



UvA-DARE (Digital Academic Repository)

Keeping an eye on the brain of perinatally HIV-infected children

Blokhuis, C.

[Link to publication](#)

Citation for published version (APA):

Blokhuis, C. (2017). Keeping an eye on the brain of perinatally HIV-infected children

General rights

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

Disclaimer/Complaints regulations

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <http://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

V - APPENDICES

ABOUT THE AUTHOR



Charlotte Blokhuis (Hilversum, 1987) graduated from Comenius College in Hilversum in 2005, and started studying medicine at the VU University Medical Center Amsterdam in the same year. With an avid passion for pediatrics, she followed her research internship and senior clinical elective at the pediatric ward of the Slotervaart Hospital in Amsterdam. Her final year of rotations included a Tropical Medicine elective in Cameroon, where she worked at the Apostolic Hospital Banga Bakundu, and was recruited for several outreach missions in the surrounding area. She obtained her medical degree in 2012.

For the following two years, Charlotte worked as a house officer at the pediatric departments of the Slotervaart Hospital in Amsterdam and the Flevo Hospital in Almere. Having developed a keen interest in pediatric infectious diseases and a curiosity for research, she started as a PhD candidate at the Emma Children's Hospital in Amsterdam in 2015. Under supervision of dr. Dasja Pajkrt, prof. dr. Taco Kuijpers, and prof. dr. Peter Reiss, she studied the microstructural and biochemical aspects of cognitive and cerebral deficits in perinatally HIV-infected children. As of 2016, she resumed part-time clinical duties at the pediatric department of the Flevo Hospital alongside her research work.

Charlotte resides in Hilversum, where she has been an active member in the Worship and Creative Arts team of Thousand Hills International Church for over a decade. Her free time is typically infused with creative endeavors, including music, graphic/web design, drawing, and photography. She aims to commence training to become a pediatrician in the near future.

CO-AUTHORS

M.D. (MICHAEL) ABRAMOFF. MD PHD

Department of Ophthalmology and Visual Sciences, Stephen A. Wynn Institute for Vision Research, University of Iowa, Iowa City, United States; Department of Biomedical Engineering and Department of Electrical and Computer Engineering, University of Iowa, Iowa City, United States

M.W.A. (MATTHAN) CAAN. PHD

Department of Radiology, Academic Medical Center, University of Amsterdam, The Netherlands

S. (SOPHIE) COHEN. MD PHD

Pediatric Hematology, Immunology, and Infectious Diseases, Emma Children's Hospital, Amsterdam, The Netherlands

Y.W. (YVONNE) VAN DALEN. MSC

Pediatric Hematology, Immunology, and Infectious Diseases, Emma Children's Hospital, Amsterdam, The Netherlands

N. (NAZLI) DEMIRKAYA. MD

Department of Ophthalmology, Academic Medical Center, University of Amsterdam, The Netherlands

S. (SUSANNE) DOELEMAN. BSC

Pediatric Hematology, Immunology, and Infectious Diseases, Emma Children's Hospital, Amsterdam, The Netherlands

M.H. (MALON) VAN DEN HOF. MD

Pediatric Hematology, Immunology, and Infectious Diseases, Emma Children's Hospital, Amsterdam, The Netherlands

N.A. (NEELTJE) KOOTSTRA. PHD

Department of Experimental Immunology, Academic Medical Centre, Amsterdam, the Netherlands

J. (JENS) KUHLE. MD PHD

Neurology, Departments of Medicine, Biomedicine and Clinical Research, University Hospital Basel, Basel, Switzerland

T.W. (TACO) KUIJPERS. MD PHD

Pediatric Hematology, Immunology, and Infectious Diseases, Emma Children's Hospital, Amsterdam, The Netherlands

C.B.L.M. (CHARLES) MAJOIE. MD PHD

Department of Radiology, Academic Medical Center, University of Amsterdam, The Netherlands

R.A.A. (RON) MATHOT. PHARM D PHD

Department of Hospital Pharmacy, Clinical Pharmacology Unit, Academic Medical Center, Amsterdam, the Netherlands

H.J.M.M. (HENRI-JEAN) MUTSAERTS. MD PHD

Department of Radiology, Academic Medical Center, University of Amsterdam, The Netherlands; Cognitive Neurology Research Unit, Sunnybrook Health Sciences Centre, Toronto, Canada

D. (DASJA) PAJKRT. MD PHD MBA

Pediatric Hematology, Immunology, and Infectious Diseases, Emma Children's Hospital, Amsterdam, The Netherlands

C.F.W. (CAREL) PEETERS. PHD

Department of Epidemiology & Biostatistics, VU University Medical Center, Amsterdam, The Netherlands

