Feline Red Blood Cell Shape and the Impacts of Cytauxzoonosis

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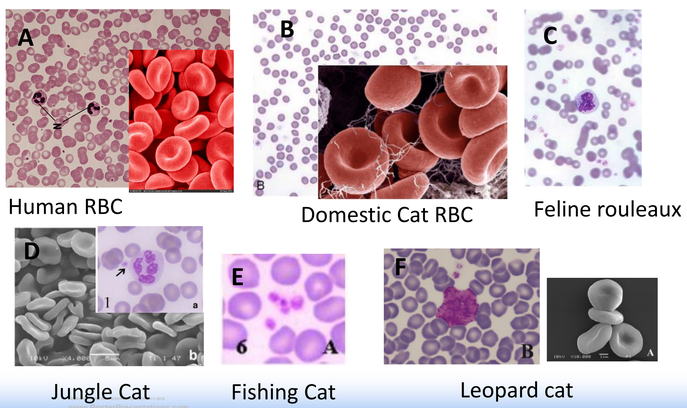
Introduction

With a role as important as carrying oxygen to tissues everywhere in the body, red blood cells (RBCs) have been well-studied, especially in humans. To meet the higher oxygen needs of large animals like humans, RBCs are the most abundant and fastest produced cells in the body. In addition, mammalian RBCs have evolved to have high surface area to volume ratio to maximize gas carrying and deformability. All mammalian RBCs lack a nucleus and some other organelles, plus they have a biconcave, disc shape giving a distinct lighter area in the center known as the central pallor that can be seen on blood smears. Further research has told us that these cells are filled with hemoglobin molecules each of which to can chemical bind to four oxygen molecules (Case, 2021).

The evolution of the biconcave shape was significant enough that most mammals evolved a similar shape. Though it seems to be less documented, the felid family was no exception. Wild species of felids, such as pumas and lynx, maintained this discoid, red blood cell shape (Wikander, Anantatat, Kang, & Reif, 2020). Even snow leopards (Panthera uncia) have this shape to their RBCs despite living in higher altitudes, where most felids would have a difficult time breathing due to lower oxygen availability (Janecka et al., 2015).

Despite the effectiveness of the biconcave disc shape, as we investigate domesticated felids, there is a clear change in shape (Fig. 1B). Rather than having a distinct central pallor, the cell is concave on one side and convex on the other creating more of a bowl shape. This deviation in shape can result in lower gas transportation and exacerbate rouleaux stacking leading to additional health problems. The red blood cells of cats are also more prone to oxidative damage and Heinz bodies (Cornell University College of Veterinary Medicine, 2014). However, there doesn't seem to be any research to indicate why or when a mutation in shape occurred or the impacts of it.

Figure 1 – RBC shape in A) humans (disc); B) domestic cats (bowl); C) the stacking or rouleaux seen in cats because of the bowl shaped RBCs. RBC shape in other similar sized cats and close related felids D) Jungle cat (*Felis*, disc); E) Fishing cat (*Prionailurus,* disc); and F) Leopard cat (*Prionailurus,* disc).

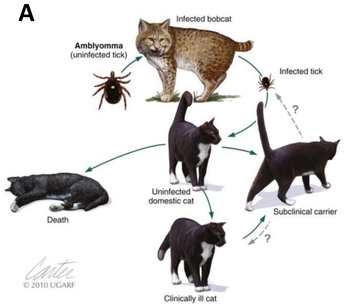


Bobcat Fever

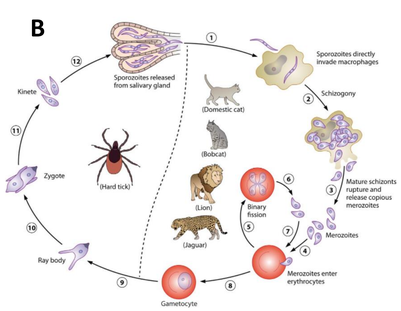
Bobcats were originally thought to be the main vector for cytauxzoonosis, commonly known as "bobcat fever." However, further research has shown the *Cytauxzoon* parasite in several species of wild felids as well as domestic felines (Wikander, Anantatat, Kang, & Reif, 2020). There is a difference is in the severity of the infection amongst felids. Wild felids such as bobcats, pumas, and panthers experience asymptomatic or mild cases of the disease, surviving to become reservoirs that perpetuate the parasite's lifecycle. In contrast, infection in domestic cats is often severe, then fatal, though there has been some recent documentation of survivors and the cats can then also become reservoirs for this protozoan parasite (Wang et al., 2017).

Cytauxzoonosis is a disease caused by the protozoan parasite *Cytauxzoon felis* carried by ticks, including the Lone Star Tick (*Amblyomma americanum*) and the American Dog Tick (*Dermacentor variabilis*), that infects red and white blood cells. Once infected with sporozoites transferred from tick saliva, the sporozoites replicate asexually inside macrophages that swell causing blockages and tissue damage until they burst, releasing piroplasms/merozoites that infect red blood cells. Since *C. felis* uses both red and white blood cells to support their proliferation, variations in these cells may impact the severity of disease experienced by the host (Byers, 2016). With the range of ticks expanding, the potential for cytauzoonosis also increases (Merck Veterinary Manual & Tarigo, 2015).

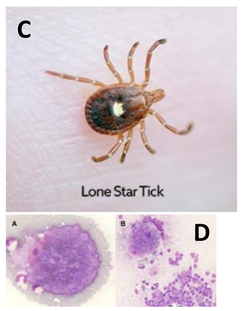
Figure 2 – A) The multiple fates of cats with cytauxzoonosis; B) Lifecycle of the protozoan, parasite *Cytauxzoon felis;* C) the Lone Star Tick, *Amblyomma americanum;* D) Cat macrophage infected by *Cytauxzoon felis;* E) Cat RBCs infected by *C. felis.*



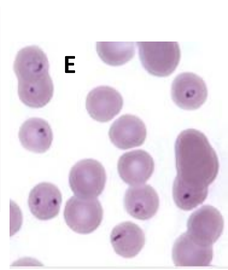
Pathway *C. felis* infections in felines



Lifecycle of *C. felis*



C. felis infected macrophage



C. felis infected RBCs

Phylogeny of the Felidae with distribution of RBC shape

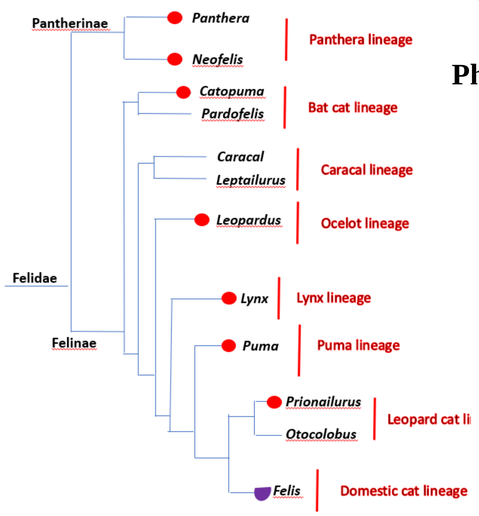
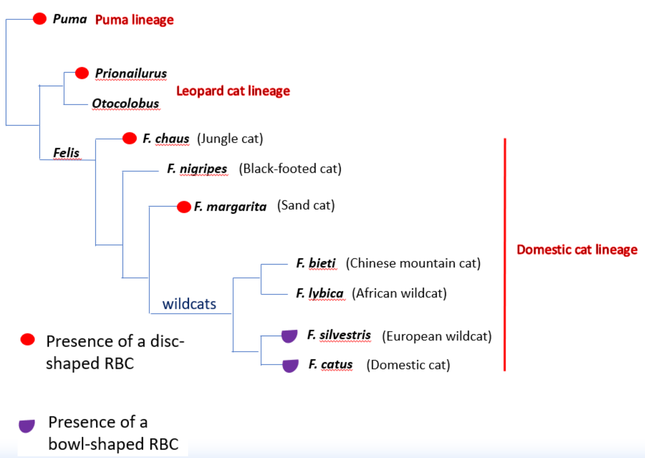


Figure 3 – DNA based phylogeny of the Family Felidae and subfamily Felinae (Johnson et al., 2006), illustrating the distribution of RBC shape within the felids from this study.

Phylogeny of the Felinae with distribution of RBC shape



RBC shape distribution and Cytauxzoonosis

The distribution of the discoid-shaped RBCs within the Felidae is similar to other families of mammals in that most species have the typical disc shape.

The oddity is the bowl-shaped RBCs found in domestic cats and its closest relatives, the wildcats especially the European wildcat, *Felis silvestris*, which appears to be to the progenitor to domestic cats as well as the other wildcats, the African and Chinese mountain cats (Yamaguchi et. Al., 2015). We have no data on RBC shape in these later two species/subspecies.

Cytauxzoonosis in domestic cat has historically been considered uniformly fatal, with a short course of illness, and most domestic cats die within 9 to 15 days post-infection. (Wang et al., 2017), whereas milder symptoms exist in other felids with disc-shaped RBCs.

Thus, there seems to be a strong, but untested, correlation between RBC shape and the severity of cytauxzoonosis in felids.

When comparing the red blood cells of hosts that experience mild infections to domestic cats, there is a noticeable difference in shape. The bowl shape seen in domestic cats could provide more cell volume that the parasite could use to proliferate, which may lead to a higher population of the parasite in the host.

Additionally, there is no literature yet published that discusses the shape change of RBCs in wildcats and domestic cats or what mutations in subsurface, plasmalemma proteins which would alter the typical biconcave disc shape into the bowl-shaped RBC shape seen domestic cats and in European wildcats.

Hypothesis

The increased volume, based on the change from disc shape to bowl shape in domestic cat RBCs, increases the risk of severe infection compared to felids with the normal discoid RBCs.

Future Research

Differences in cell volume, populations of parasites in various hosts, mutations that cause the shape variation, do normal RBCs reduce severity of infection, WBC variations.

Acknowledgements

Thank you to the McNair program for funding and support through this project.

References

See attached