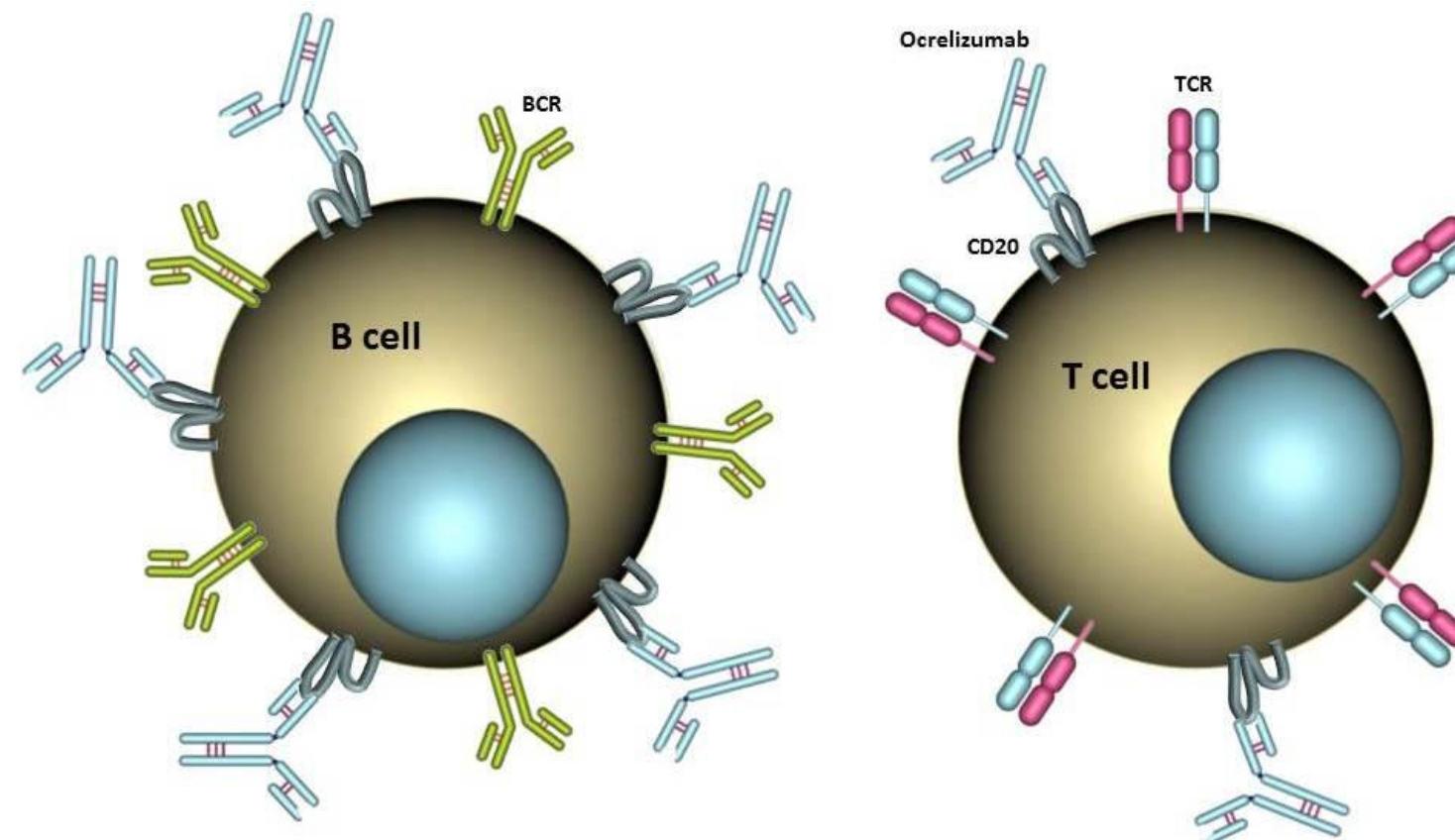


# Ocrelizumab use before pregnancy and neonatal B-cell depletion: A case report.

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## Introduction

Ocrelizumab is a recombinant humanized IgG1 monoclonal antibody that depletes B-lymphocytes by binding their surface antigen CD20 through antibody-dependent cellular phagocytosis or cellular cytotoxicity or complement-dependent cytotoxicity, approved for the relapsing forms of multiple sclerosis. Several studies reported normal neonatal B-cell counts after therapy ending shortly before conception or during early pregnancy; only two cases of B-cell depletion are reported when ocrelizumab was used during the second and third trimester of pregnancy. We report the first case of transient neonatal B-cell depletion while the drug was stopped 3 months before conception.

## Case report

We present a 28-years-old female suffering from relapsing multiple sclerosis who was treated with ocrelizumab infusion and subsequent doses of 600 mg IV infusion every 6 months with favorable response. She conceived 3 months after the last administration.



## Results

Pregnancy was uncomplicated and the patient delivered at 38 weeks gestation via cesarean section for previous caesarean section a male (weight 3500 g, APGAR 10/10). On examination he was deeply jaundiced but otherwise healthy. At birth, the percentage of postnatal CD 19+ B cells was 0.6% (range 6-25) and one month later increased to 23.4%. CD3+, CD4+ and CD8+ T cells as well as natural killer cells (CD56+CD3–) were into normal ranges. No signs of infections were observed.

### Lymphocyte Subsets in the infant

	Infant (at birth)	Ref. Range
CD19 B-Cells absolute, cell/ $\mu$ L	11	315-1383
CD19 B-Cells as % of ALC	0.6%	6-25%
CD3 T-Cells (T Total) as % of ALC	73.41%	55-84%
CD4 T-Cells (T Helper) as % of ALC	56.63%	31-60%
CD8 T-Cells (T Cytotoxic) as % of ALC	18.39%	13-41%
CD16 + CD56 (T-Cells Natural Killer) as % of ALC	26.42%	3-22%

## Conclusions

The mean half-life of ocrelizumab is 26 days while the fetal B cells circulate by the 12th week from conception. Therefore, placental transfer of ocrelizumab can start at around 16 weeks of gestation (similar to other IgG immunoglobulins) and considering five half-times for a complete elimination of the drug, it is improbable a biologic effect of ocrelizumab if the therapy is stopped 3 months before conception.

From the other hand, longer half-life of 39 days has been reported in the literature; moreover, the manufacturer reported that the longest terminal half-life recorded in women was 53 days. These observations make possible the fetal B-cell depletion as we have seen in our case. Eventually, in adults the median time to B-cell repletion is 72 weeks (range 27-175 weeks) but in our neonate there was a very quick repletion.

Since the CD20 is not expressed on progenitor B cells, thus early B-cell precursors should not have been affected by ocrelizumab treatment contributing to the fast B-cell recovery observed.