International Registry of Hereditary Calcium Urolithiasis

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Mayo Clinic Hyperoxaluria Center

Annapolis, MD
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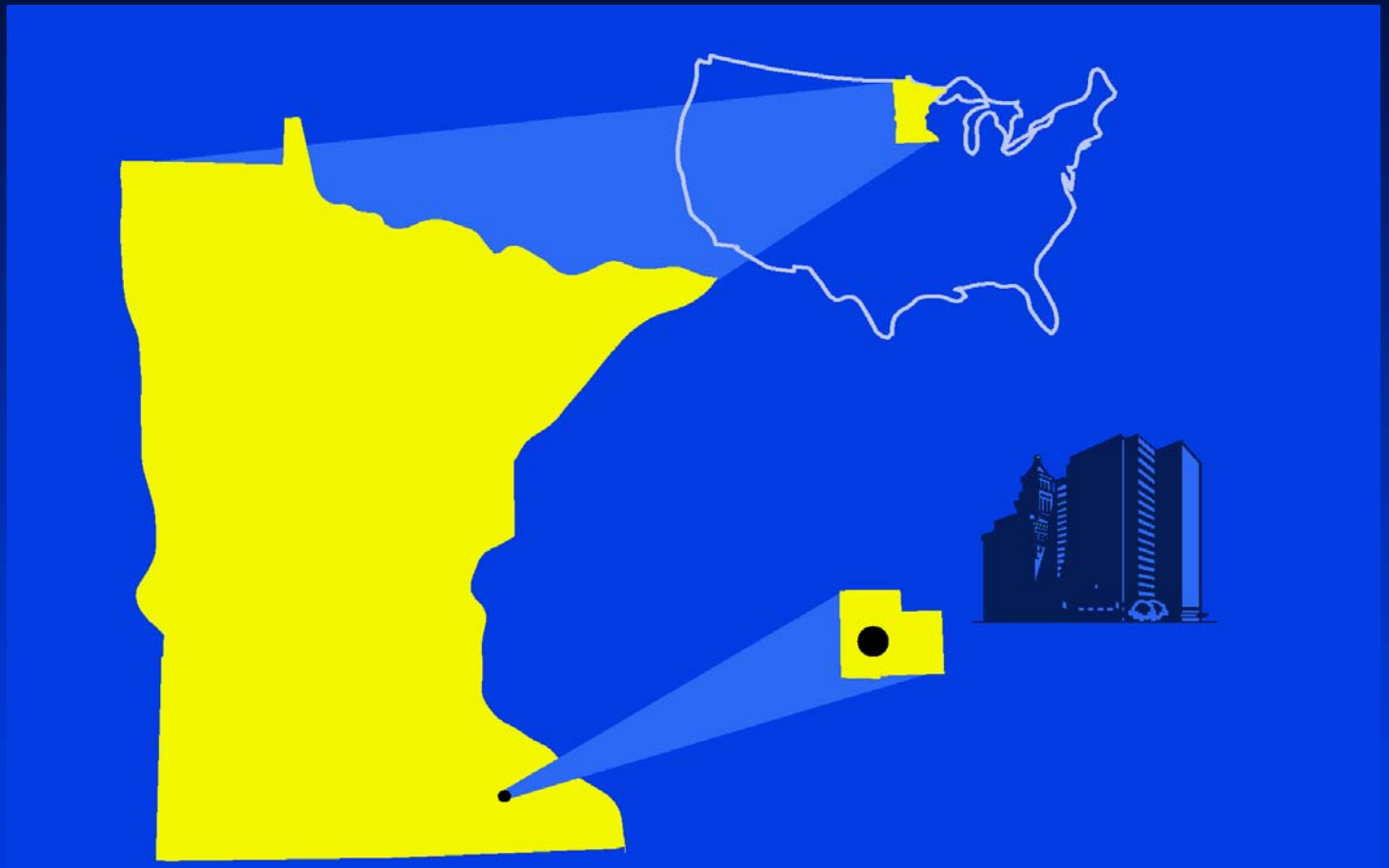
MAYO CLINIC ROCHESTER



International Registry of Hereditary Calcium Urolithiasis

- The primary aim is to establish an international registry for patients with Primary Hyperoxlauria and Dent's disease
- This voluntary registry will be populated with data provided by physicians who care for these patients, usually nephrologists or urologists