M.C.M. (MARCEL) PISTORIUS

Department of Hospital Pharmacy, Clinical Pharmacology Unit, Academic Medical Center, Amsterdam, the Netherlands

P. (PETER) REISS. MD PHD

Department of Global Health, Academic Medical Center, University of Amsterdam, and Amsterdam Institute for Global Health and Development, The Netherlands; Department of Internal Medicine, Division of Infectious Diseases, Center for Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, The Netherlands; HIV Monitoring Foundation, Amsterdam, The Netherlands

H.J. (HENRIETTE) SCHERPBIER. MD PHD

Pediatric Hematology, Immunology, and Infectious Diseases, Emma Children's Hospital, Amsterdam, The Netherlands

J.A. (JACQUELINE) TER STEGE. MSC

Psychosocial Department, Emma Children's Hospital, Academic Medical Centre, Amsterdam, the Netherlands

C.E. (CHARLOTTE) TEUNISSEN. PHD

Neurochemistry Laboratory and Biobank, Department of Clinical Chemistry, VU University Medical Centre and Neurocampus Amsterdam, the Netherlands

F.D. (FRANK) VERBRAAK. MD PHD

Department of Ophthalmology, Academic Medical Center, University of Amsterdam, The Netherlands; Department of Biomedical Engineering and Physics, Academic Medical Center, University of Amsterdam, The Netherlands

F.W.N.M. (FERDINAND) WIT. MD PHD

Department of Global Health, Academic Medical Center, University of Amsterdam, and Amsterdam Institute for Global Health and Development, The Netherlands; Department of Internal Medicine, Division of Infectious Diseases, Center for Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, The Netherlands; HIV Monitoring Foundation, Amsterdam, The Netherlands

AUTHOR CONTRIBUTIONS

CHAPTER 2

CB drafted the manuscript and illustrated figures 1 and 2. NAK, MWAC, and DP revised the manuscript.

CHAPTER 3

YwvD analyzed the data including statistical analysis, interpreted the results, and drafted the manuscript. CB analyzed the data including statistical analysis, interpreted the results, and drafted the manuscript. SC recruited patients and controls, coordinated study visits, performed MRI scans, collected blood and CSF samples, and revised the manuscript. JAtS performed neuropsychological assessments and revised the manuscript. CET performed biomarker analysis and revised the manuscript. JK performed biomarker analysis and revised the manuscript. NAK conceptualized the laboratory protocol and revised the manuscript. HJS recruited patients, supervised study design, and revised the manuscript. TWK supervised study design and revised the manuscript. PR supervised study design and revised the manuscript. CBLMM conceptualized the imaging protocol, supervised MRI scanning procedure and revised the manuscript. MWAC designed the study, conceptualized the imaging protocol, supervised MRI scanning procedure and data analysis, interpreted the results and revised the manuscript. DP designed the study, supervised study visits, interpreted the results, and revised the manuscript.

CHAPTER 4

CB analyzed the data including statistical analysis, interpreted the results, and drafted the manuscript. HJMMM performed MRI postprocessing, interpreted the results, and revised the manuscript. SC recruited patients and controls, coordinated study visits, performed MRI scans, and revised the

manuscript. HJS recruited patients, supervised study design, and revised the manuscript. MWAC designed the study, conceptualized the imaging protocol, supervised MRI scanning, and revised the manuscript. CBLMM conceptualized the imaging protocol, supervised MRI scanning, and revised the manuscript. TWK and PR supervised study design and revised the manuscript. FWNMW advised on statistical analysis and revised the manuscript. DP designed the study, supervised study visits, interpreted results, and revised the manuscript.

CHAPTER 5

CB analyzed the data including statistical analysis, interpreted the results, and drafted the manuscript. ND performed optical coherence tomography scans, interpreted the results, and drafted the manuscript. SC recruited patients and controls, coordinated study visits, performed MRI scans, and revised the manuscript. FWNMW advised on statistical analysis and revised the manuscript. MDA contributed to the ophthalmological study protocol and revised the manuscript. HJS recruited patients, supervised study design, and revised the manuscript. TWK and PR supervised study design and revised the manuscript. MWAC conceptualized the imaging protocol, supervised MRI scanning, and revised the manuscript. CBLMM conceptualized the imaging protocol, supervised MRI scanning, and revised the manuscript. FD conceptualized the ophthalmological study protocol, supervised OCT scanning, and revised the manuscript. DP designed the study, supervised study visits, interpreted results, and revised the manuscript.

