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The Biology and Husbandry of The African Spiny Mouse (*Acomys cahirinus*) and the Research Uses of a Laboratory Colony

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African spiny mice (*Acomys* spp.) are unique precocial rodents that are found in Africa, the Middle East, and southern Asia. They exhibit several interesting life-history characteristics, including precocial development, communal breeding, and a suite of physiologic adaptations to desert life. In addition to these characteristics, African spiny mice are emerging as an important animal model for tissue regeneration research. Furthermore, their important phylogenetic position among murid rodents makes them an interesting model for evolution and development studies. Here we outline the necessary components for maintaining a successful captive breeding colony, including laboratory housing, husbandry, and health monitoring aspects. We also review past and present studies focused on spiny mouse behavior, reproduction, and disease. Last, we briefly summarize various current biomedical research directions using captive-bred spiny mice.

Rodents of the genus *Acomys* are collectively referred to as 'spiny mice' due to the prominent spiny hairs that emerge from their dorsal skin.[57] *Acomys* takes its name from the Greek *acme*, meaning 'sharp point,' and *mus*, meaning 'mouse.' The International Union for the Conservation of Nature currently recognizes 18 *Acomys* species, which are distributed widely across arid environments including parts of Africa, the Middle East, and southern Asia. Historically, spiny mice served as a model to examine physiologic adaptations to a desert lifestyle and to examine temporal partitioning among sympatric rodent species in the wild.[61,90] As precocial mammals, aspects of the unique life-history of *Acomys* have been studied, and they also have proven to be a useful laboratory model for investigating diet-induced type-2 diabetes, diel rhythmicity, late-gestational development, female aggression, and parental behavior. To conduct these studies, several species of spiny mouse (for example, *A. cahirinus*, *A. russatus*, *A. dimidiatus*, *A. subspinosus*) have been maintained successfully in laboratory colonies (Figure 1). Interestingly, the reported husbandry of captive spiny mice varies.

Our own interest in these animals grew out of research investigating their weak-skin phenotype and enhanced regenerative ability (compared with other mammals).[84] Because our initial studies focused on live-trapped animals, we began keeping groups of *A. kempi* and *A. percivali* in Kenya (Figure 1). Building on this experience, we formally established a colony of *A. cahirinus* in the United States beginning in 2012 (Figure 1). Based on our own experience and that reported by others in the literature, the purpose of this paper is to describe practical aspects of spiny mouse biology, a standardized program of laboratory care and briefly review some current research uses for these rodents.

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Taxonomy and Unique Properties

Acomys spp. are members of the family Muridae, a taxonomic group that comprises nearly one third of all mammalian diversity and whose members form the most speciose family of mammals on earth.[92] *Acomys* were traditionally included within the subfamily Murinae, the Old World mice and rats, but molecular phylogenetics appears to have resolved this controversy.[92,93] Recent molecular data places *Acomys*, along with *Deomys*, *Uranomys*, and *Lophuromys*, in their own distinct subfamily, Deomyinae. The Deomyinae share a common ancestor with Gerbillinae (gerbils) and together, these subfamilies share a common ancestor with the Murinae.[92,93] Their common name (that is, spiny *mouse*), however, continues to provide some confusion among lay people and scientists who mistakenly associate them with laboratory mice.

Acomys spp. possess a number of unique biologic features. Their most notable characteristic is that of precocial development.[7] Spiny mice are considered precocial because newborn pups show an advanced stage of development, compared with all other murid rodents. Gestation in African spiny mice reportedly lasts 38 to 45 d, about twice as long as that in mice and rats.[7,12,20,42,63] Litter size tends to be small, consisting of 1 to 4 pups (normally 2) and rarely as many as 5.[20,54,95] We followed pregnant *A. cahirinus* from our own colony and corroborated previous results, finding a gestation time of 39.3 ± 1.1 d (n = 12 pregnancies, mean ± 1 SD) and a litter size of 1.7 ± 0.7 pups (n = 26 litters). Pups are born haired with eyes open and ears unfolded, and they are capable of eating dry food from the second day of life (Figure 2).[12] In addition, substantial development of the lung,[60] liver,[47] kidney,[21] and brain[8] occurs in utero, such that organogenesis is mostly completed before term. This situation contrasts with that in mice and rats, in which maturation of these organ systems happens in postnatal life. Furthermore, spiny mice complete the majority of neurogenesis prior to birth, making comprehensive behavioral assessments in neonatal spiny mice possible. Exemplified by their social interaction among strangers, spiny mice pups between 1 and 5 d old are curious and social.[79] Young pups are very mobile compared

