

# The CoolXenon Study

**Submission date**  
26/11/2010

**Recruitment status**  
No longer recruiting

**Registration date**  
26/11/2010

**Overall study status**  
Completed

**Last Edited**  
19/02/2015

**Condition category**  
Injury, Occupational Diseases, Poisoning

- ☐ Prospectively registered
- ☐ Protocol
- ☐ Statistical analysis plan
- ☒ Results
- ☐ Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
2009-014260-19

**Protocol serial number**  
Version 1.21 (as of 05/01/2011)

## Study information

**Scientific Title**

A feasibility study of adding xenon to cooling therapy in babies at high risk of brain injury following poor condition at birth

**Acronym**

CoolXenon

**Study objectives**

Our experimental work has shown that by adding the inert gas xenon (50%) while undergoing hypothermia treatment the % good outcome doubles (from 35% to 70%) in both small and large survival models. This is the first clinical feasibility study combining xenon inhalation with the established neuroprotective hypothermia treatment in newborn term after moderate and severe perinatal asphyxia.

**Further reading:**

Dingley J, Tooley J, Porter H, Thoresen M. Xenon provides short term neuroprotection in neonatal rats when administered after hypoxia-ischemia. *Stroke* 2006; 37(2): 501-6.  
<http://www.ncbi.nlm.nih.gov/pubmed/16373643>

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.  
<http://www.ncbi.nlm.nih.gov/pubmed/18292440>

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.  
<http://www.ncbi.nlm.nih.gov/pubmed/18309163>

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. *Anaesthesia and Analgesia* 2009; 109(2): 451-60.  
<http://www.ncbi.nlm.nih.gov/pubmed/19608817>

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. *Journal of Cerebral Blood Flow and Metabolism* 2009; 29(4): 707-14.  
<http://www.ncbi.nlm.nih.gov/pubmed/19142190>

Thoresen M. Patient selection and prognostication with hypothermia treatment. *Seminars in Fetal and Neonatal Medicine* 2010; 15(5): 247-52  
<http://www.ncbi.nlm.nih.gov/pubmed/20580626>

As of 01/03/2011 the target number of participants has been increased from 12 to 14

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

North Somerset and South Bristol Research Ethics Committee approved on the 16th September 2009 (ref: 09/H0106/64)

**Study design**

Interventional non-randomised single centre feasibility study

**Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Topic: Neurological; Subtopic: Neurological (all Subtopics); Disease: Nervous system disorders

**Interventions**

Adding xenon to the inspiratory gas of the ventilated infant using a MHRA approved closed loop xenon-delivery system. The xenon, oxygen, carbon dioxide (CO<sub>2</sub>) and nitrogen gas concentrations are controlled.

Follow up length: 42 months

Study entry: registration only

Added 01/03/2011: The duration of treatment with Xenon gas has been increased from 12 hours to 18 hours for recruits 12, 13 and 14

**Intervention Type**

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Xenon

**Primary outcome(s)**

Physiological changes, measured within 24 hours after end treatment

**Key secondary outcome(s)**

1. Bayley III, measured at 18 or 24 months
2. MRI, measured within 14 days after treatment

**Completion date**

01/03/2013

**Eligibility****Key inclusion criteria**

Infants will be eligible for xenon if the St Michael's standard inclusion criteria for cooling are met. Standard Hypothermia Treatment Criteria for 72 hours of cooling - all of criteria A, B, and C:

A: Infants greater than 36.0 weeks gestation (clinical assessment) with at least one of the following:

1. Apgar score of less than 5 at ten (10) minutes after birth
  2. Continued need for resuscitation, including endotracheal or mask ventilation, at ten minutes after birth
  3. Acidosis defined as either umbilical cord pH or any arterial, venous or capillary pH within 60 minutes of birth less than pH 7.00
  4. Base deficit greater than or equal to 16 mmol/L in umbilical cord blood sample or any blood sample within 60 minutes of birth (arterial or venous blood)
- If the infant meets criterion A then assess for neurological abnormality using criterion B and C (by trained personnel).

B: Moderate or severe encephalopathy as evidenced by:

1. Altered state of consciousness (reduced or absent responses or pathological irritability and hyper responsive

And at least one or more of the following:

2. Hypotonia
3. Abnormal reflexes including oculomotor or pupillary abnormalities
4. Absent or weak suck
5. Clinical seizures, as recorded by trained personnel

C: At least 30 minutes duration of amplitude integrated electroencephalography (aEEG) recording that shows abnormal background aEEG activity. The decision to cool is based on the worst section of the aEEG, not the best (al Naqeeb, et al, 1999) or seizures (clinical or electrical) thus meeting ONE of the following:

1. Normal background with some electrical seizure activity
2. Moderately abnormal activity (upper margin of trace greater than 10  $\mu$ V and lower margin less than 5  $\mu$ V)
3. Suppressed activity (upper margin of trace less than 10  $\mu$ V and lower margin of trace less than 5  $\mu$ V)
4. Definite seizure activity

Additional inclusion criteria for xenon:

Before being considered for additional inhaled xenon therapy via the breathing gas mixture, the infant would need to meet further additional entry criteria:

1. Intubated, ventilated, sedated, being cooled
2. Any seizures under control
3. Weight greater than 2.3 kg
4. No evidence of infection
5. Stable cardiovascular parameters - mean arterial pressure greater than 45mmHg
6. Oxygen requirement via mechanical ventilator less than 35%
7. Positive end expiratory pressure (PEEP) requirement less than 6 mmHg
8. Arterial pCO<sub>2</sub> within the accepted range (4.5 - 6.5 kPa)
9. Postnatal age less than 18 hours, either sex
10. Major congenital abnormalities, imperforate anus and congenital abnormalities suggestive of chromosomal anomaly or other syndromes that include brain dysgenesis

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**Key exclusion criteria**

1. Infants expected to be greater than 12 hours of age at the time of starting cooling treatment
2. Futility; where prognosis is considered to be hopeless, e.g. no cardiac output for 20 minutes
3. Failure to meet the additional inclusion criteria for xenon

**Date of first enrolment**

28/03/2010

**Date of final enrolment**

01/03/2013

**Locations****Countries of recruitment**

United Kingdom

England

**Study participating centre**

School of Clinical Sciences

Bristol

United Kingdom

BS2 8EG

**Sponsor information****Organisation**

University Hospitals Bristol NHS Foundation Trust (UK)

**ROR**

<https://ror.org/04nm1cv11>

**Funder(s)**

**Funder type**

Charity

**Funder Name**

Sparks (UK)

**Alternative Name(s)**

Sparks Charity

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Other non-profit organizations

**Location**

United Kingdom

## Results and Publications

**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/05/2014		Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes