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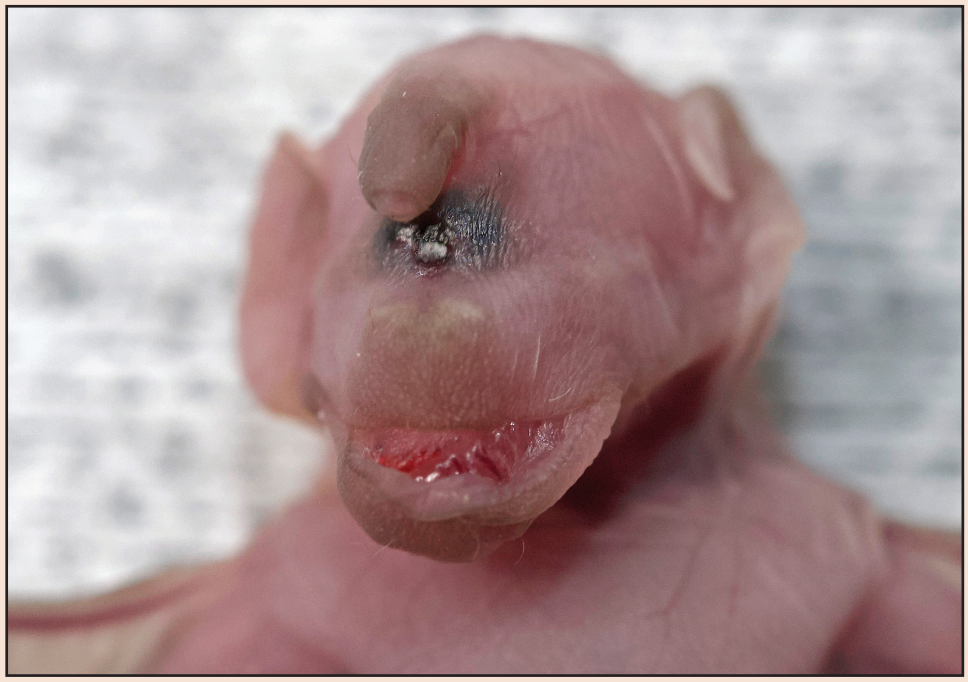

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Cover Photograph: Pup D with apparent cyclopia. Note lack of external nasal openings, a tube-like protrusion on the forehead, and a single eye in the midline. Photograph © L. Sturges and A. J. Furlow.

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First Record of Cyclopia in a Newborn Eastern Red Bat (*Lasiurus borealis*)

Abigail J. Furlow[1,*] and Leslie Sturges[1]

Abstract - In a litter of 4 premature *Lasiurus borealis* (Eastern Red Bats), 3 of the pups had obvious deformities. The upper jaw in each appeared shortened relative to the length of the mandible, possibly the result of a compressed premaxilla. In 1 affected individual, the eyes were fused into a single midline structure, external nostrils were absent, and a cylindrical appendage protruded from its forehead. These deformities are consistent with a developmental malformation termed cyclopia, which is a severe form of holoprosencephaly.

Congenital defects in humans and domesticated animals are well documented, but such abnormalities are less often described in wild mammals. Among bats, dental anomalies (Esquivel et al. 2021) and chromatic aberrations (Lucati and López-Baucells 2017) are the most common abnormalities that are reported, presumably because these defects have little effect on survival. Nevertheless, more severe anomalies like polydactyly and malformed vertebrae occasionally have been described (Kunz and Chase 1983), as well as deformities of the pinna (Ruckert da Rosa et al. 2011), tragus (Tamayo-Zuluaga et al. 2020), eye (Herazo-Callejas et al. 2024), and penis (Fuller et al. 2019). In this paper, we provide the first descriptions of severe facial abnormalities in newborn bats.