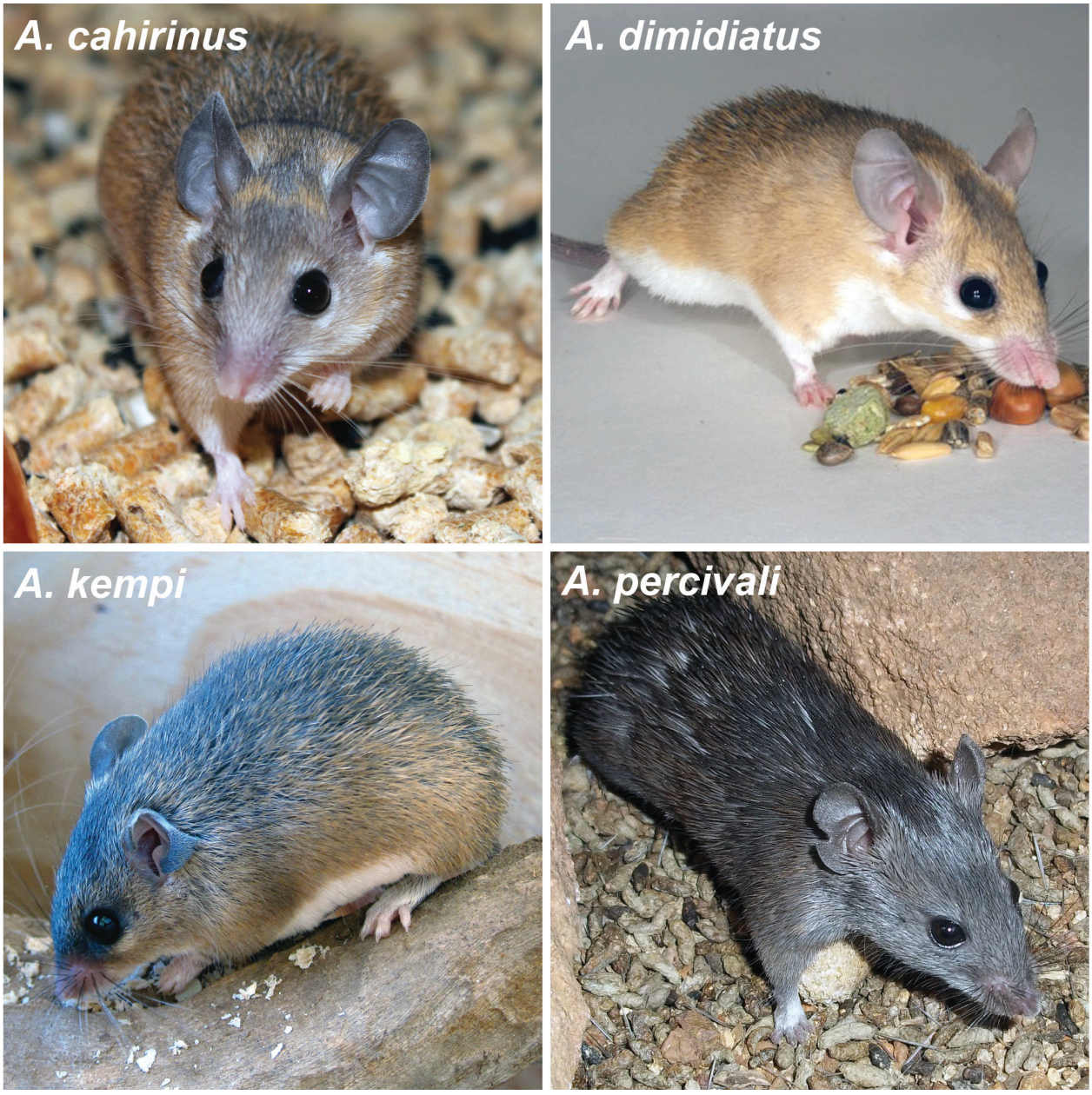

Figure 1. Four representative species of *Acomys*. Adult *A. cahirinus* from a captive breeding colony at the University of Kentucky (United States). Adult *A. dimidiatus* from a captive breeding colony at the University of Geneva (Switzerland; photo courtesy of Athanasia C Tzika). Adult *A. kempi* and *A. percivali* live-trapped in Kenya and maintained at the University of Nairobi (Kenya).

with laboratory mouse pups and have a soft gray hair coat, which is distinct from the golden brown color of adult spiny mice (Figure 2).

