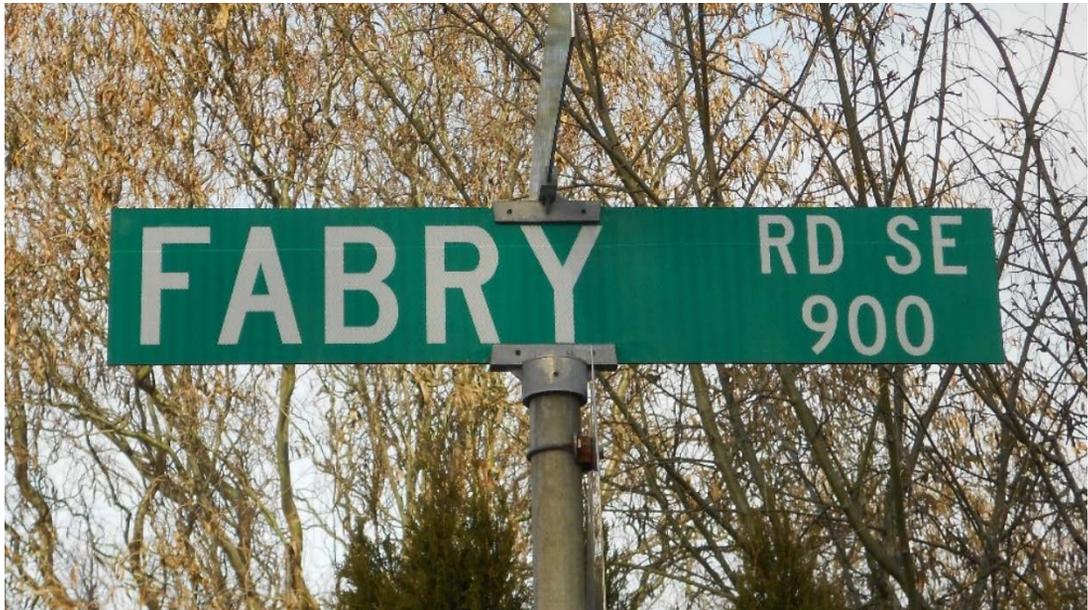


National
FABRY DISEASE
Foundation

The
Fabry Disease
Community Landscape



... a starting point on a road
less traveled

by Jerry Walter, Founder and President, NFDF

As of June 2016

Contents

Topics addressed: (comments and suggestions are welcome)

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More to come

- Fabry disease testing
- Explanation of Fabry mutations
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- Other topics?

Please send comments to Jerry Walter, at jerry.walter@fabrydisease.org

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Introduction



There is a great deal of published literature about Fabry disease and there are many resources available to support individuals with Fabry disease and their families. Still, finding the answers you are looking for and finding the resources you need are not always easy. With this document, we are trying to make your journey a little easier. This document does not focus on disease education itself but rather on common questions that arise as well as helpful information and resources.

If you have suggestions for this document, please let us know by sending an email to Jerry Walter at jerry.walter@fabrydisease.org.

Some resources we tell you about may include inaccuracies because the facts have changed since a document was written or because the author(s) has/(have) not kept up with current research. We'll address a few of these issues such as the outdated information about females with Fabry disease in many older publications.

Let's start by talking about the "F" word itself. You have probably wondered which of the names you hear is the most appropriate name.



In 1898 Dr. William Anderson from England and Dr. Johann Fabry from Germany independently described what is now most commonly referred to as Fabry disease among its many other lesser used names.

One would think Fabry disease would always be called Anderson-Fabry disease to consistently give both physicians credit. To the contrary, the most common name used in literature is simply Fabry disease. The other somewhat common names, Anderson-Fabry disease and Fabry's disease are used in literature much less.

We searched PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>) to access the U.S. National Library of Medicine's database of world-wide journal articles for Fabry disease. There are well over 3,000 articles about Fabry disease available. Looking at the article titles alone, an overwhelming majority of the articles published over the last 10 years use the name "Fabry" rather than "Anderson-Fabry" or "Fabry's".