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SPECIFIC AIMS:

- Define the spectrum of disease expression of Primary Hyperoxaluria (PH1, PH2, and unclassified PH), and Dent's disease, including identification of factors modifying expression
- Establish characteristics of disease progression over time, and identify prognostic markers
- Characterize non-PH1 and non-PH2 diseases
- Describe clinical interventions used and their outcomes. This will include guidelines for testing and response to pyridoxine administration in PHI
- Develop consensus standard methods for patient evaluation, including reference laboratories for clinical testing, and common protocols and reporting procedures
- Identify any correlations between genotype and phenotype by collecting data on mutations and polymorphisms in relation to biochemical and clinical data, including that obtained from longitudinal studies of individual patients
- Generate hypotheses for new research
- Establish well-defined patient cohorts for each disease
- Identify patients who may benefit from future clinical trials

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Characteristics of the secure web-based data collection system

- Describes the study and its goals (general accrual to-date, simple data summaries, planned analyses, abstracts, etc)
- Provides for online enrollment/certification of physicians (or designates) who wish to enter patients
- Requires the physician (or designate) a userid/password to access patient entry regions of the web site
- Verifies patient eligibility criterion and authorization for research (if applicable)
- Assign a unique numeric code number and a name code to each enrolled patient
- Allow online entry of patient data (identifiable only by coded number/name)
- Allow physician to view data only for patients that they have entered
- Generates e-mail reminders (to MD's or designates) regarding patients needing updated follow-up

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Other features of the Registry

- Summary information (e.g., descriptive statistics) will be available to all contributors
- Reimbursement provided for each patient entry ($100)

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Registry Administration
Mayo Clinic Rochester, MN

John C. Lieske, M.D.	co-PI
Dawn S. Milliner, M.D.	co-PI
Carla G. Monico, M.D.	Consultant
Julie B. Olson	Study coordinator
W. Scott Holmes	Data management
Erik Bergstralh	Biostatistician
Jeffrey Slezak	Data Entry
Rosebud Roberts, M.D.	Consultant

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Registry Scientific Advisory Board

John C. Lieske, M.D. (co-PI)	Mayo Clinic Rochester
Dawn S. Milliner, M.D. (co-PI)	Mayo Clinic Rochester
Dr. Scott Cramer	Wake Forest Univ
Dr. Chris Danpure	University College London, UK
Dr. Bernd Hoppe	Univ Children's Hosp Cologne, FRG
Dr. Neville Jamieson	Cambridge, UK
Dr. Craig Langman	Northwestern University, Chicago, IL
Dr. Jon Scheinman	Kansas Univ Children's Center, KC, MO
Dr. Steven Scheinman	SUNY Upstate Med Ctr, Syracuse, NY

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IRB (USA) or Ethics Committee (non USA)

- IRB approval may or may not be required for a clinician to participate in the data base
  - –IRB approval is always required to conduct research
  - –Definition of research rests with each IRB (Data entry of existing clinical information vs conduct of research)
  - – Approval will likely be required for participation in the data base
- Patient consent may be waived by IRB or may be required
- If no IRB available, contact study coordinator

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HIPAA categories of information

(1) De-identified Data

No authorization needed

(2) Partially De-identified Data ("Limited Data Set")

Permits dates of service, dates of birth, initials

Authorization waived

(3) Data from which patient can be identified

Authorization from patient required

- Category of data decided by each institution, privacy officer
- HIPAA not required by non U.S. sites
- STUDY COORDINATOR HAS MODEL FORMS AND IS READY AND EAGER TO HELP WITH ALL IRB AND HIPAA ISSUES!

