

HyDROPS

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Our goal is to develop a precision approach to care for non-immune hydrops fetalis by identifying the cause in each individual pregnancy



Condition studied: non-immune hydrops fetalis (NIHF)

Contact the study team: hydrops@ucsf.edu ^[1] or 1-800-RX-FETUS

What is hydrops?

Hydrops fetalis is a condition in pregnancy marked by abnormal collections of fluid in the developing fetus. There are two types of hydrops. One is immune in nature, and results from blood type incompatibility between the pregnant woman and fetus. The other type is non-immune hydrops fetalis (NIHF), which can be caused by many types of genetic abnormalities, infections, and other causes. The majority of hydrops cases today are NIHF, and this is the condition that we are studying.

NIHF carries significant risks of stillbirth during the pregnancy, as well as of early delivery and serious illness and death for the newborn. There is also risk to the pregnant woman of developing a condition called mirror syndrome, which can include high blood pressure, swelling, and damage to organs such as the kidneys and liver. These risks vary widely by the underlying cause of the NIHF.

Our research has shown that the cause of at least half of all NIHF cases remains unknown after standard-of-care testing that includes karyotype and microarray. **Importantly, without an understanding of the reason for the NIHF, prenatal care for a pregnancy with NIHF is less focused, clear plans for newborn care cannot be made, and the chance of NIHF happening again in a future pregnancy cannot be accurately estimated.**

Download the Non-Immune Hydrops Fetalis Workup ^[2] for our recommended workup for NIHF.

Why is this study important?

The **HyDROPS** study (**H**ydrops: **D**iagnosing and **R**edefining **O**utcomes with **P**recision **S**tudy) applies a broad genetic test, called trio exome sequencing, to discover genetic diseases underlying NIHF. The information resulting from this study will:

- Allow medical providers to focus prenatal management according to the underlying cause.
- Inform participants about what to expect after birth.
- Enable medical providers and parents to make clear plans for the newborn, including treatments that are best given soon after birth.
- Inform participants and medical providers about the chance of NIHF happening again in a future pregnancy.

Our goals are to develop a precision-based approach to the diagnosis and care for NIHF in order to optimize both newborn and maternal outcomes. Ultimately, our group aims to develop novel, specific in utero treatments for each underlying cause of NIHF.

Why participate?

- You will receive results from detailed genetic testing (trio exome sequencing) that are important for your pregnancy, your child, and/or future pregnancies.
- Your participation helps us to better understand NIHF and improve our care for patients with this condition.
- Findings from this study will guide development of in utero treatments for specific genetic diseases that cause NIHF.

Who may enroll in the study?

Participants may enroll in this study during pregnancy or after pregnancy. We can enroll participants remotely over video or telephone; travel to UCSF is not necessary to participate in the study.

Inclusion criteria

We are enrolling participants who are pregnant with a fetus diagnosed with NIHF, or infants who had a diagnosis of NIHF in utero, when standard genetic testing (karyotype or microarray) does not explain the NIHF. We accept a broad definition of NIHF, which includes one or more of the following:

- One or more abnormal fluid collections in the fetus (such as fluid around the heart or in the lungs, abdomen, or skin)
- Cystic hygroma
- Increased nuchal translucency ≥ 3.5 mm

Exclusion criteria

- Pregnancy with immune hydrops
- Twin pregnancy with evidence of twin-twin transfusion syndrome

What can I expect if I enroll in the study?

For NIHF pregnancies that are not clearly explained by standard genetic testing (karyotype or microarray), **we offer trio exome sequencing through our UCSF Genomic Medicine Laboratory at no cost to families participating in the study.** With trio exome sequencing, we examine more than 20,000 genes in the DNA of the fetus or infant to determine whether there are genetic variations that explain the NIHF. Samples from each biological parent are also used to determine whether these genetic changes are inherited. This testing can also be done using a sample from only one parent if both are not available. UCSF has prepared a video to explain trio exome sequencing.

Download the Study Overview chart ^[3], which outlines what to expect.