On 7 May 2024, an adult female *Lasiurus borealis* (Müller) (Eastern Red Bat) was brought to Bat Conservation and Rescue of Virginia (https://www.virginiabats.org/), a state permitted wildlife rehabilitation and education facility, located in Mount Solon, Virginia. The animal, which was originally recovered in Fairfax, Virginia, weighed 10 g and had no visible injuries. It was treated for mites using fipronil and eventually housed in an outdoor flight cage. Although the bat appeared behaviorally normal at first, it was found on the ground 4 days later, on 11 May 2024, and brought inside for observation. We housed the bat in a large canvas dog crate and closely monitored the animal for signs of pregnancy or any changes to its health; however, we avoided weighing or otherwise handling the bat to minimize stress.

At some time during the morning of 17 June 2024, the bat gave birth to 2 pups, a female (Pup A) and a male (Pup B). Only Pup A attempted to suckle, but it was unable to latch onto a nipple. Neither offspring could grasp with its hindfeet, a crucial ability for newborns, and 1 of them (Pup B) still had the placenta attached by the umbilicus (Fig. 1). The mother did not attempt to groom either offspring and seemed disinterested when we attempted to reunite them. These 2 neonates died within 24 h. About 12 h after the first births, the adult delivered 2 stillborn pups; 1 was female (Pup C), but we could not determine the sex of the fourth neonate (Pup D). The adult died about 3 weeks later, on 6 July 2024.

Three of the pups (A, C, and D) had a markedly shortened upper jaw (Fig. 2), presumably due to a deformed premaxilla. Pup D also had a cylindrical protrusion on its forehead, a single median eye, and no external nasal openings (Fig. 2). Pup B, in contrast, appeared physically normal. Although vespertilionid bats typically are born naked and with eyes closed, typical neonates are able to grasp with their hind feet and, of course, are capable of

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suckling (Kunz and Hood 2000; Kurta and Kunz 1987). However, Pup A and Pup B apparently were not able to nurse or clutch the fur of their mother. Eastern Red Bats usually weigh about 1.7 g at birth and have a forearm length of 12.7–16.6 mm (Barnard 2010). We did not weigh our neonates, but the forearm lengths were 11.5, 10.9, 11.0, and 10.7 mm for pups A–D, respectively. The small sizes of the forearms suggested that the births were premature.

The deformities in pups A, C, and D appear to be examples of holoprosencephaly (HPE), a malformation in which the forebrain fails to separate completely into 2 cerebral hemispheres (Winter et al. 2015). HPE is accompanied by a range of physical problems that are externally visible. In its simplest presentation, the condition is associated with subtle craniofacial defects. The term cyclopia denotes HPE in its most severe form, and it is characterized by anomalies of the central nervous system, absence of nasal cavities, missing or malformed facial bones, deformities in the upper and lower jaw, a median orbit containing a single eye, and, rarely, the presence of a proboscis-like structure above the eye (Noden and de Lahunta 1985, Palmquist-Gomes et al. 2019). The malady occurs in humans, as well as laboratory mice and a range of domesticated animals, including dogs, cats, goats, cows, and horses (Koch et al. 2005, Pereira et al. 2021, Rashed et al. 2014, Schell-Apacik et al. 2003). However, to our knowledge, HPE has not been described previously in any bat or any other wild mammal, other than a few ungulates (Bubenik 1982, Hellgren et al. 1984).

Our external observations suggest that Pup B was the most normal because its jaws seemed to be properly developed, whereas the other neonates apparently showed different degrees of HPE. Pups A and C had a shortened upper jaw, presumably caused by deformation of the premaxilla or other facial bones, suggesting a mild form of HPE (Noden and de

