

## 2019 UPDATE

### Summary of suggested treatments for Chronic Histiocytic Intervillositis (CHI): C. A. A. Belardo

The following are broad recommendations for treatment compiled from contributions by the various members of the site (who have previously received a diagnosis of CHI and gone on to have a successful pregnancy), emails from Doctors and Consultants who have been in direct contact with me and what can be gleaned from published, medical research papers (sources referred to at the bottom). It is not by any means a substitute for a formal medical treatment program and should not be used as such, it could however be offered to your medical professional for consideration and as a way to start putting together a treatment plan for future pregnancies.

The following information should not be regarded in isolation from other underlying autoimmune conditions such as; Crohn's disease, Antiphospholipid Syndrome, Lupus etc these may 're-classify' the 'groups' thus must also be taken into consideration. In the cases where an underlying condition has been identified it would be wise to consider number of previous successful vs. unsuccessful pregnancies combined with underlying condition findings and either refer yourself or put your medical consultant in touch with one of the CHI Centre of Excellences (CoE)

*Successful pregnancy*, for the purposes of this paper, means viable birth of live child who survives.

#### **Group A - Minor to Moderate**

A pattern seems to indicate that ladies have had prior successful, uncomplicated, live births, who then go on to have at least one birth with the CHI diagnosis, may find the following a treatment sufficient:

- Corticosteroids (*prednisolone, dexamethasone, prednisone*) (\*see footnote)
- Antitrombotics (*Heparin, Clexane, Fragmin, Lovenox, Aritax*)
- Low dose aspirin between 75mg - 100mg is typical
- Good prenatal vitamins may be sufficient treatment for subsequent pregnancies. (usually multivitamin with extra folic acid 2.2.mg, B6 25mg and vitamin B12 500mcg). For those on cortiosteroids and heparin extra calcium and Vitamin D are also essential.

#### **Group B - Moderate to Severe**

Those that have had frequent early miscarriage and/or stillbirths, with no live births to-date (or simply those that do not wish to take any risks in future pregnancies) the aforementioned:

- Corticosteroids (*prednisolone, dexamethasone, prednisone*) (\*see footnote)
- Antitrombotics (*Heparin, Clexane, Fragmin, Lovenox, Aritax*)
- Low dose aspirin 75mg - 100mg is typical
- Good prenatal vitamins may be sufficient treatment for subsequent pregnancies. (usually multivitamin with extra folic acid 2.2.mg, B6 25mg and vitamin B12 500mcg). For those on cortiosteroids and heparin extra calcium and Vitamin D are

also highly recommended.

There is now sufficient research indicating that a new group of drugs is improving the outcomes of pregnancies. These drugs are currently being prescribed 'off-label' for CHI and therefore you must refer to a CHI CoE for more information and always consult with your medical professional of choice:

- **Calcineurin Inhibitor: Tacrolimus**, also known as fujimycin or FK506, is a wide spectrum immunosuppressive drug used mainly after allogeneic organ transplant to lower the risk of organ rejection. It is safe to take in pregnancy and for CHI has been seen to be effective in very low dosages. Usually this needs to be the only drug prescribed for a healthy pregnancy and does not need to be accompanied by any of the other protocols
- **4-Aminoquinoline: Hydroxychloroquine**, sold under the brand name Plaquenil among others, is a medication used for the prevention and treatment of chloroquine-sensitive malaria. Other uses include treatment of rheumatoid arthritis, lupus, and porphyria cutanea tarda
- **TNF inhibitor: infliximab** (Remicade), **adalimumab** (Humira), **certolizumab pegol** (Cimzia), and **golimumab** (Simponi). TNF is involved in autoimmune and immune-mediated disorders such as rheumatoid arthritis, ankylosing spondylitis, inflammatory bowel disease, psoriasis, hidradenitis suppurativa and refractory asthma. This group of drugs appears third on the list as there is less proof that they have consistent success in CHI pregnancies and whilst mostly safe to use in pregnancy have more side effects.

### **Groups A & B**

In addition to the above both groups should have the following:

**Regular ultrasound scans:** every two weeks from 5-6 weeks gestation up to 12 weeks then every two-four weeks (depending on previous history) during second and third trimester and twice weekly 'stress tests' during the last month of pregnancy (or as early as 29 weeks in some cases).

**Early and then Regular Doppler scans:** it is recommended that the first doppler scan is conducted at 12 weeks then every two to four weeks to observe closely the flow of blood to the baby, early changes in flow indicate that a change of treatment or increase in dosage is advisable. From 28 weeks it is recommended to conduct weekly/fortnightly scans until birth.

**Monitor Alkaline Phosphatase (ALP) levels:** high levels observed during the pregnancy demonstrate the presence of syncytiotrophoblastic lesions due to histiocytosis in the intervillous space, before fibrin deposits cover them however this has not a consistent indicator of CHI in all pregnancies.

**Monitor PAPP-A levels:** also considered to be very important, levels should be monitored from 10 weeks. Low levels are an indicator for CHI.

**Regular Blood tests:** Pre-eclampsia, there is a new theory which will look into measuring the levels of CD68 cells during pregnancy, they would also be a good indicator as to whether the pregnancy is causing an immune response. Other markers may be MMP9 and TGFBR1 but thus far a consistent biomarker to indicate the existence of CHI in a pregnancy has yet to be identified.

**C-section delivery recommended,** usually preterm around 34 weeks after lung maturation is

recommended but ideally around 38 weeks (this is advised due to reduction in the lifespan of the placenta in patients with immune problems and avoids fetal distress).

**Dosages:** Must be discussed with your Consultant however information supplied to me by a leading Doctor in France who has written a number of papers about CHI wrote the following which is important to bear in mind when considering Corticosteroid dosages: *"In our university hospital, we recommend the use of aspirin (100 mg per day) as soon as possible in pregnancy. The use of prednisone (10 or 20 mg per day) may not prevent the disease. I think if one considers that CHI is an **autoimmune**\*\* disease, treatment of 10mg of prednisone is insufficient. However, a high-dose corticosteroid therapy has side effects maternal and has a small risk of fetal malformations. It's always a problem of benefit/risk but to my knowledge, nobody has yet tried a high-dose corticosteroid therapy to treat CHI."*\*

Sources:

- [Combining corticosteroid and aspirin for the prevention of recurrent villitis or intervillitis of unknown etiology: G. Boog, C. Le Vaillant, F. Alnoukari, F. Jossic, J. Barrier, J.-Y. Muller](#)
- [A combination treatment of prednisone, aspirin, folate, and progesterone in women with idiopathic recurrent miscarriage: a matched-pair study Clemens B. Tempfer, M.D. et al](#)
- [Chronic villitis in untreated neonatal alloimmune thrombocytopenia: An etiology for severe early intrauterine growth restriction and the effect of intravenous immunoglobulin therapy.](#)
- CD68 Immunostaining in the Evaluation of Chronic Histiocytic Intervillositis Debra S Heller MD
- [Chronic histiocytic intervillitis of unknown etiology: Clinical features in a consecutive series of 69 cases: Marchaudon et. al](#)
- Expression analysis of leukocytes attracting cytokines in chronic histiocytic intervillitis of the placenta: Lukas Freitag, Constantin von Kaisenberg, Hans Kreipe, Hussein
- Data provided from Facebook groups
- *\*Email from V. Marchaudon (translated from the French)*
- *\*\*Since this email I have more research indicating that this condition is alloimmune and not autoimmune related.*

*DISCLAIMER: the information contained in this article is advisory only and any official prescriptions must be approved and prescribed by your qualified medical professional of choice. The author of this article accepts no liability in relation to the advice given in this article.*