Along with precocial development, spiny mice are notable for large spiny hairs that form most of the dorsal pelage.[57] The rodent pelage consists of 4 types of hairs: guard, awl, auchene, and zigzag.[22,83] The characteristic spiny hairs were recently demonstrated to develop from awl hairs.[52] Prior to sexual maturity, *A. cahirinus* exhibit a gray coat on the dorsum that transitions abruptly to a white underside. Spiny hairs emerge around sexual maturity from a region on the lower dorsum and spread in a wave-like pattern to cover the entire dorsum[52] (Figure 2). These mature hairs are gray at the base, with a yellowish to orange midregion and a small black distal tip.

Acomys possess very weak skin that tears easily in response to attack or handling.[84] The tensile strength of laboratory mouse skin is 21 times greater than the tensile strength of *A. percivali* and *A. kempi* skin, and *A. cahirinus* appears similar in this regard.[84] It is presumed that this characteristic facilitates predator escape through autotomy. The weak-skin phenotype is found in all parts of the pelage, and the tail sheath in these animals is easily lost.[88] Animals trapped in the field frequently lack tails, and tail loss does not affect fecundity.[88] Interestingly, field observations suggest that *Deomys*, *Uranomys*, and *Lophuromys* (all members of Deomyinae) exhibit a similar phenotype.

Natural Habitat

Spiny mice are distributed widely across semidry and arid regions from Africa, the Middle East, and Asia.[57] *A. cahirinus* is found throughout the Middle East, and data on natural populations have been collected from animals in the extreme deserts of Israel.[57,90] In comparison, *A. kempi* and *A. percivali* are found

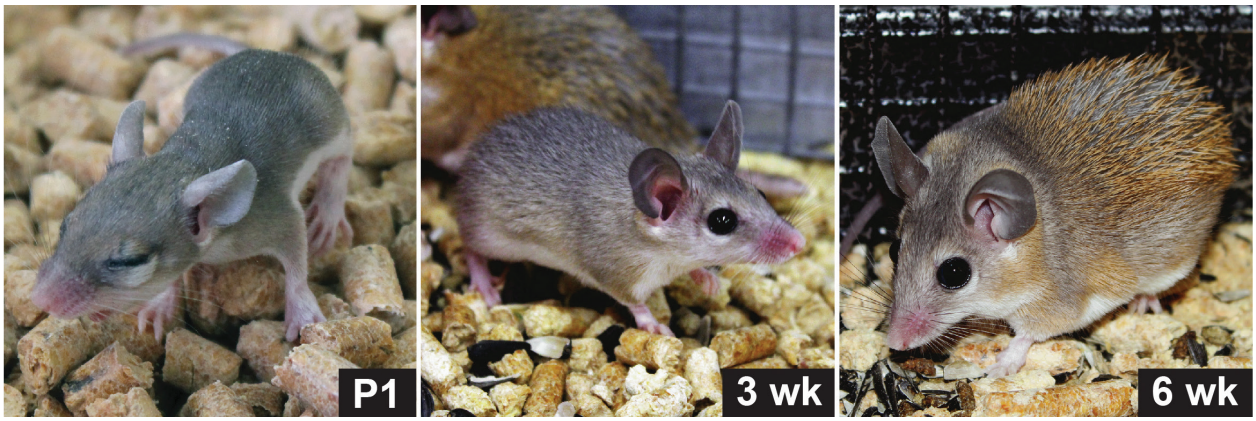

Figure 2. Postnatal development of *Acomys cahirinus*. A newborn *A. cahirinus* (P1) demonstrating precocial development. Note the open eyes, unfurled ears, hair coat, and so forth. In this 3-wk old *A. cahirinus*, the adult coat color is visible at the boundary between the white underside and gray, juvenile coat. The spiny hairs have emerged from the dorsal skin of this 6-wk old *A. cahirinus*.

in semiarid regions throughout Kenya, and both species prefer mountainous and rocky outcroppings with ample crevices for daytime shelter.[90] Spiny mice concentrate in rocky areas, like rock canyons, kopjes, near cliffs, and in the crevices of buildings. Given their predilection for rocky outcroppings and because they do not dig burrows, they are thought to rely on rock crevices and already established burrows for shelter.[14] Laboratory colonies of different *Acomys* species have been established with animals from Algeria, Egypt, India, Israel, Kenya, Libya, Morocco, South Africa, and Tanzania.