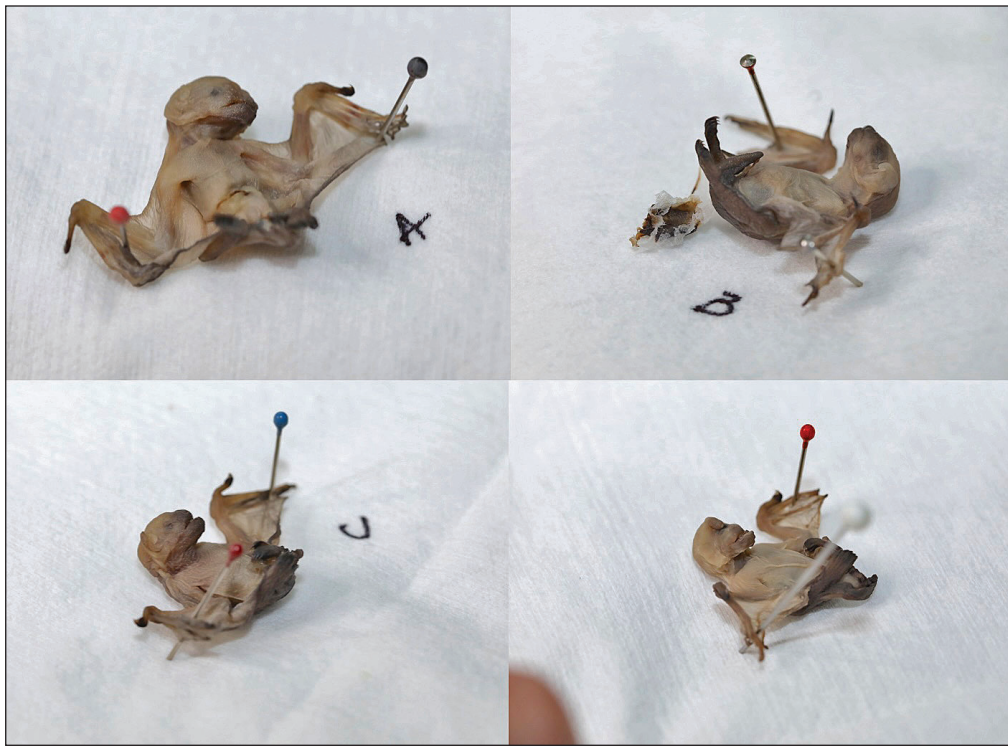

Figure 1. Side view of each newborn Eastern Red Bat. Note shortened upper jaw in A, C, and D and apparently normal jaw in B.

Lahunta 1985). Pup D, though, had a cylindrical protrusion on its forehead, a median eye, no external nostrils, and a deformed upper jaw, all of which are traits associated with cyclopia (Noden and de Lahunta 1985, Palmquist-Gomes et al. 2019).

Reasons for HPE vary and can be either genetic or environmental or a combination of such factors (Malta et al. 2024). For instance, HPE often is related to the absence or inhibition of signaling pathways involving the sonic hedgehog gene (Schell-Apacik et al. 2003). In cattle and sheep, consumption of alkaloids contained in naturally occurring plants, like *Veratrum californicum* Durand (California False Hellebore) can cause HPE (Welch et al. 2009). In humans, the likelihood of HPE developing correlates with a number of variables, including maternal allergies and exposure to acids, solvents, ochratoxins, alcohol, or tobacco (Addissie et al. 2020a, Malta et al. 2024, Matsunaga and Shiota 1977, Winter et al. 2015). Although identifying specific genetic-environmental interactions in the etiology of birth defects is challenging (Lipinski and Krauss 2023), pesticide exposure increases the risk of HPE in humans (Addissie et al. 2020b), and a component of pyrethroid insecticides (piperonyl butoxide) is known to disrupt the sonic hedgehog pathway (Wang et al. 2012).

