

- 1 Leading Bristol Neonatal Neuroscience laboratory running both experimental models and feasibility/pilot/large RCT clinical trials (newborn neuroprotection; hypothermia and added therapies like xenon).
- 2 Research staff, 3 PhD fellows (2 in Norway), 3MD fellows, 2 technicians and 1postdoctoral fellows. Local and international collaboration.
- 2 Clinical Practice. On service attending consultant for a level 3 NICU. Long term follow up clinic (Bayley examination) of all infants cooled in the south west neonatal network.
- 3 Teaching and supervision of doctors, nurses in training and research staff
- 4 The running of large international clinical trials.

PERSONAL DETAILS

Address [email]	School of Clinical Sciences, University of Bristol St Michael's Hospital, Southwell Street, Bristol BS2 8EG [marianne.thoresen@bris.ac.uk]
Date of birth	15th April 1951
Nationality	Norwegian

ACADEMIC HISTORY

1983	PhD (Institute of Physiology, University of Oslo, Norway)
1982	MD (Medicine) University of Oslo, Norway
1973	Physiotherapy, Oslo

HONORS, AWARDS and ELECTED FELLOWSHIPS

2011 June 28 th	The Vice Chancellor of University of Bristol IMPACT AWARD for 2011
2010	ACADEMIA EUROPAEA elected fellow
2007	Norwegian Academy of Science and Letters: ELECTED FELLOW
2007 October	Visiting "Tooley" Professor, named lecture University of California San Francisco (US)
1998	Royal College of Paediatrics and Child Health (UK) ELECTED FELLOW
1996-98	Visiting Professor, 2months/year Gothenburg , Sweden.Swedish Medical Research Council
1992-95	Carrier award for female scientists (3 yrs, start up grant). Norwegian Medical Research Council

RECENT EMPLOYMENT HISTORY

2003 present	Professor of Neonatal Neuroscience, University of Bristol and Honorary Consultant Neonatologist, St Michael's Hospital, Bristol, UK
In addition, from 1/9/2011	Professor of Physiology, Institute of Basic Medical Sciences, University of Oslo, Norway
2001-2003	Reader and consultant as above
1998-2001	Senior Lecturer in Neonatology, Honorary Consultant Neonatologist, UoB
1997-1997	Consultant Neonatologist, Ullevaal University Hospital, Oslo,
1996-1998	Visiting Professor, 2 mths/year Department of Physiology, University of Gothenburg (Sweden)
1992 -1995	Scientist Norwegian MRC Carrier award
1988 1992	Training in Paediatrics, Ullevaal University Hospital, Oslo, The National Centre for Epilepsy, Oslo, Norway
1985- 1988	Postdoctoral fellowship Nobel Institute of Neurophysiology, Karolinska Institute, Stockholm Sweden

PROFESSIONAL ACTIVITIES

- Adviser for NICE (National Institute of Clinical Excellence, UK) on hypothermia therapy
- Data Monitoring Cttee (Chair) for the Australian Neonatal Cooling Trial (ICE 2002-2011)
- Adviser for the French Neonatal Society on Hypothermia Treatment (2010→)
- Steering Cttee - NEST trial (co-chair)(Hypothermia during Ecmo treatment UK 2004-2012)

- Adviser for NIH on hypothermia as neuroprotection (2005, 2010 and neonatal stroke 20114)
- Reviewer for grant-giving bodies in the US, Australia, New Zealand, UK, Sweden & Norway
- Reviewer for academic journals (Ann Neurology, J Neurosci, Stroke, J Cereb Blood Flow Metab, Anaesthesiology, Brain Pathology, Pediatrics, Pediatric Research and more) and grant giving bodies (in UK, Scandinavia, NZ and US)
- Assessor for external chairs in neonatology/pediatrics
- Member of current working parties in the UK: Fetal alcohol syndrome Definitions on Perinatal Asphyxia