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Timeline of registry

- 5/03 Data Forms Development
- 9/03 Web application: PH
- 11/03 Web entry Mayo PH pts
- 12/03 Web application: Dents
- 2/04 Web entry PH: non-Mayo
- 2/04 Web entry Dents: non-Mayo
- 6/04 Web site fully open
- 6/04 Initial statistical analysis

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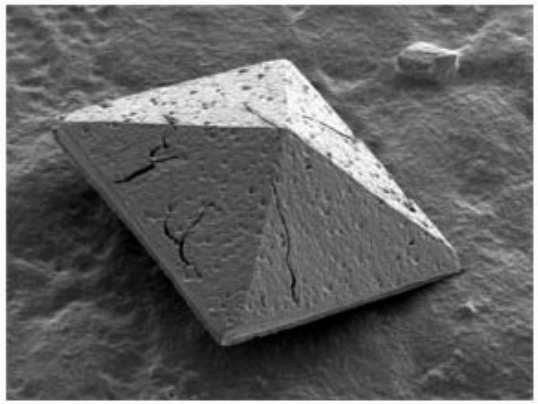
INTERNATIONAL REGISTRY FOR HEREDITARY CALCIUM STONE DISEASES



Primary Hyperoxaluria and Dent's Disease are both rare genetic disorders that can cause kidney stones, nephrocalcinosis, end stage renal failure, and death. Due to their low incidence in the general population, the experience of most physicians and medical centers is relatively limited, and research to improve patient's lives is difficult.

The purpose of this registry is to identify worldwide as many affected individuals as possible, and to collect as much clinical information about these patients as is feasible. The resulting collection of data will be much larger than any individual center could hope to accumulate, and will be available to all interested physicians and researchers internationally.

Goals of the registry are to increase understanding about these rare disorders, to provide evidence that can be used to establish patient care guidelines, and to provide the basis for future clinical trials. Participation in the registry is voluntary and at the discretion of patients and their care providers. All information regarding individuals will be carefully protected in an anonymous fashion in accordance with Mayo Clinic, United States, and international guidelines.

REGISTRY MISSION STATEMENT

The International Registry for Calcium Stone Diseases is a vehicle through which the international scientific community can pool information regarding these rare diseases, in order to collectively advance knowledge, and ultimately improve the quality of life of affected individuals and their families.

REGISTRATION FOR PHYSICIANS WISHING TO PARTICIPATE

Thank you for considering participation in the Primary Hyperoxaluria/Dent's Disease Registry. Your participation is very important for building a database of information to assist in developing therapeutic strategies for Primary Hyperoxaluria. It will help to outline more about disease expression, and also about diagnosis, therapy, transplantation procedures and outcomes. A study coordinator is available to answer questions or help in any way with data entry. To contact the study coordinator please call Julie Olson at (800) 270-4637 OR E-mail to hyperoxaluriacenter@mayo.edu

International Registry of Hereditary Calcium Urolithiasis- contacts

- Julie B. Olson: Study coordinator
  (800) 270-4637; hyperoxaluriacenter@mayo.edu
- Mayo Web page
  http://mayoresearch.mayo.edu/mayo/research/nephrology/registry.cfm
- John C. Lieske, M.D. Lieske.John@mayo.edu
- Dawn S. Milliner, M.D. Milliner.Dawn@mayo.edu

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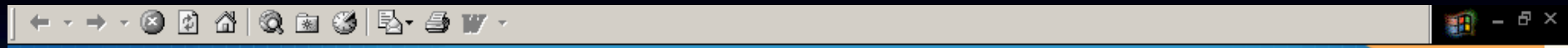


Intuit QuickBase

Support | Sign In | My QuickBase

Sign In to QuickBase

Help

What is your e-mail address? *

Do you have a QuickBase password?

- ○ No, I need to register and get a QuickBase password
- ◉ Yes, my QuickBase password is