So, with this trend among physicians and researchers, the NFDf consistently uses the name **Fabry disease** (singular). Why swim upstream and add to the confusion?

Fabry Disease Awareness Information

Commonly Asked Questions

Do we have an awareness month, day or year?

We celebrate **Fabry Disease Awareness Month** in the U.S. and in a few other countries in **April**. In the U.S. the National Fabry Disease Foundation and the Fabry Support & Information Group (FSIG) work with Fabry community members in each state to obtain as many official state governors' proclamations as possible. We recognize Fabry disease awareness in April in every state but not every state has an official program or some states will only grant a week or a day.



Every first Saturday in April we celebrate International Fabry Women's Day, an initiative started by the Fabry Support and Information Group Netherlands.

Do we have a color for ribbons and other awareness materials?

Based on community input the NFDF, FSIG and the Canadian Fabry Association (CFA) use dark blue as our awareness color. On the PMS color chart it is PMS 541 shown to the right.



Do we have a ribbon?

The Fabry community's ribbon is a product of many Fabry community members and the support organizations working together. We use the ribbon design in electronic media as well as to make awareness products such as car magnets, lapel pins, ribbon pins, etc.



Do we have a T-shirt?

In 2013 an NFDF volunteer designed the "I define me" T-shirt for our annual Fabry Family Conference. We adopted it as our hallmark T-shirt. The NFDF provides the T-shirt at our annual national conference and by mail.

Do we have wristbands? The NFDF (royal blue), FSIG (light blue) and the CFA all have awareness wristbands and FSIG has a medical alert wristband (red).

Fabry Medical Alert Cards are available. The FSIG has a wallet alert card and the NFDF has a wallet USB drive alert card for Fabry community members upon request.

NFDF T-shirts, wristbands and USB alert cards and other products are available by sending an email jerry.walter@fabrydisease.org.

Primary Fabry Family Support Organizations

There are two primary patient support organizations in the United States that are dedicated solely to Fabry disease. Both organizations are registered IRS 501(c)(3) non-profit charitable organizations.



Our organization the **National Fabry Disease Foundation (NFDF)**, founded in 2005, is currently led by Jerry Walter.

Website: www.fabrydisease.org Email: info@fabrydisease.org Phone: 800-651-9131. See the NFDF's program handout in the Featured Resources Section of our website.



The **Fabry Support & Information Group (FSIG)** was founded in 1996 and is currently led by Jack Johnson.

Website: www.fabry.org Email: info@fabry.org Phone: (660) 463-1355

The two complimentary U.S. organizations have common broad goals to support the Fabry community and between us we have a very diverse set of valuable programs and services to support people with Fabry disease and their families.



In Canada, the Fabry community is supported by the **Canadian Fabry Association (CFA)** currently led by Gina Costantino. Website: www.fabrycanada.com



Many other countries have similar Fabry disease support organizations. To find other country organizations, visit the members section of www.fabrynetwork.org.

The primary aim of The Fabry International Network (FIN) is to facilitate collaboration between patient organizations to support those affected by Fabry Disease.



Patient Services Incorporated (PSI) at www.patientservicesinc.org is non-profit organization in the U.S. who provides financial insurance premium assistance and prescription copayment support as well as support for additional expenses related to Fabry healthcare needs.

Among their many other programs the NFDF and the FSIG also have financial assistance programs called the **Urgent and Unmet Needs Program** and the **Rapid Assistance Fund support** Program, respectively. Genzyme offers **Co-Pay Assistance** to support eligible out-of-pocket drug and infusion-related costs (not infusion medication itself). <https://www.genzyme.com/promos/fzcopy.aspx>

Where to find information

You can find thousands of peer-reviewed articles about Fabry disease at PubMed - NCBI, PubMed Central (only full-text articles), Europe PubMed Central, PubMed Central Canada, and possibly other countries' library sites by typing "Fabry disease" in each sites' search field? <http://www.ncbi.nlm.nih.gov/pubmed>.