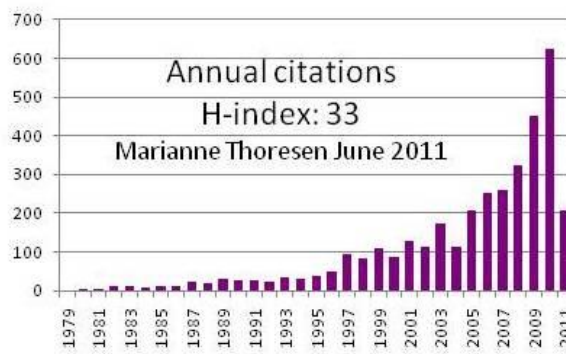
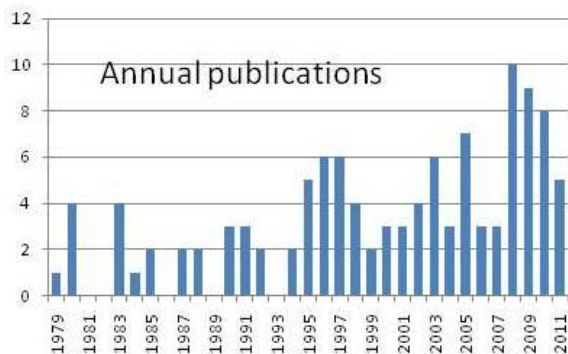
Grants awarded 1998-20011 (UK)as PI ~£ 2.30 mill + £2.0 as co-PI

Previous Grant Awards –1978-1997 in Norway £ 644 000

SELECTED INVITED KEYNOTE LECTURES - LAST 4 YEARS (A=ADULT MEDICINE)

- 2011 Association of Paediatric Anaesthetists of Great Britain & Ireland. 20 May. *Neuroprotection with cooling and the added benefits of xenon*
- 2011 Amsterdam, Netherlands. 12-14 February 6th Int Conf on Brain Monitoring: *How therapeutic hypothermia changes outcome predictors*
- 2011 Bristol, UK. Neonatal Brain Club. 5-6 February
- 2010 Washington US: “Hot topics in neonatology” 8-10 Dec. Cooling and Xenon
- 2010 Bristol: Masterclass in Neurology October
- 2010 London, Imperial College: “Update in Neonatology” November 27th
- 2010 Cartagena, Colombia: Biannual intensive care and neonatology conference of South America. 20-23 Oct. 3 lectures
- 2010 Washington, 10-12 August. Hypothermia, implication for clinical practice. NIH working group.
- 2010 Tours, France L’egide de la Commission Recommendations de la Societe Francaise de Neonatologie Jan 29th I. Physiology and adverse effects during hypothermia and II. Cooling in Clinical practice: In the delivery room, during transport and in the nursery.
- 2009 Lisboa, Portugal, Portuguese Society for Intensive care and Neonatal Medicine 12-14 Nov . “Neonatal neuroprotection”
- 2009 British Association of Perinatal Medicine, Leeds – 11 September 2009
“Clinical effectiveness and safety issues of combined hypothermia and Xenon inhalation as neuroprotection after hypoxia-ischaemia in small and large animal models”
- 2009A Lund, Sweden – 2-5 September 2009 “Xenon as neuroprotection”, 4th international Hypothermia Meeting, Member of Organising Committee and Faculty.
- 2009 Pediatric Academic Societies Annual Meeting – Baltimore, USA 2-5 May
“Enhancing Newborn Neuroprotection: Hypothermia plus ?”
- 2009 4th Neonatal Brain Monitoring Conference – Orlando, Florida 20-22 Feb 2009
“Outcome of clinical cooling trials, aEEG during cooling and a clinical protocol outside a randomised trial”
- 2009 Royal Society for Medicine (UK): Advances and outcomes in neonatology, 22 Jan
“The term brain - Birth asphyxia and treatment options”
- 2008A Therapeutic Temperature Management Congress 1-4 October 2008 Barcelona
“Neonatal Asphyxia – State of the Art Hypothermia for neonatal asphyxia”
“Hypothermia plus ...? Experimental work on neonatal combination therapy”
- 2008 Newborn Brain Symposium and hypothermia workshop St Louis, USA, Sept 2008
Symposium: Mechanisms of injury – Term brain : “Hypothermia”
- 2008 Conference with Directors of Neonatology in Israel on Cooling – Tel Aviv June 2008 22 June: Planning Israel’s treatment plan for asphyxiated infants
23 June: Keynote Lecture at the Annual Israeli Obstetric/Neonatal Meeting
- 2008A European Resuscitation Council 9th Scientific Congress – Belgium 22-24 May 2008
Session: ‘Pro-Con - Therapeutic Hypothermia in Neonates’,
- 2008 European Pediatric Intensive Care Society, Ljubljana, Slovenia – 6-8 March 2008
“Therapeutic hypothermia and neuroprotective drugs in HIE of the newborn”
“Safety of therapeutic hypothermia, feasibility before and during transport to tertiary center”
- 2008 Neonatal Brain Monitoring Conference, Vienna 16-18 January 2008
Session: Neuroprotection – “Supportive care of infants during brain cooling”
- 2007 Visiting “Tooley” Professor – UCSF: Delivering The 2007 “Tooley Lecture” – Sept 2007

