

The PHACE Registry: Update and Review of Accomplishments

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 PHACE Syndrome Community Conference
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PHACE syndrome International Clinical Registry and Genetic Repository

- Established in 2006 at UCSF with Dr. Ilona Frieden
- Merged with the Texas Children's PHACE Registry Directed by Denise Metry in 2011
- 310 individuals with PHACE and their families enrolled
- Ongoing efforts include natural history studies and gene discovery

What Happens When You Enroll?

- We will do consent forms
- We will review the medical history
- We will order a small blood draw from the child (or adult with PHACE) and both parents if available or we can also use saliva kits
- We may collect a tissue sample
- We will collect reports MRI's and other test results and do a survey



The Research: Clinical and Genetic

- We are also trying to understand the spectrum of medical issues in PHACE syndrome
- We want to understand the natural history, what do we need to watch out for in adulthood?
- We are using sequencing techniques to look for small changes in the DNA to find the cause of PHACE

Why participate in research?

- Your participation in the registry makes the research possible to publish the papers that help educate your doctors



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PHACE Syndrome: Consensus-Derived Diagnosis and Care Recommendations

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[The Journal of Pediatrics](http://www.jpeds.com)
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PHACE Syndrome: Consensus-Derived Diagnosis and Care Recommendations

- 28 physicians from 14 institutions, 9 pediatric specialties,
 - Neuroradiology
 - Neurosurgery
 - Neurology
 - Cardiology
 - Cardiothoracic surgery
 - Dermatology
 - Otolaryngology
 - Hematology-oncology
 - Plastic surgery

Garzon et al. J Pediatr. 2016

Consensus statement on PHACE syndrome diagnostic criteria

- Multidisciplinary group met in Houston, Texas at the PHACE research conference in 2008
- **Definite PHACE:**
 - Segmental hemangioma or hemangioma > 5 cm on the face or scalp PLUS 1 major criterion OR 2 minor criteria
- **Possible PHACE:**
 - Segmental hemangioma > 5 cm on the face or scalp PLUS 1 minor criterion

Metry D, Heyer G, Hess C, et al. Consensus Statement on Diagnostic Criteria for PHACE Syndrome. *Pediatrics* 2009;124:1447-56.

Variations of PHACE syndrome

Expanding the spectrum of PHACE

- Many individuals have major criteria for PHACE but lack the characteristic "facial" location of their large segmental hemangioma
 - Examples include the scalp, upper chest and arm
 - Some people have PHACE-related changes without a hemangioma on the skin
 - Large hemangioma can occur behind the eye with no extension to the skin surface

- Segmental or regional presentation of hemangioma along with classic PHACE anomalies not coincidental but a part of the continuum

Inheritance

- The PHACE registry has over 310 enrolled, no familial recurrence seen
- One set of monozygotic twins with only one affected
- All cases to date have been sporadic

Registry study of structural changes

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ORIGINAL ARTICLE WILEY WILEY-LISSA INTERNATIONAL medical genetics

Structural malformations of the brain, eye, and pituitary gland in PHACE syndrome

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- Cerebellar hypoplasia 25%
- Dandy Walker 9%
- Malformations of cortical development 7%
- Intracranial hemangiomas 18%
- Optic nerve changes 11%

THE JOURNAL OF PEDIATRICS • www.jpeds.com CLINICAL AND LABORATORY OBSERVATIONS

Prenatal Risk Factors for PHACE Syndrome: A Study Using the PHACE Syndrome International Clinical Registry and Genetic Repository

Joy Wan, MD¹, Jack Steiner, BS², Eulalia Baselga, MD¹, Francine Blei, MD¹, Maria Cordisco, MD³, Maria C. Garzon, MD¹⁷, Deborah S. Goddard, MD³, Anita Haggstrom, MD³, Alfons Krol, MD^{18,11}, Ilona J. Frieden, MD¹², Denise Metry, MD¹³, Kimberly D. Morel, MD¹⁷, Judith M. A. Verhagen, MD¹⁴, Orii Wargon, MD¹⁵, Beth A. Drolet, MD¹⁶, and Dawn H. Siegel, MD¹⁶

The cause of PHACE syndrome is unknown. In a study of 218 patients, we examined potential prenatal risk factors for PHACE syndrome. Rates of pre-eclampsia and placenta previa in affected individuals were significantly greater than in the general population. No significant risk factor differences were detected between male and female subjects. (*J Pediatr* 2017;190:275-9).

- Rates of pre-eclampsia and placenta previa significantly higher than general population
- Number of miscarriages also slightly higher

Collaborators

- Medical College of Wisconsin
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 - Wendy Demos
 - Beth Drolet
 - Liz Worthey
 - Shawna Brown
 - Katherine Mueller
 - Angela Beltrame
 - Uli Brockel
 - John Jensen
 - Paula North
 - Patricia Burrows
- UCSF
 - Ilona Frieden
 - Erin Mathes
 - Kelly Cordoro
 - Bill Hoffman
 - Chris Hess
 - Pui Kwok
 - Joseph Shieh
 - Deborah Goddard
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- Australia
 - Orii Wargon
- Netherlands
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 - Johannes M.P.J. Breur
- Ireland
 - Rosemary Watson

And many more!
Thank you!