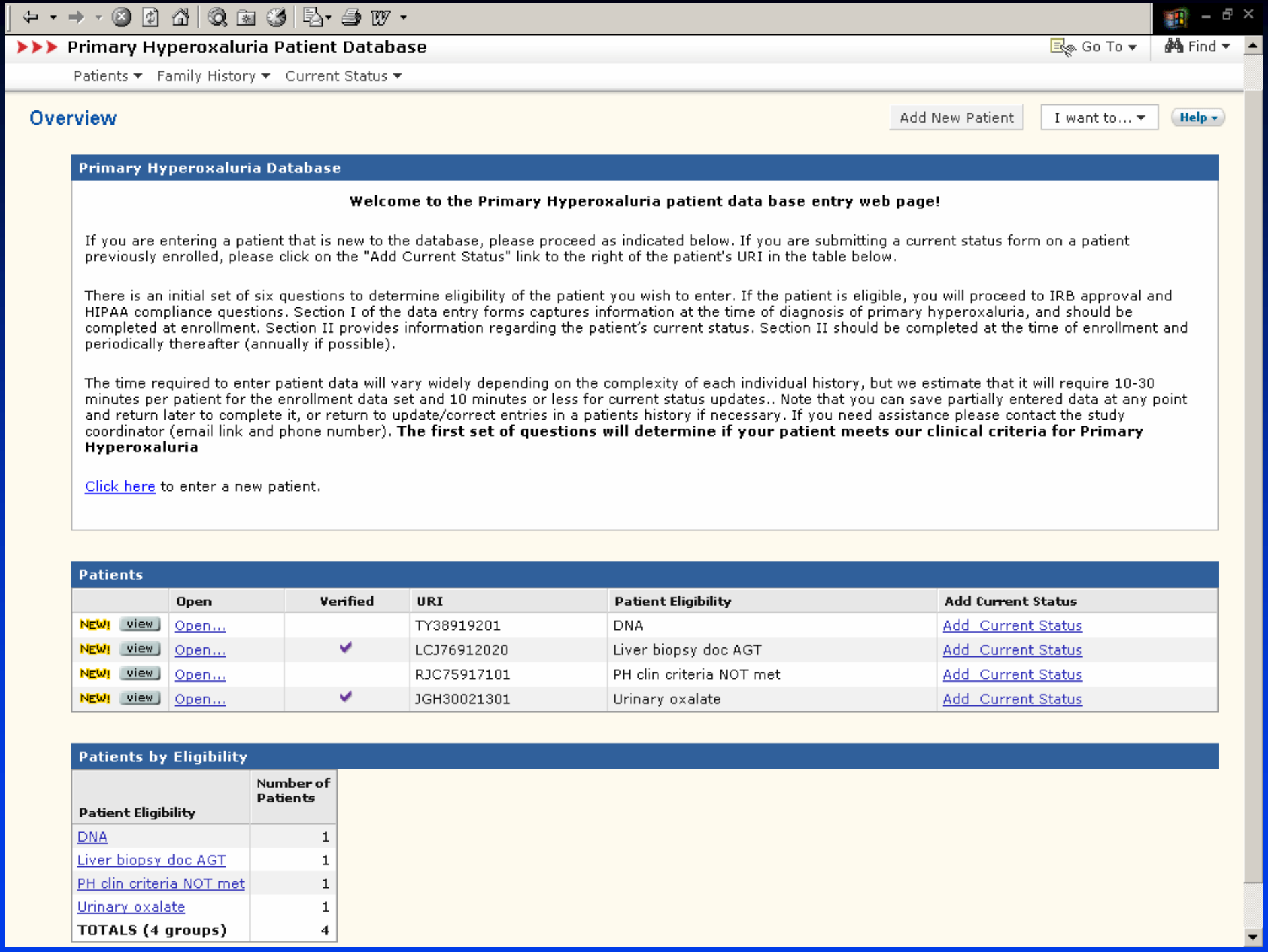
Sign In

Forgot your password?

☐ Keep me signed in on this computer unless I sign out

* Or your QuickBase screen name if you have one

⚠ **The page you have requested can be viewed only by users who have signed in. Please sign in to proceed.**


Primary Hyperoxaluria Patient Database
Go To
Find
Patients
Family History
Current Status
Overview
Add New Patient
I want to...
Help
Primary Hyperoxaluria Database
Welcome to the Primary Hyperoxaluria patient data base entry web page!
If you are entering a patient that is new to the database, please proceed as indicated below. If you are submitting a current status form on a patient previously enrolled, please click on the "Add Current Status" link to the right of the patient's URI in the table below.
There is an initial set of six questions to determine eligibility of the patient you wish to enter. If the patient is eligible, you will proceed to IRB approval and HIPAA compliance questions. Section I of the data entry forms captures information at the time of diagnosis of primary hyperoxaluria, and should be completed at enrollment. Section II provides information regarding the patient's current status. Section II should be completed at the time of enrollment and periodically thereafter (annually if possible).
The time required to enter patient data will vary widely depending on the complexity of each individual history, but we estimate that it will require 10-30 minutes per patient for the enrollment data set and 10 minutes or less for current status updates.. Note that you can save partially entered data at any point and return later to complete it, or return to update/correct entries in a patients history if necessary. If you need assistance please contact the study coordinator (email link and phone number). The first set of questions will determine if your patient meets our clinical criteria for Primary Hyperoxaluria
Click here to enter a new patient.
Patients
Open
Verified
URI
Patient Eligibility
Add Current Status
NEW! view
Open...
TY38919201
DNA
Add Current Status
NEW! view
Open...
LCJ76912020
Liver biopsy doc AGT
Add Current Status
NEW! view
Open...
RJC75917101
PH clin criteria NOT met
Add Current Status
NEW! view
Open...
JGH30021301
Urinary oxalate
Add Current Status
Patients by Eligibility
Patient Eligibility
Number of Patients
DNA 1
Liver biopsy doc AGT 1
PH clin criteria NOT met 1
Urinary oxalate 1
TOTALS (4 groups) 4