Publication activity: I was cited 700 times in 2010 and my H-index is 33.



Published papers 2008-2012 R=review or chapter

98 (2008) Aquilina K, Hobbs C, Cherian S, Tucker A, Porter H, Whitelaw A, **Thoresen M**. A neonatal piglet model of intraventricular hemorrhage and post-hemorrhagic ventricular dilatation. *J Neurosurg (2 Suppl Pediatrics)* 2008; 107:126-136

99 (2008) Gunn A, Wyatt JS, Whitelaw A, Barks J, Azzopardi D, Ballard R, Edwards AD, Ferriero D, Gluckman PD, Polin RA, Robertson CM, **Thoresen M**. CoolCap Study Group. Therapeutic Hypothermia Changes the Prognostic Value of Clinical Evaluation of Neonatal Encephalopathy. *J Pediatrics* 2008; 152(1): 55-58

100 (2008) Gressens P, Dingley J, Plaisant F, Porter H, Schwendimann L, Verney C, Tooley J, **Thoresen M**. Analysis of Neuronal, Glial, Endothelial, Axonal and Apoptotic Markers following moderate Therapeutic Hypothermia and Anaesthesia in the Developing Piglet Brain. *Brain Pathology* 2008; 18(1): 10-20

101 (2008) Hobbs C, **Thoresen M**, Tucker AM, Aquilina K, Chakkarapani E, Dingley J. Xenon and hypothermia combine additively offering long term functional and histopathological neuroprotection after neonatal hypoxia-ischemia. *Stroke* 2008; 39(4) 1307-13

102 (2008) Dingley J, Hobbs C, Ferguson J, **Thoresen M**. Xenon/hypothermia neuroprotection regimes in spontaneously breathing neonatal rats after hypoxic-ischemic insult: respiratory and sedative effects. *Anaesthesia and Analgesia* 2008; 106: 916-923

103 (2008) Karlsson M, Tooley J, Satas S, Hobbs H, Chakkarapani E, Stone J, Porter H, **Thoresen M**. Delayed hypothermia as selective head cooling or whole body cooling does not protect brain or body in newborn piglets. *Ped Res* 2008; 64(1):74-80

104 (2008) Tucker A, Aquilina K, Chakkarapani E, Hobbs C, **Thoresen M**. Development of amplitude-integrated EEG and interburst interval in the rat. *Pediatric Research e-pub 20.8.08 Vol 65(1)2009;62-66*

105 (2008) Aquilina K, Hobbs CE, Tucker AM, Whitelaw A, **Thoresen M**. Do drugs that block Transforming Growth Factor Beta reduce post-haemorrhagic ventricular dilatation in a neonatal rat model ? *Acta Paediatrica* 2008 Sep;97(9):1181-6

106 (2008) Azzopardi D, Brocklehurst P, Edwards D, Halliday H, Levene M, **Thoresen M**, Whitelaw A. The TOBY Study: Whole body hypothermia for the treatment of perinatal asphyxial encephalopathy:a randomised controlled trial. *BMC Pediatrics* 2008; 8(1):17 e-pub ahead of print

107 (2008) **Thoresen M**. Supportive care during neuroprotective hypothermia in the term newborn - adverse effects and their prevention. *Clinics in Perinatology - Neuroprotection issue.* 2008 35;749-763

108 (2008) Azzopardi D, Strohm B, Brocklehurst P, Edwards AD, Halliday H, Juszczak J, Levene M, **Thoresen M**, Whitelaw A, on behalf of the steering group and TOBY Cooling Register Participants. Treatment of asphyxiated newborns with moderate hypothermia in routine clinical practice: How cooling is managed in UK outside a clinical trial. *Arch Dis Child Fetal Neonatal Ed.* 2009 Jul;94(4):F260-4. e-pub 5.12.08

