Hypertensive mice are more susceptible to experimental malaria

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Background: Global prevalence of hypertension is on the rise, especially in developing countries where infectious diseases, such as malaria, are also rampant. Whether hypertension could predispose or increase susceptibility to malaria, however, has not been extensively explored. Previously, we reported that hypertension is associated with abnormal erythrocyte physiology and anemia. Since erythrocytes are target host cells for malarial parasite, *Plasmodium*, we hypothesized that hypertensive patients with abnormal erythrocytes physiology are at greater risk or susceptibility to *Plasmodium* infection.

Method: To test this hypothesis, eight weeks old normotensive (BPN/3J) and hypertensive (BPH/2J) mice were characterized for their erythrocyte physiology and subsequently infected with green fluorescent protein-tagged *Plasmodium yoelii* (*P. yoelii*), a murine-specific non-lethal strain.

Results: When compared to BPN mice, BPH mice displayed microcytic anemia and their erythrocytes were highly resistant to osmotic hemolysis. Further, BPH erythrocytes exhibited an increase in membrane rigidity and an altered lipid composition, as evidenced by higher levels of phospholipids and saturated fatty acid, such as stearate (C18:0), along with lower levels of polyunsaturated fatty acid like arachidonate (C20:4). Moreover, BPH mice had significantly greater circulating $Ter119^{+}$ $CD71^{+}$ reticulocytes, or immature erythrocytes. Upon infection with *P. yoelii*, BPH mice experienced significant body weight loss accompanied by sustained parasitemia, indices of anemia, and substantial increase in systemic pro-inflammatory mediators, compared to BPN mice, indicating that BPH mice were incompetent in clearing *P. yoelii* infection.

Conclusions: Collectively, these data demonstrate that aberrant erythrocyte physiology observed in hypertensive BPH mice contributes to an increased susceptibility to *P. yoelii* infection and malaria-associated pathology.

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