
Swallowing	I NI W						
Insomnia	I NI W						
Other:							
Psychiatric Symptoms							
Absent	X						
Present	X						
Anxiety	I NI W						
Depression	I NI W						
Mood swings	I NI W						
Other:							

INITIAL EVALUATION	Date	Result
Liver Biopsy		
Hepatic copper content (mcg/g dry weight)		
Histology		
Narrative:		
Molecular Studies		
Mutation Analysis		
Haplotype Analysis		
Narrative:		
Immunology		
Hepatitis A immune status		
Hepatitis B immune status		
Hepatitis C immune status		
Liver Imaging		
CT scan		
MRI		
Sonogram		
Neurological Imaging		
CT Scan		
MRI		
PET		
Other		

DATE	ADDITIONAL NOTES

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