109R(2008) Gunn AJ, Hoehn T, Hansmann G, Bührer C, Simbruner G, Yager J, Levene M, Hamrick SEG, Shankaran S and **Thoresen M**. Hypothermia: An evolving treatment for neonatal hypoxic ischemic encephalopathy. *Pediatrics* 2008;121: 648-649 (Commentary - Letter to Editor)

110R (2008) Hoehn T, Hansmann G, Bührer C, Simbruner G, Gunn AJ, Yager J, Levene M, Hamrick SEG, Shankaran S, **Thoresen M**. Therapeutic hypothermia in neonates. Review of current clinical data, ILCOR recommendations and suggestions for implementation in neonatal intensive care units. *Resuscitation* 2008; 78:7-12

111 (2009) **Thoresen M**, Hobbs C, Wood T, Chakkarapani E, Dingley J. Cooling combined with immediate or delayed Xenon inhalation provides equivalent long-term neuroprotection after neonatal hypoxia-ischemia. *J Cereb Blood Flow Metab* 2009 Apr; 29(4): 707-14 E-pub Jan 14

112 (2009) Malcolm R. Battin, **Marianne Thoresen**, Elizabeth Robinson, Richard A. Polin, A. David Edwards, Alistair Jan Gunn, on behalf of the Cool Cap Trial Group. Does head cooling with mild systemic hypothermia affect requirement for blood pressure support? *Pediatrics* 2009 Mar;123(3):1031-6

113 (2009) M Karlsson, S Satas, J Stone, H Porter, **M Thoresen**. Liver enzymes cannot be used to predict liver damage after global hypoxia-ischemia in a neonatal pig model. *Neonatology* 2009 Apr; 96: 211-218

114 (2009) Liu X, Borooah M, Stone J, Chakkarapani E, **Thoresen M**. The effect of 3-day therapeutic hypothermia on serum gentamicin levels in new born encephalopathic infants. *Pediatrics* 2009 July; 124(1):310-15