CHAPTER 6

CB and CFWP analyzed the data including statistical analysis and interpreted the results; CB drafted

and CFWP revised the manuscript. SC recruited patients and controls, coordinated study visits, collected blood and CSF samples, and revised the manuscript. HJS recruited patients, supervised study design, and revised the manuscript. NAK conceptualized the laboratory protocol, performed biomarker analysis, and revised the manuscript. TWK and PR supervised study design and revised the manuscript. CET conceptualized the laboratory protocol, performed biomarker analysis, interpreted results, and revised the manuscript. DP designed the study, supervised study visits, interpreted results, and revised the manuscript.

patients, supervised study design, and revised the manuscript. FWNMW advised on statistical analysis and revised the manuscript. MCMP performed liquid chromatography-mass spectrometry analysis and revised the manuscript. NAK and CET conceptualized the laboratory protocol and revised the manuscript. RAAM supervised liquid chromatography-mass spectrometry analysis, interpreted results, and revised the manuscript. DP designed the study, supervised study visits, interpreted results, and revised the manuscript.

CHAPTER 7

CB and SD analyzed the data including statistical analysis, interpreted the results, and drafted the manuscript. SC recruited patients and controls, coordinated study visits, collected blood and CSF samples, and revised the manuscript. ND performed optical coherence tomography scans and revised the manuscript. HJS recruited patients, supervised study design, and revised the manuscript. NAK and CET conceptualized the laboratory protocol, performed biomarker analysis, and revised the manuscript. JK performed biomarker analysis and revised the manuscript. FD conceptualized the ophthalmological study protocol, supervised OCT scanning, and revised the manuscript. DP designed the study, supervised study visits, interpreted results, and revised the manuscript.

CHAPTER 8

MvdH and CB analyzed the data including statistical analysis, interpreted the results, and drafted the manuscript. SC recruited patients and controls, coordinated study visits, collected blood and CSF samples, and revised the manuscript. HJS recruited

PHD PORTFOLIO

Name: Charlotte Blokhuis
PhD period: January 2015 – September 2017
Promotores: Prof. dr. T.W. Kuijpers; Prof. dr. P. Reiss
Copromotor: Dr. D. Pajkrt
Department: Pediatric Hematology, Immunology, and Infectious Diseases

PHD TRAINING

	COURSES	ECTS
2015	AMC World of Science	0.7
2015	Practical Biostatistics	1.1
2015	Unix	0.6
2015	Scientific Writing in English	1.5
2016	Basic Legislation in Science	0.9
2016	Project Management	0.6
	SEMINARS, WORKSHOPS, MASTERCLASSES	
2015	AMC Ruysch Masterclass by prof. dr. J. Ananworanich <i>Amsterdam, The Netherlands</i>	0.2
2015	AMC Ruysch Lecture by prof. dr. J. Ananworanich <i>Amsterdam, The Netherlands</i>	0.1
2015-16	AMC HIV Journal Club (monthly) <i>Amsterdam, The Netherlands</i>	1.0
2015-16	AMC Laboratory for Viral Immune Pathogenesis research meetings (weekly) <i>Amsterdam, The Netherlands</i>	2.0
2015-17	AMC Pediatric Hematology, Immunology and Infectious Diseases research meeting (monthly) <i>Amsterdam, The Netherlands</i>	1.0
2015	Spinoza Centre for Neuroimaging user meetings (weekly) <i>Amsterdam, The Netherlands</i>	1.0
	ORAL PRESENTATIONS AT SCIENTIFIC CONFERENCES	
2015	Netherlands HIV Treatment Association (NVHB) biannual meeting <i>Utrecht, The Netherlands</i>	0.5
2016	Amsterdam Kindersymposium <i>Amsterdam, The Netherlands</i>	0.5
2017	European Society for Pediatric Infectious Diseases Annual Meeting <i>Madrid, Spain</i>	0.5

POSTER PRESENTATIONS AT SCIENTIFIC CONFERENCES		ECTS
2015	European AIDS Clinical Society Conference <i>Barcelona, Spain</i>	0.5
2016	Netherlands Conference on HIV Pathogenesis, Treatment and Prevention <i>Amsterdam, The Netherlands</i>	0.5
2017	Conference on Retroviruses and Opportunistic Infections <i>Seattle, United States</i>	0.5
2017	European Society for Pediatric Infectious Diseases Annual Meeting <i>Madrid, Spain</i>	0.5
(INTER)NATIONAL CONFERENCES		
2015	Amsterdam Kindersymposium <i>Amsterdam, The Netherlands</i>	0.25
2015	European AIDS Clinical Society Conference <i>Barcelona, Spain</i>	1.0
2015	Netherlands Conference on HIV Pathogenesis, Treatment and Prevention <i>Amsterdam, The Netherlands</i>	0.25
2016	Conference on Retroviruses and Opportunistic Infections <i>Boston, United States</i>	1.0
2016	Amsterdam Kindersymposium <i>Amsterdam, The Netherlands</i>	0.25
2016	Netherlands Conference on HIV Pathogenesis, Treatment and Prevention <i>Amsterdam, The Netherlands</i>	0.25
2017	Conference on Retroviruses and Opportunistic Infections <i>Seattle, United States</i>	1.0
2017	European Society for Pediatric Infectious Diseases Annual Meeting <i>Madrid, Spain</i>	0.75