You can find out about Fabry disease research/clinical trials at the U.S. clinical trials registry site at www.clinicaltrials.gov and many other clinical trial registry sites in other countries? Clinical trials in www.clinicaltrials.gov also include information about the non-U.S. clinical trial sites for those trials listed. You can search "Fabry disease" then narrow your search by checking the open studies box.

At GeneReviews (<http://www.ncbi.nlm.nih.gov/books/NBK1116/>) you can find expert-authored, peer-reviewed disease descriptions ("chapters") presented in a standardized format and focused on clinically relevant and medically actionable information on the diagnosis, management, and genetic counseling of patients and families with specific inherited conditions.

You can find laboratories around the world who test for the Fabry disease GLA gene using the website GeneTests (<https://www.genetests.org/>) by typing Fabry disease in the search box, then by selecting the "Tests" tab. In the U.S. LabCorp also tests for Fabry disease but they are not listed in GeneTests.

You can find information about Fabry disease in the Genetics Home Reference at <http://ghr.nlm.nih.gov/condition/fabry-disease?>

Pharmaceuticals companies involved in Fabry disease have various forms of Fabry disease literature available upon request.

You can subscribe to Google Alerts for Fabry disease news. However, you will also receive many alerts about pharmaceutical company news along with other Fabry community news.

A WORD OF CAUTION: When searching the internet for Fabry disease information you will find information that is inaccurate or not up-to-date. The best sources of information for disease education are peer-reviewed journal articles and patient reported outcomes survey reports of large numbers of participants.

The virtual community (face book)

There are quite a few social media sites available for the Fabry disease community.

The difference between face book Pages and Groups: Pages allow organizations, businesses, etc to communicate broadly with people who like them. According to face book, Pages may only be created and managed by organization representatives. Groups provide a space for people to communicate about shared interests. Groups can be created by anyone. We would recommend using existing sites rather than creating new ones. We already have a lot to choose from and keeping up with too many sites can be difficult.

The **National Fabry Disease Foundation** has a face book **Page** with over 2,000 “Likes” at www.facebook.com/FabryDisease. We encourage everyone to “Like” and follow our page. Much of the information we provide to you is posted here first before our newsletter or website.

Pages mostly offer information shared by the organization or entity. **Groups** have more active discussions and provide a great deal of information and mutual support. It is great to be able to interact with people who are so geographically dispersed that you may never meet in person. Although increased local, regional and national meetings allow more opportunities to meet.

The other most popular/most used Pages and Groups that we know about are below. Current

Fabry’s Disease Info and Support (Not to be confused with Fabry Support & Information Group) at <https://www.facebook.com/groups/Fabry.Disease.Info.and.Support/>. Closed group for privacy reasons. You may request membership.

Fabry Support & Information Group at <https://www.facebook.com/Fabry.org/>.

Fabry Support Group at <https://www.facebook.com/groups/fabrysupport/>. Members can add others to this group. It is a secret group for privacy reasons.

Fighting Fabry Disease at <https://www.facebook.com/fightingfabry/>.

Not Defined by Fabry at <https://www.facebook.com/groups/1508471869386119/>.

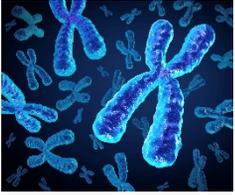
Canadian Fabry Association at <https://www.facebook.com/groups/27694413535/>.

Fabry Australia at <https://www.facebook.com/groups/FabryAustralia/>.

Morbus Fabry Interessengemeinschaft (Germany) at <https://www.facebook.com/morbusfabry.interessengemeinschaft>

Please keep in mind that each of us with Fabry disease is an expert about our own disease but what may be true for one person may not be true for another. If you read information about symptoms, medications, management, etc. please ask your physician before taking the advice of a fellow patient or family member. Please verify information before you share something you’ve heard from someone else or read on face book as it may not be accurate for everyone.