General Characteristics

Acomys species have a lifespan of 2 to 4 y, although there have been reports that *A. cahirinus* can live as long as 7 y in captivity.[5,55] Several adult *A. cahirinus* that were colony founders remain in our colony today and are at least 3 y old (although likely older). *Acomys* have large ears, large black eyes, and long noses with prominent long whiskers. Spiny mice exhibit sexual dimorphism, with males being slightly larger than females.[17] On a 14% protein diet supplemented with sunflower seeds, 6-mo-old adult *A. cahirinus* typically weigh between 30 and 50 g. There are reports of *A. cahirinus* reaching weights of 100 g, but this is on modified diets designed to extenuate a natural propensity for obesity.[29,41,65] The adult body length (nose to rump) varies from 9 to 13 cm, with a tail slightly less than or equal to 100% of body length. The tail itself is scaly with small hairs.

The color and location of spiny hairs can help discriminate separate *Acomys* species (Figure 1). Adult *A. cahirinus* have a light-brown dorsal coat and cream-colored undersides. Spiny hairs are present from their tails to halfway up their back. *A. kempi* resembles *A. cahirinus* but has a slightly darker coat with a reddish tint and white undersides with spiny hairs present from the tail to halfway up the back. *A. percivali*, in contrast, maintains a gray coat even after sexual maturity and has a white underside; spiny hairs cover the back from tail to neck.

Reproductive Biology

Both male and female *A. cahirinus* are sexually mature at 2 to 3 mo of age.[95] Sexual maturity is coincident with the emergence of spiny hairs that have a light-golden color[52] (Figure 2). Captive females are reported to continually mate and produce offspring in the lab for years under optimal conditions.[95] However, *A. cahirinus* appears to exhibit seasonal breeding in the wild, showing a preference for copulation after long rains so that young are born during lush times,[5,15,56] and testis development in *A. spinosissimus* is seasonal[51] and photo-responsive.[50] Interestingly, although captive females cycle year round, we find few pups born from December through February. On average, females begin cycling at 45 d old, with the onset of the opening of the vagina.[63] The female estrus cycle is approximately 11 d long, although this is variable, and natural ovulation results in 2 to 5 oocytes.[63] Although it is not easy to identify estrus stage by vaginal smear compared with lab mice, the longer estrus cycle suggests an uncharacteristically long luteal phase for a rodent.[63] After ovulation, functionally active corpora lutea are spontaneously present in *A. cahirinus*[63] and *A. spinosissimus*.[13] This is in contrast with most laboratory rodents, where vaginocervical stimulation is required for the formation of functional corpora lutea (that is, pseudopregnancy).[32,91] A superovulation protocol has been developed for *A. cahirinus* that successfully produces a 5-fold increase in 2-cell embryos compared with natural ovulation, allowing a large number of embryos to be collected for developmental experiments.[62]

Male *A. cahirinus* start producing spermatozoa between 5 and 6 wk of age and can begin impregnating females at approximately 7 wk old.[64] Although males have a full complement of accessory sex glands (prostate, seminal vesicles, coagulating glands, and ampullary glands), they are unique among rodents in not having preputial glands.[64,94] In addition, male spiny mice have large lateral prostate glands, compared with lab mice and rats.[64,94] Male copulatory behavior exhibits multiple intromissions, no thrusting, single to few ejaculations, and a short incipient lock, the last 2 of which are rare among murids.[17] The presence of a semen plug after copulation varies. Dissection of the reproductive tracts of mated female spiny mice revealed prominent semen plugs in one study,[17] whereas others have not noted readily observable plugs after mating.[6,20] In support of these findings, we closely examined *A. cahirinus* females set for breeding (n = 34) and never observed plugs in those that became pregnant. Studies on spiny mouse coagulation extract and semen revealed that spiny mouse extract has subeffective coagulation abilities.[64] However, plugs are readily seen after superovulation,[62] suggesting that female *A. cahirinus* can affect coagulation of male semen. Similar to other rodents, spiny mice experience postpartum estrus, which allows for estimation of fetal age for developmental studies.[54]

Behavior

The social dynamics of spiny mice in the wild are unknown. However, behavioral data from captive-bred colonies

demonstrates they are communal breeders.[25,26,68,95] Our own observations of captive *A. cahirinus*, *A. kempi*, and *A. percivali* indicate that they spend considerable time huddling together in groups. Social interactions between individuals appears dependent on familiarity, kinship, and sibling recognition.[75] Increased group size as measured by number of sexually mature females positively affects litter size and breeding efficiency.[26] There are reports that some *Acomys* species will create nests,[30,31] but our observations of *A. cahrinius*, *A. kempi*, and *A. percivali* suggest they do not.