SAVE | SAVE & DONE

Welcome to the Primary Hyperoxaluria patient data base entry web page!

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If you need assistance please contact the study coordinator (email link and phone number). **The first set of questions will determine if your patient meets our clinical criteria for Primary Hyperoxaluria.**

®=Required data items

Patient Eligibility Criteria ®, i.e., must enter data that confirm eligibility

All patients meeting criterion (1), (2), (3) or (4) are eligible:

○ 1a) **Liver biopsy** documenting AGT activity below the normal reference range **confirming PH1.**

- or -

○ 1b) **Liver biopsy** documenting GR/HPR activity below the normal reference range confirming **PH2.**

○ 2) **Molecular genetic analysis** (DNA testing) confirming a mutation known to cause PH1 or PH2.

○ 3) Urinary oxalate excretion of greater than 0.8 mmol/1.73 m 2 /day (>60 mg/1.73 m 2 /day) in the absence of a gastrointestinal disease known to cause hyperoxaluria (enteric hyperoxaluria).

4) If the patient presented in end stage renal failure, and neither a liver biopsy or mutational analysis were obtained, **(4a and 4b) or 4c** must be fulfilled:

○ 4a) Pre dialysis plasma oxalate greater than 60 umol/L **AND**
4b) Renal biopsy confirming extensive oxalate deposition

4c) Evidence of systemic oxalosis (one of the following):

4) If the patient presented in end stage renal failure, and neither a liver biopsy or mutational analysis were obtained, **(4a and 4b) or 4c** must be fulfilled:

- ○ 4a) Pre dialysis plasma oxalate greater than 60 umol/L **AND**
  4b) Renal biopsy confirming extensive oxalate deposition

4c) Evidence of systemic oxalosis (one of the following):

- ○ 4c i) retinal oxalate deposits
- ○ 4c ii) oxalate deposits in bone marrow, skin, or other tissue (histologically confirmed)
- ○ 4c iii) nephrocalcinosis
- ○ 4c iv) calcium oxalate nephrolithiasis

5) Family history of PH in a sibling is supportive. Affected sibling? ○ Yes ○ No

Age & sex of siblings [ ] Sibling diagnosis [ ]

○ 6) This patient does not meet these clinical criteria for PH.

If you believe the patient has PH, please contact us.

You may also still continue to enter data if you choose, although it may not be incorporated into the database unless the diagnosis of PH can be confirmed by registry staff.

Institutional Review Board (IRB) Authorization and HIPAA Compliance

For all USA sites, before any data is entered the following IRB/HIPAA information is required. For non-USA sites, please answer the questions below regarding your local review body for studies involving human patients. Click here for more information regarding IRB or HIPAA compliance, including model forms. A study coordinator is available to answer questions or to help facilitate submission of the appropriate information to your local IRB. To contact the study coordinator please call (800) 270-4637 OR click here for e-mail.

1. (IRB) Approval) Before information may be provided, you must obtain approval from your IRB, Ethics Committee or other appropriate body to provide the information, or a statement that such approval is not required. If approval is required, your IRB or Ethics Committee may waive the requirement to obtain informed consent, or may require you to obtain the patient's informed consent prior to submitting the information.

USA Sites

- ○ I have received permission from our local IRB to share information about this patient with the registry, and have complied with IRB requirements for informed consent, if any.

