Laboratory Mice Shipped From Sea Level to High Altitude Experience Minimal Hematologic and Cytokine Changes

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Introduction

●Hematologic and physiologic changes that occur during travel from low to high altitude include:
- ➢ Increases in erythrocyte and erythropoietin (EPO) production and reticulocytosis
- ➢ Increases in cytokines interleukin 6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interleukin 10 (IL-10)
- ➢ Increases in C-reactive protein (CRP).

● Hematologic and physiologic effects associated with shipping laboratory mice from sea level to a location at higher altitude have not been published.
● Since most major vendors exist at sea level, it may be necessary to extend acclimatization periods for laboratory mice following transport to altitudes over 1500m.

Objective

● To assess hematologic and cytokine changes over time associated with shipping mice from sea level to higher altitudes to determine acclimatization requirements.

Materials and Methods

● 50, 9-week old female ICR mice were purchased from Charles River Laboratories (Wilmington, MA) at an altitude of 25 meters.
● 60, 8-week old female C57BL/6J mice were purchased from Jackson Laboratories (Bar Harbor, ME) at an altitude of 25 meters.
● Ten mice of each strain were euthanized via CO2 asphyxiation and bled via cardiac puncture on the day of arrival, and 3, 7, 14, and 21 days post arrival.
● Hematologic parameters were determined using an automated hematology analyzer.
● TNF-α, IL-6, IL-10, CRP and EPO were analyzed using bead-based immunoassay (Luminex Technology and Millipore kits).

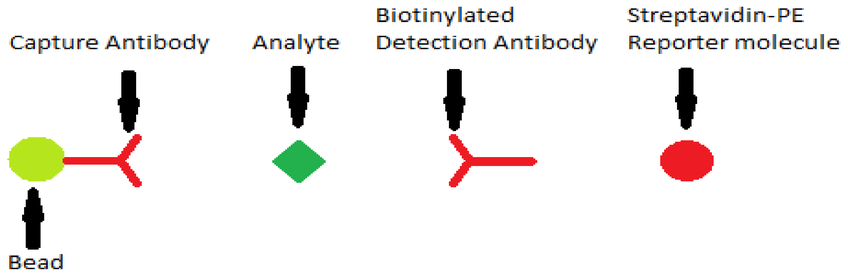


Figure 1: *Bead-based immunoassay*

● Capture reagent is coupled to bead with known ratio of two internal dyes
● Incubate beads with the sample
● Incubate beads with a biotinylated detection antibody followed by binding to streptavidin-PE reporter molecule
● Red laser reads the internal dye of the bead and green laser reads the amount of streptavidin-PE per bead and analyte concentration calculated

Results

Figure 2

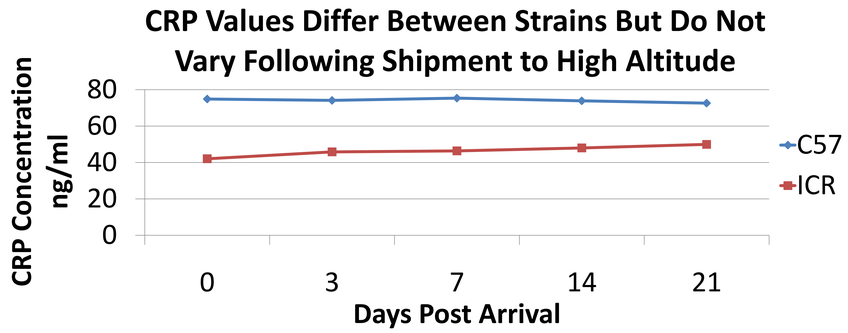
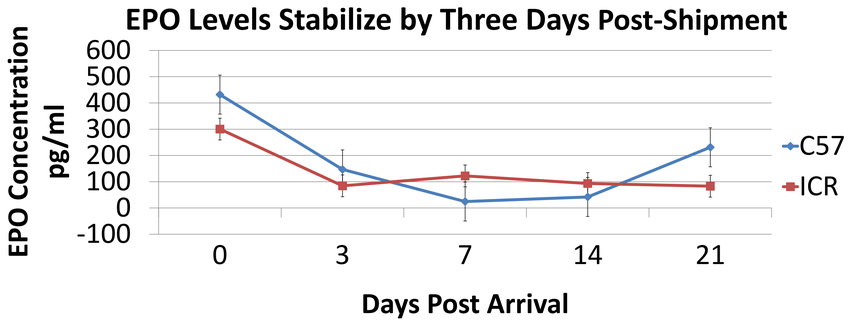


Figure 3



Results Continued

Figure 4

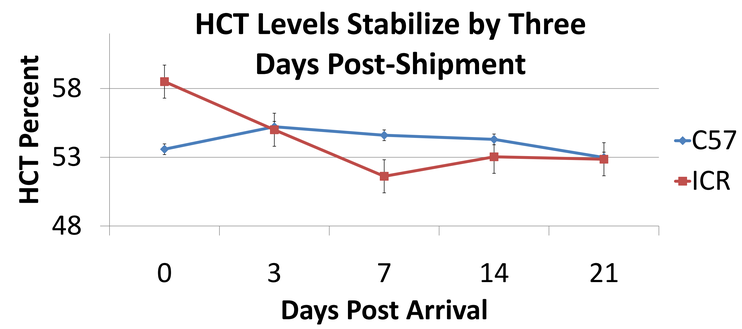
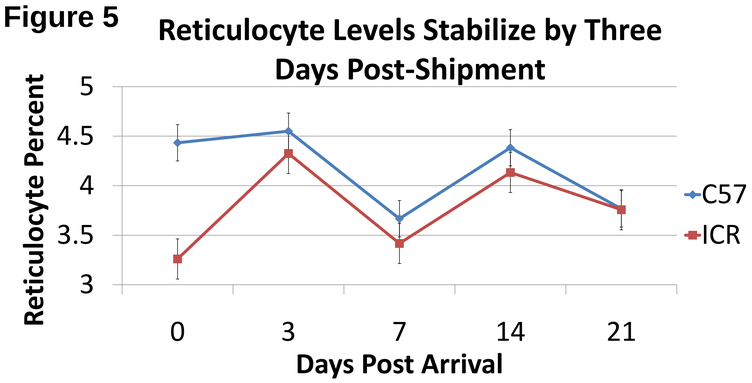


Figure 5



Conclusion

● Reticulocyte, HCT, and EPO levels stabilized by three days post-shipment
● CRP values remained constant following shipment but differed between strains
● TNF- α, IL-6, and IL-10 levels in the majority of mice were below detectable limits
● A minimum three day acclimatization period is recommended for laboratory mice shipped from sea level to a higher altitude such as Colorado

Acknowledgements

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C57 & ICR Mice HCT Values