We find that *A. cahirinus*, *A. kempi*, and *A. percivali* appear to be healthiest living in small groups consisting of 1 to 2 males, several females, and their progeny. A series of experiments explored social bonds between kin by using a number of cues, including vision, touch, and olfaction as well as the preference among young *Acomys* for the nest, milk, and a lactating mother's diet.[67,69-74,76-78] Taken together, these studies provide clear evidence that young *A. cahirinus* exhibit both group and kin recognition through olfactory cues. Pheromones produced by parents and the smell of the mother's milk and siblings all help behavioral imprinting that lasts into adulthood. Both male and female spiny mice provide parental care to juveniles belonging to their group. Females group-foster pups, in that individuals have been observed suckling from multiple lactating females.[95] Males display parental care, with juveniles spending more time with the male than the female.[49] Forced weaning can occur as early as 2 wk of age, although mothers will continue to nurse young beyond this time.[20,42,63,95] Juveniles have been observed suckling from a lactating female for weeks despite also eating solid food.[16] Newborn pups huddle vigorously with parents and littermates, but this huddling decreases after 2 to 3 wk.[7] In our colony, we routinely wean male and female pups during cage changes (3 to 4 wk after birth).

Both wild and captive-bred *Acomys* species are very curious.[4] *A. cahirinus* are less ambivalent when compared with lab mice by using several behavioral tests.[3,5] Remarkably, wild *Acomys* appear to ignore predator stimuli (owl calls, snake, and fox odor) and do not change their behavior after exposure.[10,23,33,40] Aggression studies have found that chasing, not fighting, is the primary aggressive behavior between individuals.[66] The environment of home cage compared with strange cage also affects levels of aggression. Adult female spiny mice typically are more aggressive and dominant over their male companions when in the female's home cage.[66] Both males and females were equally aggressive when in the males' home cage, and less overall aggression was observed in the males' cages.[66] This pattern suggests that females regard males as intruders to their territory, but males do not regard females as intruders.[66] Interestingly, when female spiny mice are paired with sexually experienced and inexperienced males, females are more likely to treat sexually inexperienced males as intruders than males with previous breeding experience.[1]

Housing

Spiny mice can do well in a variety of housing scenarios, and captive colonies have reported housing in typical mouse and rat enclosures.[20,42,54,95] However, 2 factors make these types of enclosures less than ideal. First, spiny mice are communal breeders and prefer living in groups, thus making standard mouse enclosures too small. Second, *Acomys* are very inquisitive and like to explore their environment. They are also avid climbers and jumpers. Therefore, we house spiny mice in nonsterile open cages. Although we have used large 20-gal aquariums with ventilated wire (1/4-in. spacing) mesh lids as suitable enclosures, given the exploratory behavior and large group sizes of these species, we now exclusively use 24 in. × 18 in. × 16 in. powder-coated galvanized steel cages with wire sides and lids (1/4-in. wire). The floors of these cages are solid, galvanized steel pans. Cages to these specifications are available from Quality Cage Company (Portland, OR) and are suitable for groups of 10 to 20 mice (Figure 3). The wire walls and ceiling of these cages provide extra enrichment that *Acomys* routinely use for climbing. The enclosures are safe, escape proof, easy to clean, provide good ventilation, and have doors that are easy to open and close. In the event that an animal is injured, standard mouse enclosures (Allentown Caging, Allentown, PA) can be used for short-term temporary housing. We have found that when we isolate individual *A. cahirinus* (even uninjured animals), they appear relatively inactive and lethargic. Although nighttime video recordings suggest they exhibit bursts of activity at light and dark onset, they move very little during the day when isolated. This behavior is in contrast to animals in our large group cages, which are active throughout the day. However, when isolated spiny mice are placed back into group housing, their activity levels return to normal.