- 115 (2009) Chakkarapani E, **Thoresen M**, Hobbs C, Aquilina K, Liu X, Dingley J. A closed-circuit neonatal xenon delivery system: technical neuroprotection feasibility study in newborn pigs. *Anesthesia & Analgesia* 2009 Aug;109(2):451-60 (e-pub 1.6.09)
- 116 (2009) Azzopardi D, Strohm B, Edwards AD, Dyet L, Halliday H, Juszcak J, Kapellou O, Levene M, Marlow N, Porter E, **Thoresen M**, Whitelaw A, Brocklehurst P. Moderate Hypothermia to Treat Perinatal Asphyxial Encephalopathy: The TOBY Randomized Controlled Trial. *N Engl J Med*. 2009 Oct 1;361(14):1349-58
- 117 (2009) Chakkarapani E, Harding D, Stoddart P, Garrett-Cox R, **Thoresen M**. Therapeutic hypothermia: surgical infant with neonatal encephalopathy. *Acta Paediatrica* 2009 Nov;98(11):1844-6 e-pub 10.8.09
- 118 (2009) Mary Rutherford, Luca A Ramenghi, A. David Edwards, Peter Brocklehurst, Henry Halliday, Malcolm Levene, Brenda Strohm, **Marianne Thoresen**, Andrew Whitelaw, Denis Azzopardi. Assessment of brain tissue injury following moderate hypothermia in neonates with hypoxic ischaemic encephalopathy: a nested substudy of a randomised controlled trial. *Lancet Neurology* 2009 Nov 5. E-pub ahead of print
- 119 (2010) Chakkarapani E, Liu X, Hoque N, Aquilina K, Porter H, Dingley J, **Thoresen M**. Xenon hypothermia combination enhances neuroprotection after perinatal asphyxia. *Annals of Neurology* 2010 E-pub 8 Mar doi:10.1002/ana.22016
- 120 (2010) **Thoresen M**, Hellstrom-Westas L, Liu X, de Vries L. Effect of Hypothermia Treatment on the Predictive Value of Amplitude Integrated Electroencephalogram in Infants with Moderate and Severe Perinatal Asphyxia. *Pediatrics* 2010 Jul;126(1):e131-9. Epub Jun 21
- 121 (2010) Edwards AD, Brocklehurst P, Gunn AJ, Halliday H, Juszcak E, Levene M, Strohm B, **Thoresen M**, Whitelaw A, Azzopardi D. Neurological outcome at 18 months of age following moderate hypothermia in newborn infants with hypoxic ischaemic encephalopathy. *Br Med J* 2010;340:c363
- 122R(2010) Whitelaw A, **Thoresen M**. Clinical assessment and therapeutic interventions for hypoxic-ischemic encephalopathy in the full term infant. In: 'The Newborn Brain: Neuroscience and Clinical Applications' 2nd edn Eds: Lagercrantz H, Hanson M, Evrard P, Rodeck C. Cambridge University Press 2010
- 123R(2010) **Thoresen M**. Hypothermia after perinatal asphyxia, selection for treatment and cooling protocol. *Journal of Pediatrics, Asphyxia Supplement* 2011 (Feb); 158(2)Suppl 1: e45-49 doi: 10.1016/j.jpeds.2010.11.013
- 124R(2010) **Thoresen M**. Patient selection and prognostication with hypothermia treatment In: *Hypothermia: an emerging therapy; Seminars in Neonatology* 2010 (15); 247-252 doi:10.1016/j.siny.2010.05.008 E-pub 25 June
- 125 (2010) Hoque N, Chakkarapani E, Liu X, **Thoresen M**. A Comparison of Cooling Methods used in Therapeutic Hypothermia for Perinatal Asphyxia. *Pediatrics* 2010 Jul;126(1):e124-30. Epub 2010 Jun 7
- 126(2010) Strohm B, Azzopardi D, on behalf of the UK TOBY Cooling Register Study Group. Temperature control during therapeutic moderate whole-body hypothermia for neonatal encephalopathy. *Arch Dis Child Fetal Neonatal Ed* 2010;95:F373-F375 doi:10.1136/adc.2009.163816
- 127 (2010) Karlsson M, Wiberg-Itzel E, Blennow M, Winbladh B, **Thoresen M** Lactate dehydrogenase predicts hypoxic-ischemic encephalopathy in newborn infants: a preliminary study. *Acta Paediatr* 2010 Aug;99(8):1139-44 Epub 19.03.2010
- 128(2010) Liu X, Chakkarapani E, Hoque N, **Thoresen M**. Environmental cooling of the newborn pig brain during whole body cooling. *Acta Paediatrica* Jan 2011; 100(1): 29-35 e-pub August 2010 DOI:10.1111/j.1651-2227.2010.01956.x
- 129 (2010) Aquilina K, Chakkarapani E, Love S, **Thoresen M**. Neonatal rat model of intraventricular haemorrhage and post-haemorrhagic ventricular dilatation with long-term survival into adulthood. *Neuropathology and Applied Neurobiology* 2011; **37**: 156–165 doi: 10.1111/j.1365-2990.2010.01118.x
- 130R(2010) Chakkarapani E, **Thoresen M**. Use of Hypothermia in the Asphyxiated Infant *Perinatology* 2010; 3:20-29. <http://www.perinatology.com/perinatology/Volume1-Issue3/Use%20of%20Hypothermia%20in%20the%20Asphyxiated%20Infant.htm>
- 131(2011) Aquilina K, **Thoresen M**, Chakkarapani E, Pople IK, Coakham HB, Edwards RJ. Preliminary Evaluation of a Novel Intraparenchymal Capacitive Intracranial Pressure Monitor *J Neurosurg*. E-pub 27.5.11. DOI: 10.3171/2011.4.JNS101920
- 132 (2011) Hoque N, **Thoresen M**, Aquilina K, Hogan S, Whitelaw A. Decorin and Colchicine as potential treatments for post-haemorrhagic ventricular dilatation in a neonatal rat model. (*Neonatology March 2011*)
- 133 (2011) Liu X, Tooley J, Løberg E, Suleiman S, **Thoresen M**. Immediate hypothermia reduces cardiac troponin I following hypoxic-ischemic encephalopathy in newborn pigs. *Ped Res* (in press August 2011)
- 134 (2011) Elstad M, Whitelaw A and **Thoresen M**. Cerebral Resistance index is less predictive in hypothermic encephalopathic newborns. *Acta Paediatrica* e-pub 18.5.2011. DOI: 10.1111/j.1651-2227.2011.02327.x
- 135(2011) Dalen ML, Liu X, Elstad M, Løberg EM, Saugstad OD, Rootwelt T, Thoresen M*. Resuscitation with 100% Oxygen Counteracts the Neuroprotective Effect of Therapeutic Hypothermia in the Neonatal Rat. (*In press, Pediatric Research*)
- 136R(2011) Higgins R, Raju T, Edwards AD, Azzopardi DV, Bose CL, Clark RH, Ferriero DM, Guillet R, Gunn AJ, Hagberg H, Hirtz D, Inder TE, Jacobs SE, Jenkins D, Juul S, Laptook AR, Lucey JF, Maze M, Palmer C, Papile L, Pfister RH, Robertson NJ, Rutherford M, Shankaran S, Silverstein FS, Soll R, **Thoresen M**, Walsh WF. Hypothermia and Other Treatment Options for Neonatal Encephalopathy: An Executive Summary of the Eunice Kennedy Shriver National Institute of Child Health and Human Development Workshop. *J Pediatr*. 2011 Nov;159(5):851-858.e1. Epub 2011 Aug 27