Inheritance



The Fabry disease gene (GLA) is on the X-chromosome. Therefore Fabry disease is inherited in an X-linked manner. The X and Y chromosomes, two of the 23 pairs of chromosomes in the body, among many other functions, determine the sex of an individual. Females have two X chromosomes. Males have one X chromosome and one Y chromosome.

Fabry affected males pass their X chromosome to all of their daughters. In this way, all daughters of affected males will have the gene for Fabry disease. This is assuming paternity is not of concern.

Affected males do not pass the Fabry disease gene to any of their sons. Sons receive their father's Y chromosome and cannot inherit FD from their father.

Every time a female with the Fabry gene has a child, there is a 50% chance that she will pass her affected X chromosome to the child, and a 50% chance that she will pass her normal X chromosome to the child. This means there is a 50% chance that every daughter and every son born to a female with the Fabry gene will inherit the affected X chromosome and have the Fabry gene.

As recently as 2001 it was believed that Fabry disease was a typical X-linked recessive disease in which females were carriers only and could not have symptoms. However, researchers and treating physicians have learned that females without Fabry disease symptoms are the exception not the rule.

Many females have symptoms as severe as males with classic Fabry disease, while others may be seemingly asymptomatic, only experience mild symptoms, or exhibit any degree of symptoms in between. A high percentage of females carrying the Fabry disease gene are affected and have many significant symptoms. One study reports 69% of females have symptoms and signs of Fabry disease.

It is generally preferred to refer to a female with a disease causing Fabry mutation but who doesn't have symptoms as an asymptomatic female rather than a "carrier". In medicine, the term "carrier" is usually reserved for a female who is a carrier but CANNOT have symptoms such as with an X-linked recessive disease.

When a gene mutation spontaneously occurs in a family for the first time rather than by inheritance, it is called a de novo mutation.

How many people have Fabry disease?

If you are an individual with Fabry disease or a family member, knowing how many people have Fabry disease is probably not that useful but it's interesting. To researchers, policy makers, drug suppliers, investors, businesses that provide support to care, etc. the number is probably much more useful.

The numbers reported are usually discussed in at least three ways: Incidence, prevalence and the number of people affected.

Incidence (rate of appearance): the number of new cases in a given period of time (day, month, year). Fabry disease newborn screening is a good example. The 2013 six-month, full-state population screening in Missouri revealed a Fabry gene mutation detection rate of a staggering one in 2,913 newborns. Ongoing research indicates many of these detected gene mutations may not cause Fabry disease symptoms but there will still likely be many more people with classic and non-classic Fabry disease than historical estimates indicate.

Prevalence: the proportion of cases at a specific point in time. It is usually expressed as a fraction, a percentage or a number per 10,000 or 100,000 people, etc., such as the commonly used U.S. estimate for Fabry disease described in the National Institutes of Health Genetics Home Reference which states "Fabry disease affects an estimated 1 in 40,000 to 60,000 males." This enables one to calculate an estimate of how many people have Fabry disease at any point in time. But the math is not easy for all categories of people with Fabry (males with a classic mutation, females with a classic mutation, males with a non-classic mutation, females with a non-classic mutation, people with a non-disease causing mutation).

Why are the numbers usually quoted in terms of males? What about females, they are affected also?

The statistics are often quoted in terms of males because with an X-linked inheritance pattern the estimated numbers of males with Fabry disease are easier to determine.

The number of people that have Fabry disease is a very difficult number to calculate. No one really knows how many people are affected but we'll provide some possible numbers and further explanations on the following page.

Fabry Population (one possible scenario)

To follow up on the previous explanation of how many people have Fabry disease, here is an estimate of the U.S. population using the prevalence of 1 in 40,000 to 60,000 (average 1 in 50,000) males cited by the National Institutes of health.