Soft, dust-free bedding for cage bottoms is ideal, and in our experience, the optimal bedding for *A. cahirinus* is fragrance-free, pelleted-pine bedding. With use of good absorbent bedding and reasonable population densities of up to 20 mice per cage, cage changes can occur at 3- to 4-wk intervals, or more often as needed. *Acomys* species have desert-adapted physiologies and are capable of meeting their water needs through food sources.[90] However, if dry food is used, multiple drinking bottles (4 to 8 oz in size) attached to the outside of the cage provide an ample water source. Hydrogels are another option, and spiny mice readily use these if provided. Spiny mice are omnivorous and will eat food directly from ceramic bowls placed on the cage floor or from a feed hopper. Water bottles and feed are changed at least twice weekly, or as often as needed. The use of environmental enrichment provides hiding opportunities and limits fighting. Although the cage itself provides enrichment, spiny mice enjoy hiding tubes, rodent igloos, and shelters with multiple openings. Wood blocks and nylon bones provide material for gnawing.

Environmental Parameters

Spiny mice are desert adapted and prefer warm temperatures. However, *A. cahirinus*, *A. kempi*, and *A. percivali* are found in habitats that exhibit low nighttime temperatures, and *A. cahirinus* is capable of maintaining its core body temperature at environmental temperatures as low as 5 °C (41 °F).[90] In addition, *A. cahirinus* does not exhibit hyperthermia until 32.5 °C (90.5 °F).[90] In captivity, *A. cahirinus* lives and breeds well in a temperature range between 21 and 26 °C (70° to 80 °F). Humidity is maintained as per the *Guide* standard for rodents: 30% to 70%.[36] Although spiny mice are reported to be nocturnal, at least one species (*A. russatus*) is known to exhibit diurnal activity patterns.[11,89] We have used both a 12:12-h controlled artificial (fluorescent) light cycle and a light:dark regimen using natural light exposure through windows. We recently changed to using natural light exclusively in attempt to mimic seasonality and find that under these light conditions mice breed well.

Nutrition

Acomys species are omnivorous and are known to ingest insects, snails, and seeds and other plant material.[27,44] Captive

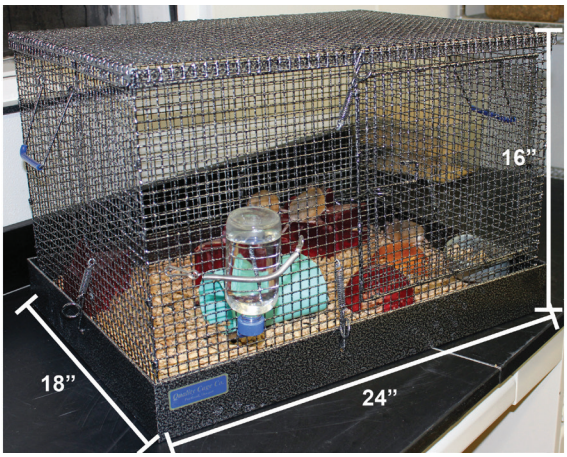

Figure 3. Wire cages used for housing the *A. cahirinus* colony at our institution. Cages (width, 24 in.; height, 18 in.; depth, 16 in.; Quality Cage Company, Portland, OR) are made from 1/4-in. galvanized-steel wire and can be disassembled for processing through a cage washer. The wire sides and top provide excellent enrichment.

colonies have been maintained on a variety of foodstuffs, and there is likely no preferred diet. However, caution should be exercised regarding fat content in the diet, given that nearly 15% to 30% of *A. cahirinus* can spontaneously become diabetic on mouse chow and fatty seeds.[28,41,65] Obesity is also a health concern with spiny mice possibly because of a tendency to overeat.[7,86] Long-term maintenance of spiny mice on a high-sucrose diet can have deleterious effects on reproduction and survival.[87] Given these concerns, we primarily use a 3:1 mixture of low-protein mouse pellets (14.3% protein, 4% fat with 2.9 kcal/g; Harlan Teklad 2014, Harlan Laboratories, Indianapolis, IN) and black-oil sunflower seeds (14% minimum protein, 20% minimum fat with 5.8 kcal/g; Pennington Seed, Madison, GA). We have observed spiny mice preferentially eating the sunflower seeds first, followed by the mouse pellets.