TEACHING

	LECTURING	ECTS
2016	Guest lecture at International Federation of Medical Students Association "House MD" seminar Amsterdam, The Netherlands	0.2
	TUTORING, MENTORING, SUPERVISING	
2015	Y.W. van Dalen, BSc <i>Master thesis</i>	2.0
2016	P.N.D. Elders <i>Bachelor thesis</i>	2.0
2016	A.M. Dasler, BSc <i>Extracurricular project</i>	1.0
2016	S. Doeleman <i>Bachelor thesis</i>	2.0
2016	M. van Zanten, MD <i>Extracurricular project</i>	1.0
2017	M. Klein Haneveld <i>Bachelor thesis</i>	0.7
2017	A.M. Weijnsfeld <i>Master thesis</i>	1.0

PARAMETERS OF ESTEEM

2016	AMC PhD Poster Award (2nd prize)
2017	Amsterdam Infection & Immunity Travel Award
2017	European Society for Pediatric Infectious Diseases Annual Meeting Travel Award

PUBLICATIONS

INTERNATIONAL PUBLICATIONS

THIS THESIS

Higher subcortical and white matter cerebral blood flow in perinatally HIV-infected children

C. Blokhuis, H.J.M.M. Mutsaerts, S. Cohen, H.J. Scherpbier, M.W.A. Caan, C.B.L.M. Majoie, T.W. Kuijpers, P. Reiss, F.W.N.M. Wit, D. Pajkrt
Medicine (Baltimore). 2017 Feb;96(7):e5891

The Eye as a Window to the Brain: Neuroretinal Thickness Is Associated With Microstructural White Matter Injury in HIV-Infected Children

C. Blokhuis*, N. Demirkaya*, S. Cohen, F.W.N.M. Wit, H.J. Scherpbier, P. Reiss, M.D. Abramoff, M.W.A. Caan, C.B.L.M. Majoie, F.D. Verbraak, D. Pajkrt.
Invest Ophthalmol Vis Sci. 2016 Jul 1;57(8):3864-71

Neurometabolite Alterations Associated With Cognitive Performance in Perinatally HIV-Infected Children

Y.W. Van Dalen*, C. Blokhuis*, S. Cohen, J.A. Ter Stege, C.E. Teunissen, J. Kuhle, N.A. Kootstra, H.J. Scherpbier, T.W. Kuijpers, P. Reiss, C.B.L.M. Majoie, M.W.A. Caan, D. Pajkrt.
Medicine (Baltimore). 2016 Mar;95(12):e3093

Neurodevelopmental delay in pediatric HIV/AIDS: current perspectives

C. Blokhuis, N.A. Kootstra, M.W.A. Caan, D. Pajkrt.
Neurobehav HIV Med. 2016 Jan;7(1):1-13.

* denotes equal contributors

OTHER

Virological and Social Outcomes of HIV-Infected Adolescents and Young Adults in The Netherlands Before and After Transition to Adult Care

A.M. Weijnsfeld, C. Smit, S. Cohen, F.W.N.M. Wit, M. Mutschelknauss, L.C. van der Knaap, L.M. van Zonneveld, B.J. Zomer, N. Nauta, J.C. Patist, M.H.J. Kuipers-Jansen, E.P. Smit, C. Blokhuis, D. Pajkrt, for the Dutch HIV Adolescents and Young Adults (AYA) Study Group.

Clin Infect Dis. 2016 Oct 15;63(8):1105-12

Intermittent fasting during Ramadan causes a transient increase in total, LDL, and HDL cholesterol and hs-CRP in ethnic obese adolescents

N.N.E. Radhakishun, C. Blokhuis, M. van Vliet, I.A. von Rosenstiel, O. Weijer, M.W. Heymans, J.H. Beijnen, D.P. Brandjes, M. Diamant.

Eur J Pediatr. 2014 Aug;173(8):1103-6

ACKNOWLEDGEMENTS

“Gratitude bestows reverence, allowing us to encounter everyday epiphanies, those transcendent moments of awe that change forever how we experience life and the world.”

