Short and long-term effects of congenital iron deficiency on hematopoietic cell lineages

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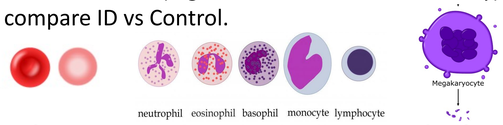
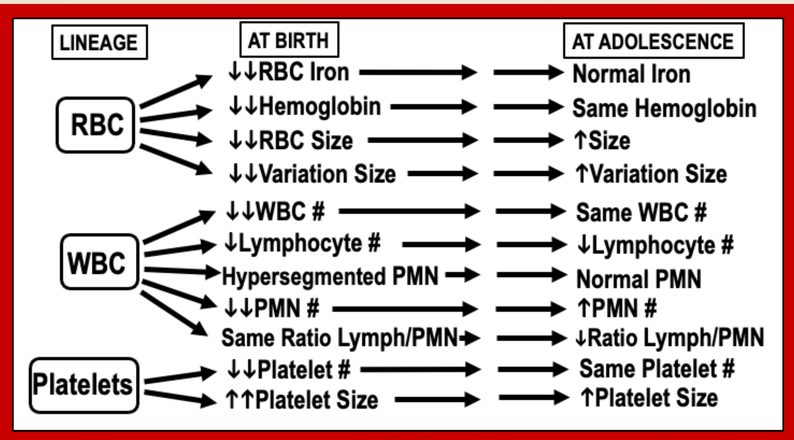
BACKGROUND

- In early life, iron is prioritized for RBC production at the expense of other developing tissues & cellular processes.
- Iron deficiency (ID) can impact immune function in childhood.
- Erythropoietin may rise in ID & may increase platelet numbers in adults.
- However, less is known about how ID affects other cell lineages, including granulocytes, monocytes, lymphocytes, and thrombocytes (platelets).
- Leverage established Sprague Dawley rat model of gestational ID (Siddappa, 2003; Sun, 2016) to understand marrow & thymus hematopoietic cell lineages of offspring.
- **Goal:** examine numbers & morphology of hematopoietic cell lineages during congenital ID & its long-term effects, through weaning & adolescence.

METHODS

- Randomized, controlled study of gestational ID pregnancies vs. controls to examine offspring hematopoietic numbers & cell morphology.
- ID model: ID rat diet (<6 mg/kg iron) from gestational day 2 of pregnancy until postnatal (P) day 7 vs. control nutrient-sufficient control diet (198 mg/kg iron)
- Pups weaned from dam milk to a normal nutrient-sufficient control diet at 22.
- At both P2-3, and P45, pups were euthanized & blood samples collected, defining our age groups.
- RBC iron was measured by Zinc protoporphyrin/ heme ratio, which rises in iron deficiency.
- Complete blood cells (CBCs) measured hemoglobin, mean cell volume, and red blood cell (RBC distribution width.
- Manual counting of reticulocytes (Brilliant Cresyl Blue) and Wright-Giemsa (W-G) smears for manual nucleated red blood cell counts (nRBC), which was used to correct the and White blood cell (WBC) count and the manual differential counts.
- Paired comparisons at each time point. Distributions were examined (log conversion or Mann-Whitney) to compare ID vs Control.





At birth vs. controls:

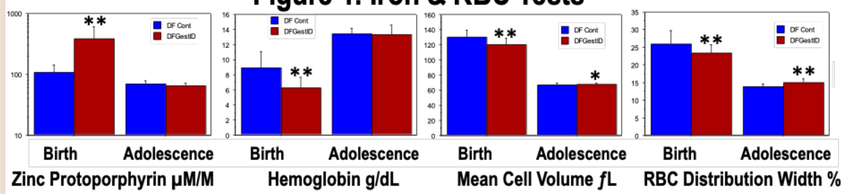
- ID ZnPP/H ratios 350% higher.
- ID hemoglobin levels 30% lower.
- ID WBC 35 lower, lymphocyte 32% lower, PMN 63% lower.
- ID platelet #s 25% lower, but ↑ size.

At P45, 38 d post-normal nutrient diet vs. controls:

- Formerly ID iron ZnPP/H same.
- Formerly ID hemoglobin levels same.
- Formerly ID total WBC did not differ, but lower lymphocyte #s 16% lower & PMN #s 27% higher.
- Formerly ID platelet #s same, but ↑ size.

RESULTS

Figure 1. Iron & RBC Tests



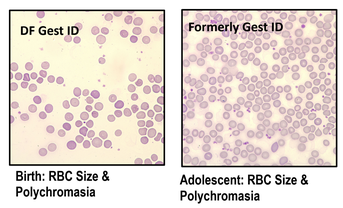
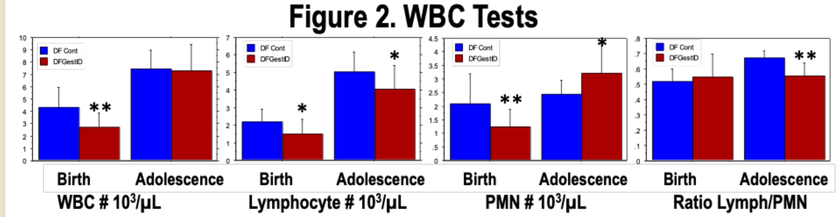


Figure 2. WBC Tests



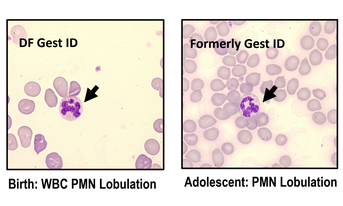


Figure 3. Platelet Tests

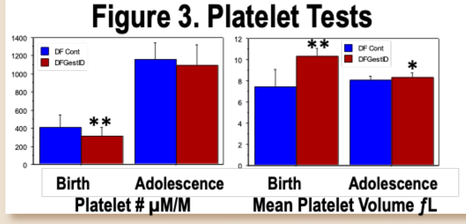


Figure 1. Iron & RBC Tests & Photomicrographs of W-G Smears at Birth & Adolescence.
Figure 2. WBC Tests & Photomicrographs of W-G Smears at Birth & Adolescence.
Figure 3. Platelet Tests.
Dam fed control (DF Cont) in blue vs. DF Gestational ID (Gest ID) in red. * indicates p<0.05-p≤0.005, ** indicates p<0.005.

Discussion/ Conclusions

- Birth: RBC iron ↓, Hemoglobin↓, WBC ↓, platelet ↓.
- At P45, equivalent to adolescence: some abnormalities in RBC, WBCs, & platelets are found despite having normal iron & hemoglobin status.
- ID has a qualitative & quantitative impact on all blood cell lineages in short- and long-term observations & this study adds to already known functional differences in WBC cytokine responses.

Additional Resources

Additional Resources

- **Sun MY,** et al. Repro Fertil Dev 2016;15: 10.1071/RD15358. doi: 10.1071/RD15358.
- **Siddappa AJ**, et al. Pediatr Res 2003;53:800. doi: 10.1203/01.PDR.0000058922.67035.D5.

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