- 137(2011) Chakkarapani E, Liu X, Dingley J, **Thoresen M**. Xenon enhances cardiostability in hypothermic asphyxiated newborn pigs. *J of Intensive Care Medicine*, e-pub 13.12.11 DOI: 10.1007/s00134-011-2442-7
- 138(2011) Guillet R, Edwards E, Thoresen M, Ferriero DM, Gluckman PD, Whitelaw A, Gunn AJ. 7-8 Year Follow-up of the CoolCap Trial of Head Cooling for Neonatal Encephalopathy. *In press Pediatric Research – Nov 2011*
- 139(2011) Ylva Carlsson, Xiaoyang Wang, Leslie Schwendimann, Catherine I. Rousset, Etienne Jacotot, Pierre Gressens, Marianne Thoresen, Carina Mallard, Henrik Hagberg. Combined effect of hypothermia and Caspase-2 gene deficiency on neonatal hypoxic-ischemic brain injury. *(In press Pediatric Research)*
- 140(2011) Strohm B, Hobson A, Brocklehurst P, Edwards AD, **Azzopardi D**; UK TOBY Cooling Register. Subcutaneous fat necrosis after moderate therapeutic hypothermia in neonates. *Pediatrics*. 2011 Aug;128(2):e450-2. Epub Jul 4
- 141(2012) Sabir H, Jary S, Tooley J, Liu X, Thoresen M. Hyperoxia and Hypocarbia in the First Hours of Life and Their Association with Outcome in Infants Treated with Therapeutic Hypothermia after Perinatal Asphyxia. *In press J Pediatrics March 2012*

Current research group in Bristol

Three PhD fellows (co supervising 2), 2 MD fellows, 1 postdoctoral fellow, 2 research technicians. Ongoing collaboration with UK, the Netherlands, Sweden, Norway and the US.

In 1993 I initiated collaborative investigations in Oslo, Gothenburg and London on the feasibility of mild cooling after a hypoxic-ischemic injury. I developed a new, piglet animal model. I used this and an established neonatal rat model in short and long term survival experiments to examine the neuroprotective effect of different durations, delays and modes (ie head cooling or body cooling) of hypothermia after asphyxia^{44,46,56,67,76}. We characterised the mechanisms involved in protection like reduced apoptosis, reduced production of excitotoxic aminoacids and reduced cerebral energy failure, reduced lactate and maintained ATP as examined by magnetic resonance spectroscopy (MRS P³¹ 1H)^{37,50,57}.

We have translated experimental research into clinical trial and now changed clinical practice. Our cooling pilot trial⁶² showed that 76hrs of reduced body temperature was feasible with no adverse effects reported. Together with 25 hospitals we examined the effect of cooling after asphyxia in 235 infants and found at 18 months follow up that the outcome in the cooled group was improved with less cerebral palsy diagnosed 85. Our second large clinical hypothermia trial which used total body cooling was published in Oct 2009¹¹⁶ and showed significantly more normal survivors in the cooled group. This trial is the only neonatal hypothermia trial powered to reliably look at long term outcome (age 6-8 years, start 2010)) for which we have received MRC funding.

Further work on experimental cooling

We have shown that cooling is more protective if stress is avoided⁶⁷. We have investigated other substances for neuroprotection as we seek to find a combination therapy that improves outcome more than cooling alone. Recently we published that the inert gas Xenon was very neuroprotective in a rodent model⁹¹. Adding Xenon to hypothermia increases the neuroprotection from 35% to 70 % in the rodent model¹⁰¹. Adding Xenon also increases the effective time window¹¹¹. Recently we have investigated the effect of Xenon Hypothermia in our survival piglet neonatal asphyxia model¹¹⁹ and shown that the doubling of neuroprotection is similar to that seen in the rodent model (XeHT- 73% neuroprotection). We have developed a specific ventilator for the use and recirculation of the expensive gas xenon⁸⁴. During these studies we not only examine the final neuropathological outcome but also monitor all relevant clinical effects of XeHT treatment (EEG, cerebral autoregulation and regional brain perfusion, effect on blood pressure and cardiac output, as well as a series of biochemical markers of brain and body injury). Unlike selective brain injury models^{37,42} my model allows examination of the effect of new therapies on all organs since this model is a global hypoxic-ischemic model. Our experimental data were found highly relevant and approval was given for a clinical feasibility study. This successful study recruited the 14 patients through 2010-2011 and is the basis for a Phase 2 small randomised trial 28/3. If xenon is equally effective in babies as in animals, the combined treatment will double neuroprotection as compared to hypothermia alone.

Hydrocephalus after intraventricular haemorrhage –clinical and experimental work

In collaboration with Andrew Whitelaw we have found in premature infants with posthaemorrhagic hydrocephalus (dilatation of the cerebral ventricles due to obstruction after haemorrhage in premature infants) that the cerebrospinal fluid contains high levels of Transforming Growth Factor β 1, which are predictive of later shunt dependence (ventriculoperitoneal shunt to treat permanent hydrocephalus). We have developed a piglet⁹⁸ and a rat model of posthaemorrhagic ventricular dilatation to mimic the condition in premature babies^{78,83,84}. We have used this rat model to determine whether humanized monoclonal anti-TGF β 1 or a series of drugs with anti TGF β properties can prevent the development of

hydrocephalus after intraventricular blood have caused ventricular dilatation. Using the pig model we recently showed that a telemetric ICP monitor could be implanted into the ventricles of pigs with PHVD. We have (PI Professor Andrew Whitelaw) carried out a Phase 1 trial as well as a randomised trial of intraventricular fibrinolytic therapy and 72 hours of irrigation (flushing the ventricular system) with artificial CSF in premature babies who developed posthaemorrhagic ventricular dilatation^{79,96}. These studies showed that only 30 % of infants needed shunting in the CSF irrigation group as compared to 65 % in the conventional treatment group. Due to the invasiveness and risk of secondary bleeds of this treatment we are pursuing developing drug strategies that inhibit the development of hydrocephalus. Hydrocephalus as a complication of intraventricular haemorrhage in premature infants results in 70 % of patients having poor neurological outcome.

Laboratory

My Bristol laboratory is purpose built and equipped to undertake acute as well as long term survival experiments of newborn animals both small (rodents) and large (pigs) and this is unique in the UK. The Neonatal Medicine Service in Bristol is amongst the largest in Britain and offers excellent opportunities for clinical investigation and trials of experimental therapy. Such translational research is well suited for external supervision (I am currently involved in the newborn hypothermia program in Oslo as a co-supervisor for both a clinical and experimental PhD). The line of future research is a parallel one; with emphasis on experimental research on the mechanisms of damage and repair of neonatal cerebral injury paralleled with physiological changes in healthy subjects.

PRESENTATIONS TO THE PUBLIC

- Many TV and radio interviews about research projects including "Womans hour BBC4", Radio science programs in Sweden ("Vetenskap April 5nd) and Norway ("Verdt aa vite" April 9th 2010),
- Magazine and newspaper interviews, UK and international
- Charity meetings for fundraising
- Television programs regarding neuroprotection (Discovery channel "Protecting the newborn brain" TV science program "Horizon" BBC2 September 2010).