The estimated U.S. population in 2016 is about 323 million people. The percentage of males and females per year is usually about 50% each.

Estimated males with classic Fabry disease: Half of 323,000,000 people equals 161,500,000 males. Therefore, males with FD equals $161,500,000/50,000$ for a total of 3,230 males in the U.S.

Genetic math states twice as many females inherit an X-linked gene as males which equals about 6,460 females with the Fabry gene in the U.S.

A 2008 study of 1077 females in the Fabry Registry indicated 69.4% females had symptoms and signs of Fabry disease. This yields an estimate of about 4,483 affected females and a total estimated U.S. Fabry population (males and females) of **7,713** based on the current prevalence rate. Only about 4,000 to 5,000 people are known in the U.S. so far.

Now consider the 2013 Missouri newborn screening result with a 1 in 2,913 detection rate applied to the entire U.S. population of 323 million people. $323,000,000/2,913$ is about 110,882 people with a Fabry gene mutation. Even if only 25% of those detected have a mutation that causes symptoms, the estimated population would be about **27,720** people with classic and non-classic Fabry disease in the U.S. alone.

Please do not quote these numbers as proven population numbers but they represent a very real possibility and may still be very conservative numbers.

Many in the Missouri study will likely have a non-classic form of disease (which could still cause significant symptoms especially heart and kidney problems) or a non-disease causing form of the Fabry mutation. More to come!

Bottom line: We suggest there are thousands of people unknowingly living with classic and non-classic Fabry disease in the U.S. and around the world.



Emergency Information



In an emergency patients should report they have Fabry disease. Emergency medical personnel should be made aware Fabry patients may experience cardiovascular, cerebrovascular and renal disease at a younger age which may include coronary disease, arrhythmias, heart failure, TIA/stroke, proteinuria and other symptoms of kidney dysfunction. Emergency medical personnel may want to check kidney function as it can be low in Fabry patients and this may affect which type of initial testing is obtained and also alert care providers about prescribing any medications potentially toxic to the kidneys.

Items to always have with you

1. Primary and secondary emergency contact information
2. Who can make medical decisions in the event you cannot communicate them yourself and the location of living will, medical power of attorney, DNR order, etc.
3. Contact information for your primary Fabry physician, primary care physician if different, and key specialists such your cardiologist, nephrologist, neurologist, and others as needed
4. Insurance cards
5. A list of allergies (medication, food and environmental allergies)
6. A list of prescription medications, over the counter medications and supplements
7. Things that have not worked in the past especially for pain, severe lymphedema
8. A copy of your most recent EKG especially if you have an abnormal EKG
9. Existing conditions/chronic illnesses: (Fabry disease, Chronic Kidney Disease, etc.)
10. Existing Fabry symptoms like angiokeratomas, lymphedema, or other visible manifestations
11. Any major illnesses/events with dates: such as heart attack, stroke, kidney failure and others major illnesses bacterial meningitis, Guillain-Barre, rheumatoid arthritis, etc
12. Past Hospitalizations with dates
13. Past Surgeries with dates
14. Vaccinations: Flu, tetanus, pneumonia, TB screen, etc.
15. Physical limitations: corrected vision/eyeglasses, hearing loss/hearing aids, impaired mobility

Thank you for contributions to this page from these experienced Fabry disease physicians: Dr. Rob Hopkin (Geneticist), Dr. William Wilcox (Geneticist), Dr. John Jefferies (Cardiologist), Dr. Andrew Lundquist (Nephrologist), Dr. Katherine Sims (Neurologist), and Dr. David Warnock (Nephrologist).

Please request a copy of the NFDf's booklet entitled **"My Health Handbook and Emergency Information"** by emailing Jerry at jerry.walter@fabrydisease.org.

More about the National Fabry Disease Foundation

Established by Jerry Walter, Founder and President, in June 2005 as a U.S. Internal Revenue Service (IRS) 501(c)(3) non-profit charitable organization.