- ○ I have received notification from our local IRB that approval is not required.

1. (IRB) Approval) Before information may be provided, you must obtain approval from your IRB, Ethics Committee or other appropriate body to provide the information, or a statement that such approval is not required. If approval is required, your IRB or Ethics Committee may waive the requirement to obtain informed consent, or may require you to obtain the patient's informed consent prior to submitting the information.

USA Sites

○ I have received permission from our local IRB to share information about this patient with the registry, and have complied with IRB requirements for informed consent, if any.

○ I have received notification from our local IRB that approval is not required.

○ There is no IRB at our institution (the study coordinator will contact you with required information)

Non-USA Sites

○ I have received approval to share information about this patient from the Ethics Committee or appropriate body that reviews human studies for our institution (specify name: _____ , and complied with Ethics Committee requirements for informed consent, if any.

○ I have received notification from our Ethics Committee or other appropriate body that approval is not required by our institution before entering patient data in this registry.

2. HIPAA Compliance issues (**applies to USA sites only**)

Following initial provision of limited demographic information (patient initials, and date of birth) a unique alphanumeric identifier will be assigned. From that time on, all information will be exchanged using this alphanumeric identifier only. The individual patient will not be able to be identified.

Because some of the information will include identifying information (as defined under HIPAA), you must check with your IRB or Privacy Board to determine whether additional steps may need to be taken to provide the data. We suggest that this information be described to your IRB or Privacy Board as a Limited Data Set. If approved in this manner, your IRB or Privacy Board would likely not require you to obtain the patient's HIPAA authorization to provide the information to the database.

Please indicate below how your institution has elected to handle this information.

○ Our IRB has required me to obtain the patient's HIPAA authorization, and I have complied with this requirement.

○ Our IRB or Privacy Board has waived HIPAA authorization for this study

○ Our IRB or Privacy Board will treat this as a limited data set with a data use agreement, in which case HIPAA authorization is not required.

Thank you very much for your efforts! We are trying to be as complete as possible, but we understand that not all, or even most of the sections will be completed for many patients. The time required to enter patient data will vary widely depending on the complexity of each individual history, but we estimate that

Section I will collect data about the patient AT THE TIME OF DIAGNOSIS with Primary Hyperoxaluria.

I. Presentation

A. General Information & Presenting Signs and Symptoms

1). **Date of PH Diagnosis ®** MM-DD-YYYY

Patient Initials ® (will be used to generate a unique number and letter code)

Sex ® M F **D.O.B. ®** MM-DD-YYYY

Age at Diagnosis with PH yrs

Height ® (20-230) cm **Weight ®** (1-250) kg

Head Circumf (if < 3 yo) (1-60) units: cm in

Blood Pressure (SBP/DBP) / (20-250) mmHg / (20-250) mmHg

2) Country of origin: Ethnicity selection (select one):

- Hispanic or Latino
- American Indian or Alaska Native
- Asian
- Black or African
- Native Hawaiian or Other Pacific Islander
- White
- Middle Eastern/Arabic
- Indian Subcontinent
- Unknown
- Other

Date of first symptom ® MM-DD-YYYY

Signs and symptoms

If a symptom is selected please enter age or date symptom initially manifested.

Urolithiasis

Yes No

Age (yrs.) (1-120)

Date MM-DD-YYYY

B. **Laboratory Parameters at the time of Initial Diagnosis with PH**

1. Urinary studies at the time of diagnosis with PH

a) 24-urine collection at the time of diagnosis with PH date: MM-DD-YYYY

Please list the values in the format reported by your lab.

	Value	Units **(must specify) ®:**
Volume		ml/24 h (50-10,000) liter/24 h(0.05-10)
Creatine		umol/24 h (150-40,000) mmol/24 h (0.15-40) mg/24 h (20-5000) other
Creatinine concentration		umol/L (15-400) mg/dl (0.2-5) other
Oxalate		umol/24 h (15-400) mg/24 h (0.2-5) other
Oxalate Concentration		mmol/L (0.01-10) mg/L (0.1-1000) other

Lab performing oxalate assay, if known

Calcium		mmol/24 h (0.25-25) mg/24 h (1-1000) other
Calcium concentration		mmol/L (0.05-50) mg/L (2-20000) other
Citrate		mmol/24 h (0-8) mg/24 h (0-1500) other
Citrate concentration		mmol/L (0-0.1) mg/dl (0-16) other

Were other urinary risk factors for urolithiasis measured (e.g., uric acid, magnesium, super saturation)?
If so, please list with units.