— John Milton

This thesis would not exist without the help and contributions of many. And on top of that, the things I have learned in the past few years go *far beyond* the content of this thesis.

Naturally, I gladly express my thankfulness to a colorful multitude of talented, genuine, and inspiring people that I have had the absolute honor of working with, learning from, and being supported by.

THANK YOU...

SUPERVISORS

Dasja – countless coffees, emails, meetings, and pep-talks later, here we are! You possess an unparalleled, steadfast tenacity and contagious drive that fuel motivation and keep this train in motion. Thank you for having me on board, from ‘novice’ to this milestone, and for your confidence and advice.

Prof. dr. T.W. Kuijpers, prof. dr. P. Reiss – Taco, Peter – for your highly valued input and direction.

COMMITTEE

My immense gratitude to prof. dr. Jintanat Ananworanich, prof. dr. Peter Portegies, prof. dr. Marceline van Furth, prof. dr. Liesbeth Reneman, prof. dr. Michael Boele van Hensbroek, and dr. Kim C.E. Sigaloff, for your critical appraisal of this thesis and your willingness to be part of the doctoral committee.

NOVICE STUDY TEAM

Thank you for curiosity and continuing efforts to keep discovering more about cognitive and cerebral health in pediatric HIV.

Sophie – thank you for paving the way and showing me how. Malon – for taking over with such fresh avidity and precision. Henriëtte – for your tremendous contribution to pediatric HIV care and research, and further igniting my interest for pediatric infectious diseases. Annuschka – for your incredible resolve, thoroughness, and perseverance (we’ll get there one day!). Atie – for your great effort in recruiting and caring for patients.

Co-authors – it’s been such a pleasure to work with you and learn something new from each of you in such a wide range of expertise: Experimental Immunology (Neeltje Kootstra), Radiology (Matthan Caan, Henk-Jan Mutsaerts, Charles Majoie), Ophthalmology (Nazli Demirkaya, Frank Verbraak, Michael Abramoff), Pharmacology (Ron Mathôt, Marcel Pistorius), and Pediatric Psychosocial department (Jacqueline ter Stege) at the Academic Medical Center, Plasma Proteins at Sanquin (Joost Meijer), the HIV Monitoring Foundation (Ferdinand Wit), Neurology at the University Hospital Basel (Jens Kuhle), Neurochemistry Laboratory and Biobank (Charlotte Teunissen) and Epidemiology and Biostatistics (Carel Peeters) at the VU Medical Center – for such enjoyable and beneficial collaborations with a generous dose of diligence.

Students – for your remarkable endeavor, enthusiasm, and teachability.

To every single study participant and their parents/caregivers – thank you so much for your willingness to contribute. None of this would have been possible without you.

H8 CREW

To all of you amazing PhD-hunting champions passing through the top floor over the years – thank you for advice, fellowship, and so much laughter. And coffee. And lunch. (And one more coffee.)

PEDIATRICS – SLOTERVAARTZIEKENHUIS

Thank you for facilitating the transition from student to doctor, and recommending to approach Dasja for a research project.

PEDIATRICS – FLEVOZIEKENHUIS

I wouldn't be half the doctor I am now if it weren't for this outstanding team. Pediatricians – thank you for guidance, trust, and inspiration. Katja – for hiring me (twice!) and sending me on my way to pediatric residency. Fellow house officers – for the morning coffees (I see a theme here...), impeccable team spirit, and keeping it real.

THOUSAND HILLS INTERNATIONAL CHURCH

Thank you for endless encouragement and opportunities to be creative, grow, and be part of a team that so vastly surpasses the sum of parts. I'm counting my blessings.

FRIENDS

Old and new, near and far – thank for allowing our paths to cross and for letting that bring out the best in each other. Mirte – for a friendship that cannot be contained in words (although '*laugh it up, fuzball!*' probably explains a lot). Denise – for always adding that fabulous sparkle. Fellow gig aficionados – for sharing passion and making memories. I cannot thank you enough.

FAMILY

Otis – de gekste Lego-bedenksels, team-tekeningen, maffe voetbalspelletjes, goeie moppen, proestende washandjes, duizelige treintjes, omgebouwde slaapliedjes... wat kunnen wij goed samen lachen hè? Marius – for playing things, at times. (And other things at other times.) Daphne and Susanne – for always being by my side. Sam and Nathan – for taking such good care of them. Leo, Ricky – for your unending supply of conversation, music, and a good whisky every now and then. Petra – for your unconditional love and always being my safe haven.