

# Gestational surrogacy for women with recurrent pregnancy loss due to refractory chronic histiocytic intervillitis: Research Letter

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## Running title

Gestational surrogacy in chronic histiocytic intervillitis

## Introduction

Chronic histiocytic intervillitis (CHI) is a rare placental disorder that affects approximately 1 in 600 pregnancies.<sup>1</sup> It is diagnosed when at least 5% of the intervillous space is occupied by maternal CD68+ immune cells (histiocytes) and is often accompanied by massive perivillous fibrin deposition.<sup>2</sup> CHI is strongly associated with miscarriage (24%), stillbirth (29%), fetal growth restriction (72%) and preterm birth (68%).<sup>2</sup> It carries a high risk of recurrence in subsequent pregnancies.<sup>1,2</sup>

The aetiology of CHI is unclear, but its association with maternal autoimmunity and its histological similarity to rejected solid organ allografts suggest a maternal immune “rejection” of the placenta.<sup>3</sup>

While maternal immunosuppression reduces the histological severity of CHI and can improve live birth rate,<sup>4</sup> some patients have refractory disease in which every successive pregnancy is affected. In these women, gestational surrogacy offers an alternative route to parenthood. However, there is only one published case of successful surrogate pregnancy in this context.<sup>5</sup>

We report the outcomes of 17 surrogate pregnancies in which the embryos came from 13 women with recurrent adverse pregnancy outcomes due to CHI (n=54).

## Methods

Eligible women were identified through an online CHI support group. This study was approved by the London Research Ethics Committee (Fulham, 19/LO/0105). All participants provided written informed consent for publication.

## Results

Thirteen women with recurrent CHI participated in the study. These women had carried 54 pregnancies themselves (51 singleton, 3 dichorionic-diamniotic). These pregnancies resulted in high rates of adverse perinatal outcomes (Table). Of the 9 babies born alive, 2 died in the neonatal period (2/9, 22%), meaning only 7/54 pregnancies (13%) resulted in surviving children. In 8/54 (15%) pregnancies, the mother received antenatal immunosuppression including one or more of prednisolone, hydroxychloroquine, tacrolimus and intravenous immunoglobulin.

Following attempts to carry a pregnancy themselves, all 13 women underwent IVF using their own oocytes and their partner’s sperm followed by embryo transfer into a surrogate mother. This led to 17 successful surrogate conceptions (12 singleton, 5 dichorionic-diamniotic), of which 15/17 (88%) ended in term or near-term live birth. The two remaining pregnancies ended in first-trimester miscarriage, one due to confirmed fetal trisomy 21 and the other with no identified cause. There were two failed embryo transfers. None of the surrogate mothers received immunosuppression.

There was no recurrent CHI detected in any of the completed surrogate pregnancies, although most placentas (13/17) were not tested due to a good pregnancy outcome.

One of the patients included in this cohort had a late miscarriage and two early miscarriages due to CHI before undergoing IVF and gestational surrogacy. This led to two successful surrogate pregnancies. The first of these was described in the cited article by Reus et al.,<sup>5</sup> but the second has not been reported until now, hence her inclusion in this cohort.

The parents of the fetus with trisomy 21 subsequently underwent further IVF using donor oocytes and had healthy dichorionic-diamniotic twins delivered at 36 weeks’ gestation by a surrogate mother.

The INTERGROWTH-21<sup>st</sup> birthweight centile calculator is available from: <http://intergrowth21.ndog.ox.ac.uk/en/ManualEntry>

## Conclusions

This study demonstrates that when a surrogate mother carries the embryo of a couple affected by recurrent pregnancy loss due to refractory CHI, pregnancy outcomes are normalised. Although surrogacy is not universally available or acceptable, it should therefore be considered an alternative route to parenthood for these women.

Changing the maternal “host” appears to be highly effective in preventing recurrent CHI. This observation reinforces the hypothesis that CHI is driven by an abnormal maternal immune response against the placenta.

## Disclosure of interests

The authors report no conflict of interest.

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## Contribution to authorship

EFC, CAAB and DJW conceived and planned the study. TCRM and RT contributed to study design. EFC and CAAB collected data. EFC, TCRM, RT and DJW analysed the data. All authors contributed to writing and editing the manuscript.

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## Details of ethics approval

This study was approved by the London Research Ethics Committee (Fulham, 19/LO/0105) on 06 February 2019.

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