---

b) Random/spot urine specimens at the time of diagnosis with PH date: MM-DD-YYYY

Was the sample obtained fasting? Yes No Unknown

Please list the values in the format reported by your lab.

	Value	Units ®:
Oxalate		umol/L (1-10,000) mmol/L (0.001-10) mg/L (0.1-1000) other

Lab performing oxalate assay, if known

Creatinine		mmol/dl (1.5-40) mol/L (0.015-0.4) mg/dl (0.2-5) other
Oxalate to Creatinine ratio		umol/mmol (0.002-2) mmol/mmol (2-2000) mmol/mol mg/mg (0.002-2) other
Calcium		umol/l (50-50,000) mmol/l (0.05-50) other
Calcium to Creatinine ratio		umol/mmol (0.00002-0.15) mmol/mmol (0.02-15) mmol/mol (20-15,000) mg/mg (0.01-5) other
Citrate		mmol/L (0-0.1) mg/dl (0-16) other

SAVE | SAVE & DONE

Section II will collect information about the CURRENT STATUS of the patient and will be completed at enrollment and each follow-up period (annually if possible).

®=Required data items

II. Current status

A. Demographic data

Unique Registry ID::

1) **Most recent contact with patient ®:** MM-DD-YYYY

2) **Patient still alive? ®** Yes No

Date of death: MM-DD-YYYY Autopsy performed? Yes No

Cause:

Complete form with information from last visit

Most recent BP (SBP) / (DBP) / mmHg (20-230) mmHg (20-230) mmHg

Comments about current status:

B.

1. Renal Stone events (indicate those present)

Stone pain since previous report? Yes No

Stones passed since previous report? Number

Cystoscopic surgeries for stone removal since previous report? Number

ESWL treatments since previous report? Number

Open or percutaneous stone surgeries since previous report? Number

Urinary tract infection since previous report? Yes No

---

2. Markers of systemic oxalosis (mark those present):

Oxalate osteopathy Livido reticularis

Primary Hyperoxaluria Patient Database

Go To | Find

Patients | Family History | Current Status

Overview

Add New Patient | I want to... | Help

Primary Hyperoxaluria Database

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Click here to enter a new patient.

Patients

	Open	Verified	URI	Patient Eligibility	Add Current Status
NEW! view	Open...		TY38919201	DNA	Add Current Status
NEW! view	Open...	✔	LCJ76912020	Liver biopsy doc AGT	Add Current Status
NEW! view	Open...		RJC75917101	PH clin criteria NOT met	Add Current Status
NEW! view	Open...	✔	JGH30021301	Urinary oxalate	Add Current Status

Patients by Eligibility

Patient Eligibility	Number of Patients
DNA	1
Liver biopsy doc AGT	1
PH clin criteria NOT met	1
Urinary oxalate	1
TOTALS (4 groups)	**4**

Patients | Patient #61

Add a New Patient
Help

EDIT E-MAIL DONE

URI TY38919201

Add Current Status Add Current Status

Relationships

	Relationship	Age (Yrs)	Sex	Urolithiasis	Hyperoxaluria	Renal failure	Genetic mutation detected
NEW! view	Mother	50	F	Yes	Yes	Yes	Yes
NEW! view	Father	55	M	No	No	No	Unk
NEW! view	Siblings	12	M	No	No	No	No
NEW! view	Children	15	M	Yes	No	Unk	Yes

Previous Status

	Verified	Open	URI	Date Created	Patient alive?	Autopsy?
NEW! view		Open...	TY38919201	10-31-2003 12:52 PM	Yes	No

Owner: von Roesgen, Claude
Created: OCT-29-2003 9:55 AM (PST)
Last Modified: NOV-10-2003 5:02 AM (PST) by von Roesgen, Claude

EDIT E-MAIL DONE

Special Thanks

- NIDDK and Rebekah Rasooly
- Oxalosis and Hyperoxaluria Foundation
- W. Scott Holmes

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