

Cord Reinfusion in Diabetes (CORD) Pilot Study – Can cord blood prevent or delay type 1 diabetes?

The CORD study is a pilot study investigating whether cord blood can be used to prevent or delay the development of type 1 diabetes (T1D) in children at risk of developing the condition. The study is being led by Professor Maria Craig, a Paediatric Endocrinologist at The Children's Hospital at Westmead in New South Wales.

Study Rationale

There is increasing evidence that immune therapies, particularly those based on restoration of peripheral immune tolerance, may prevent autoimmune diseases such as T1D.

Abnormalities of regulatory T-cell (Treg) function and/or number have been identified in people with T1D. Umbilical cord blood contains highly functional populations of Tregs and therefore may have a role in immunomodulation.

In the non-obese diabetic (NOD) mouse model of T1D, infusion of Tregs prevented the development of T1D. However, no studies in humans have examined whether cord blood can prevent or delay T1D.

The primary hypothesis of the study is that the infusion of autologous cord blood will restore immune tolerance in children with islet autoimmunity and delay or prevent the progression of T1D.

Study Objectives

The primary aim of the study is to assess the feasibility of the reinfusion of autologous cord blood in children at high risk of T1D.

The secondary aims are to:

1. Confirm the safety of reinfusion of autologous cord blood in a pre-diabetic population; and
2. Establish and refine protocols for participant identification, recruitment, investigation and cord blood reinfusion, which will inform a future randomised controlled trial.

Study Population

The study population is children aged 1 to 15 years, at high risk of developing T1D, who have autologous cord blood banked with a private cord blood bank.

Study Design

There are two phases to the study:

1. Screening Phase: A total of 1000 eligible children will have annual screening the detection of antibodies to > 2 pancreatic islet antigens;

Treatment and Follow-up Phase: Children who are confirmed to have antibodies to > 2 islet antigens will be invited to receive an infusion of their cord blood. It is estimated that approximately 20 children will receive the infusion. All infusions will be performed at The Children's Hospital at Westmead. These children will then be followed for 3 years.

Study Outcomes

Primary:

1. Feasibility of the recruitment and screening of children who have stored and have a first degree relative with T1D or have previously been tested for islet antibodies; and
2. Prevalence of islet autoimmunity in children with a first degree relative with T1D.

Secondary:

3. Safety (adverse event profile after reinfusion of cord blood);
4. Development of dysglycaemia or diabetes as defined by the American Diabetes Association criteria;
5. Changes in immunological markers including islet autoantibody titres, cytokine levels and regulatory T- cell (Treg) phenotype and function; and
6. Differences in inflammatory markers, vitamin D and prevalence of viral infection in antibody positive versus negative children.

What does the study involve?

The screening phase involves testing for Insulin, GAD, IA2 and ZnT8 autoantibodies. Participants with negative antibodies will be invited to return for repeat screening in 12 months. If two or more antibodies to islet antigens are present, conferring a high risk of progression to T1D, the child will be invited to participate in the treatment phase of the study.

In the treatment phase, participants will receive a single intravenous infusion of autologous cord blood containing $>5 \times 10^6$ Total Nucleated Cells per kilogram of recipient body weight. Cord blood will be reinfused over a period of 1 hour. All of the cord blood will be used.

Other Information

The study is sponsored by the Sydney Children's Hospitals Network and is funded by Cell Care, Australia's largest private cord blood bank.

The study has been approved by the Sydney Children's Hospitals Network Human Research Ethics Committee. If you have any concerns about the conduct of this study, please do not hesitate to contact the Secretary of the Ethics Committee on (02) 9845 1253 and quote reference number **11/SCHN/211**.

For further information about the study, please contact the CORD Study Coordinator/Nurse at The Children's Hospital at Westmead via:

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