Participants will meet twice with the study team by telephone or video (or potentially in person if the participant is already a UCSF patient). During the first meeting, we will explain the study and genetic testing, and answer all questions about participation. During the second meeting, we will return results of the trio exome sequencing and answer all questions about the results. We also provide a formal report of the results that participants can keep for their records.

For ongoing pregnancies and live infants, we expedite testing and return results in approximately 2-4 weeks. For non-continuing pregnancies, we return results in approximately 8-10 weeks. For each case, a multidisciplinary panel of experts at UCSF carefully reviews the testing results and determines the significance of genetic variations found.

What types of samples can be used for the genetic testing?

Only one sample type is needed for the fetus or infant, as well as for each biological parent. Fetal and newborn samples can be obtained from procedures already performed, such as a prior amniocentesis.

- Fetus: cultured amniocytes, extracted DNA, cord blood, or other types of samples
- Newborn: blood, buccal (cheek) swab, or other types of samples
- Parent: blood or saliva (NOTE: We can ship saliva kits to participants' homes with pre-paid shipping labels for easy return to our lab at UCSF.)

How can I participate?

If you would like to participate in the study or want more information, please either email our study team at hydrops@ucsf.edu [4] or call 1-800-RX-FETUS.

Study Team



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Fetal Exome Sequencing video

Fetal Exome Sequencing [13]

Fetal Exome Sequencing (Spanish Translation) [14]

Fetal Exome Sequencing (Mandarin Translation) [15]

Publications by our group

Published Manuscripts:

Mardy AH, Rangwala N, Hernandez-Cruz Y, Gosnell KA, Gonzalez JM, Norton ME, Sparks TN. Utility of chromosomal microarray for diagnosis in cases of nonimmune hydrops fetalis. *Prenat Diagn* 2020; Epub ahead of print. (PubMed ^[16])

Sparks TN, Thao K, Lianoglou BR, Boe NM, Bruce KG, Datkhaeva I, Field NT, Fratto VM, Jolley J, Laurent LC, Mardy AH, Murphy AM, Ngan E, Rangwala N, Rottkamp CAM, Wilson L, Wu E, Uy CC, Valdez Lopez P, Norton ME on behalf of the University of California Fetal-Maternal Consortium (UCfC). Nonimmune hydrops fetalis: identifying the underlying genetic etiology. *Genet Med* 2019; 21(6):1339-1344. (PubMed ^[17])

Mardy AH, Chetty SP, Norton ME, Sparks TN. A system-based approach to the genetic etiologies of non-immune hydrops fetalis. *Prenat Diagn* 2019; 39(9):732-750. (PubMed ^[18])

Berger VK, Sparks TN, Jelin AC, Derderian C, Jeanty C, Gosnell K, MacKenzie T, Gonzalez JM. Non-immune hydrops fetalis: Do placentomegaly and polyhydramnios matter? *J Ultrasound Med* 2018; 37(5):1185-1191. (PubMed ^[19])

Conference Presentations:

Sparks TN, Lianoglou BR, Patel S, Adami R, Rangwala N, Datkhaeva I, Holliman K, Downum S, Amezcua J, Boe N, Laurent LC, MacKenzie TC, Murphy A, Sanders S, Slavotinek AM, Norton ME on behalf of the University of California Fetal-Maternal Consortium (UCfC). HyDROPS study: Exome sequencing identifies genetic disorders causing non-immune hydrops fetalis. Presented in oral format at: Annual Meeting of the Society for Maternal-Fetal Medicine (SMFM); Dallas, TX. February 3-8, 2020. (Abstract ^[20])

Sparks TN, Chen F, Lianoglou BR, Rego S, Patel S, Slavotinek AM, Koenig B, Norton ME. Agreement to secondary findings with exome sequencing in pre- and postnatal settings. Presented in poster format at: Annual Meeting of the Society for Maternal-Fetal Medicine (SMFM); Dallas, TX. February 3-8, 2020. (Abstract ^[21])

Mardy AH, Hernandez-Cruz Y, Rangwala N, Gosnell KA, Gonzalez JM, Norton ME, Sparks TN. Utility of chromosomal microarray in cases of non-immune hydrops fetalis. Poster presented at: Annual Meeting of the Society for Maternal-Fetal Medicine (SMFM); Las Vegas, NV. February 11-16, 2019. (Abstract ^[22])

Sparks TN, Thao K, Lianoglou B, Boe N, Bruce K, Datkaeva I, Field N, Fratto V, Jolley J, Laurent L, Mardy AH, Murphy AM, Rangwala N, Valdez Lopez P, Ngan E, Rottkamp C, Wilson L, Wu E, Uy C, Norton ME for University of California Fetal-Maternal Consortium. Underlying etiologies in prenatally-diagnosed non-immune hydrops fetalis. Poster presented at: Annual Meeting of the Society for Maternal-Fetal Medicine (SMFM); Dallas, TX. January 29-February 3, 2018. (Abstract ^[23])

Study Brochures

[Download HyDROPS Brochure for Participant](#) ^[24]

[Download HyDROPS Brochure for Medical Provider](#) ^[25]

Webinar: When Is Exome Sequencing Valuable in Prenatal Diagnosis?

View the webinar ^[26], with maternal-fetal medicine specialist, Mary E. Norton, MD, discussing genetic testing options, with a focus on when exome sequencing has value to families. Also, perinatologist, Teresa N. Sparks, MD, presents specifics on exome sequencing for nonimmune hydrops fetalis, caused by many single-gene disorders, plus a look at findings from her current NIHF study.

Study Sponsors

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ClinicalTrials.gov Identifier

NCT03412760 ^[27]

Contact Us
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Source URL: <https://fetus.ucsf.edu/hydrops-study>

Links

- [1] <mailto:hydrops@ucsf.edu?subject=Hydrops%20Study>
- [2] <https://fetus.ucsf.edu/sites/fetus.ucsf.edu/files/wysiwyg/UCSF%20NIHF%20Workup%202-2020.pdf>
- [3] https://fetus.ucsf.edu/sites/fetus.ucsf.edu/files/wysiwyg/UCSF_HyDROPS_Study_Overview_7-2020.pdf
- [4] <mailto:hydrops@ucsf.edu?subject=Hyrdops%20Study>
- [5] <https://fetus.ucsf.edu/our-team/teresa-sparks-md>
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- [11] <https://profiles.ucsf.edu/sarah.downum>
- [12] <mailto:Sarah.Downum@ucsf.edu>
- [13] <https://www.youtube.com/watch?v=mYxFAExLxVI>
- [14] <https://bit.ly/3h99JAv>
- [15] <https://bit.ly/322ZXtj>
- [16] <https://www.ncbi.nlm.nih.gov/pubmed/31981373>
- [17] <https://www.ncbi.nlm.nih.gov/pubmed/30410095>
- [18] <https://www.ncbi.nlm.nih.gov/pubmed/31087399>
- [19] <https://www.ncbi.nlm.nih.gov/pubmed/29076544>

- [20] [https://www.ajog.org/article/S0002-9378\(19\)31469-3/fulltext](https://www.ajog.org/article/S0002-9378(19)31469-3/fulltext)
- [21] [https://www.ajog.org/article/S0002-9378\(19\)32285-9/fulltext](https://www.ajog.org/article/S0002-9378(19)32285-9/fulltext)
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- [23] [https://www.ajog.org/article/S0002-9378\(17\)31611-3/fulltext](https://www.ajog.org/article/S0002-9378(17)31611-3/fulltext)
- [24] https://fetus.ucsf.edu/sites/fetus.ucsf.edu/files/wysiwyg/UCSF_HyDROPS_Patient_Brochure_6-2020.pdf
- [25] https://fetus.ucsf.edu/sites/fetus.ucsf.edu/files/wysiwyg/UCSF_HyDROPS_Provider_Brochure_Insert%20-2020.pdf
- [26] <https://medconnection.ucsfhealth.org/videos/genetic-testing-update-when-is-exome-sequencing-valuable-in-prenatal-diagnosis>
- [27] <https://clinicaltrials.gov/ct2/show/NCT03412760>