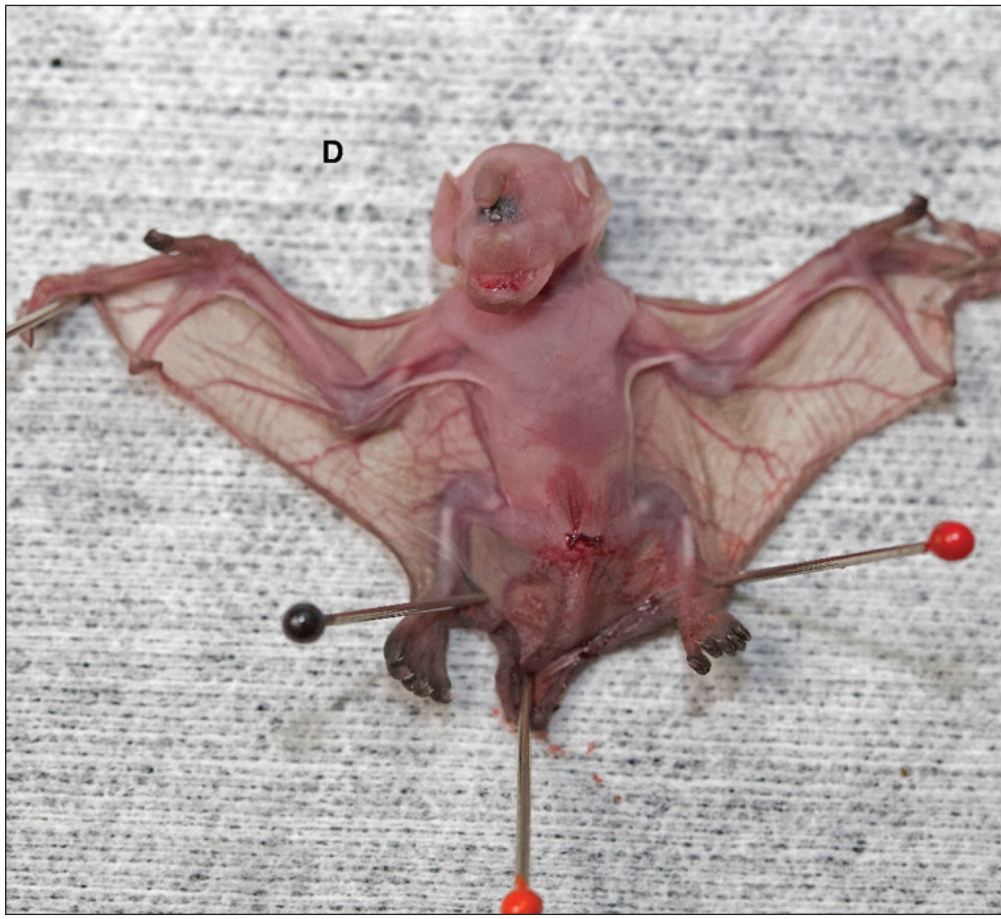

Figure 2. Pup D with apparent cyclopia. Note lack of external nasal openings, a tube-like protrusion on the forehead, and a single eye in the midline.

Deformities related to HPE appear during early gestation—for example, weeks 3–4 in humans and days 7–8.5 in mice (Lipinski et al. 2010). Eastern Red Bats have a gestation of about 80–90 days (Jackson 1961), but the adult bat spent only 41 days in our care prior to parturition. Hence, the malformations that we recorded likely were not related to anything that the mother experienced while at our facility.

Although HPE is somewhat common among humans, occurring in 1 of every 250 conceptuses and 1 of every 16,000 births (Winter et al. 2015), the frequency of HPE or other developmental abnormalities among bats is unknown and difficult to quantify. The Eastern Red Bat, for example, is a solitary foliage-roosting species (Carter and Menzel 2007), and tiny aborted fetuses or stillborns would simply drop to the forest floor and not likely be recorded by biologists. Many bat populations, though, are decreasing (Frick et al. 2020; Soto-Centeno and Calderón-Acevedo 2023), including those of the Eastern Red Bat (Mallinger et al. 2023, Winhold et al. 2008), and when studying these declines, wildlife managers concentrate on the causes of adult mortality, like disease and wind turbines. However, factors that decrease the production of viable young should also be considered. Although we do not know the specific reason for the HPE that we observed or its frequency in nature, the increased use of insecticides following arrival of white-nose syndrome has led to a higher rate of infant mortality in humans (Frank 2024), and increased pre- or post-birth mortality may also be occurring in wildlife.

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