Vision: No longer will any individual's quality of life be diminished, nor will their lives be shortened because of Fabry disease.

Mission: To help ensure all individuals with Fabry disease are identified, diagnosed and treated in time to avoid a diminished quality of life or life threatening consequences, to provide assistance to individuals with Fabry disease and their families, to provide Fabry disease education and awareness, to promote continued data-gathering and research to improve treatment opportunities and to find a cure.

Slogans the NFDF uses:

Giving more life to our children's years and more year's to our children's lives!
(slogan adapted from the Belgium Fabry disease support organization.)

Fighting Fabry Disease ... Living better Longer (on our wristband)

Fighting Fabry disease for better and longer lives

Trademarked Programs:

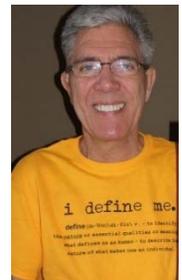
Work up a sweat for someone who can't™

Break a sweat for those who can't™

Hallmark programs:

- We have a **R.A.R.E.** opportunity to **Recognize And Rescue Everyone** with Fabry disease.
- The Eyes Have It campaign (working with eye doctors)
- The Connecting the Dots campaign (working with dermatologists)
- The Fabry Legion – the Fabry community's Army fighting Fabry disease

Our T-shirt theme: The "I define me." T-shirt was first designed and distributed in 2013. T-shirt front: "I define me." T-shirt back: "Fighting Fabry Disease ... Living Better Longer"



Please request our Program Handout for information about our many programs and services.

Please request the NFDF's "My Health Handbook and Emergency Information" booklet.

Please share information widely about our programs, services and materials.

Website: www.fabrydisease.org | Email: info@fabrydisease.org

U.S. Toll Free: 800-651-9131 or non-toll-free phone: 919-932-7785

How does the National Fabry Disease Foundation contribute to research?

The NFDF occasionally provides funding for small research projects but with limited resources we usually contribute to research in other important ways.

At the NFDF annual conference and occasionally throughout the year we facilitate participation in research being conducted by the medical community. The NFDF has made a significant contribution to the successful completion of many published research articles.

Patient Reported Outcomes Surveys (PROS) – Learning from the pros

Beginning in 2014 the NFDF began administering periodic surveys to the Fabry community. This program provides a great deal of useful information for the following purposes.

- To learn about symptom trends among people with Fabry disease to help identify future research needs
- To provide individuals with Fabry disease questions to ask their physicians based on the symptom trends of others
- To understand the Fabry community's needs to enable us to revise and expand the NFDF's programs and services as needed
- To understand the collective voice of the Fabry community so the NFDF may represent the community according to your opinions on important issues. We do not want the medical community making critical decisions on important issues without knowing what our community thinks.

In 2016, the NFDF will again offer periodic surveys in a contest format which was very successful in 2014. **Having the greatest number of survey participants possible helps to ensure the survey findings are a good representation of the overall Fabry community.**

PLEASE PARTICIPATE IN NFDF SURVEYS WHEN THEY ARE ANNOUNCED.

Topics to be added in the next version of this document:

- Explanation of Fabry gene mutations
- Testing for Fabry
- Fabry treating physicians
- ... and more

We appreciate your suggestions on how to improve this document. Email suggestions to Jerry Walter at jerry.walter@fabrydisease.org

We will avoid too much disease education in this document. From the perspective of a new person finding out they have Fabry, what would you like to have known?

Keep in touch to stay informed. We are always adding and improving our programs.

Please subscribe to our e-newsletter at the top right of our website homepage at www.fabrydisease.org

Please like and follow our face book page at www.facebook.com/FabryDisease

We learn from the PROS (Patient Reported Outcomes Survey) program. That means you! Please take our periodic surveys to help answer questions about our disease and our community.

Sincerely, Jerry Walter