Handling and Restraint

Spiny mice are normally friendly, and gentle handling can promote acclimation to researchers and husbandry staff. However, spiny mice are agile and can become excited quickly. Care should be exercised when performing routine cage cleaning because spiny mice often times jump out of the cages. We have found that spiny mice acclimate to being handled and become accustomed to their caregivers. It is best to handle them by either gently scooping or cupping them in the hand or by grabbing the entire body from the dorsal side. Caution must be used when handling a spiny mouse because of their weak skin. We do not recommend handling spiny mice by their tails because the tail sheath can be easily detached due to a separation plane in the connective tissue between the skin and underlying muscle.[88] After loss of the tail sheath, spiny mice are reported to consume the remaining tissue.[88] Whether cage mates contribute to consumption of the remaining tail tissue is unknown. However, because the tail is gone the following day, surgical intervention is unnecessary. Individual identification is important for tracking experimental animals. Use of an ear punch is not effective because the holes close. Although we have attempted to use ear tags, due to the weak skin of spiny mice, the tags are almost always torn out. Instead, we have found the use of an implantable microchip (Bio Medic Data Systems, Seaford, DE) to be an easy and reliable method to track individual animals.

Health Issues and Disease Monitoring

New introductions into established housing groups will usually result in fighting. Tail injuries are the most common type of injury, and these wounds heal quickly. In addition, skin wounds result from fighting and heal well, although serious injuries may require isolation of the injured animal. Substantial injuries that encompass a prominent depth and surface area have a guarded to poor prognosis when the injured animal is left with the group. Often cage occupants will attack an injured mouse. Cannibalism is not uncommon, and few remains may be found of the deceased. Similar to other rodents, cannibalism of pups can occur when there is a smaller pup that is unlikely to survive or with a first litter.[20]

As stated earlier, *Acomys* species are prone to obesity in captivity. Obesity can result from a high-fat diet and, coupled with a normally low insulin response, can lead to diabetes mellitus.[86,87] Diabetes mellitus can lead to glycosuria and hypertrophy and eventual rupture of the islets of Langerhans, quickly causing death.[28,65,87]

As with all rodents, spiny mice are susceptible to external and internal parasites. A recent study of flea host specificity found that *Parapulex chephrenis* occurs on, and prefers, *A. cahirinus* compared with a cooccuring gerbil, *Gerbillus dasyurus*.[43] Endoparasites detected in wild spiny mice in specific locations in Africa have been principally cestodes and oxyurid nematodes.[2,48] In addition, spiny mice can harbor the oxyurids *Syphacia minuta* and *Aspicularis africana*.[2] Fecal infections of *Eimeria cahirinensis* (coccidia) have been noted in wild-trapped *Acomys dimidiatus*.[46] Oocysts from infected mice successfully orally inoculated naïve *A. cahirinus* and *A. dimidiatus*, and transmission of coccidia was 100%.[46] In contrast, coccidia were not transmissible to SCID mice or 2 other African rodents (*Mastomys coucha* and *Lemniscomys striatus*), thus supporting the known host specificity for this parasite.[46]

Reports of overt disease in captive spiny mice colonies are uncommon, and there are few reports of infectious agents in wild spiny mice. However, several studies investigating the prevalence of *Bartonella* spp. in wild rodents have identified this pathogen in *A. cahirinus*.[53,82] One study[82] isolated 4 novel strains of *Bartonella* from the blood of wild-captured *A. cahirinus*, and another[53] detected *Bartonella* most closely related to *B. eliazbethae* in spleen samples from the same species.

Although captive spiny mouse colonies are typically many generations removed from the wild, infectious disease screening should be performed on any new animals entering a captive colony from an outside source to ensure they do not harbor common transmissible rodent pathogens. In addition, infectious disease screening is recommended when establishing a new colony. Although serologic testing reagents specific for spiny mice are not commercially available, PCR assays and standard fecal floats, pelage, and tape tests for internal and external parasites can be used to determine the pathogen-free status of the colony. We have used mouse molecular diagnostics infectious disease PCR panels (IDEXX RADIL, Columbia, MO) to screen for the following murine pathogens in our *A. cahirinus* colony: mouse adenovirus 1 and 2, mouse hepatitis virus, mouse parvovirus/minute virus of mice, epizootic diarrhea of infant mice, sialodacryoadenitis virus, rat parvovirus, Theiler murine encephalomyelitis virus, cilia-associated respiratory bacillus, *Corynebacterium rodentium*, *C. piliforme*, *C. kutscheri*, *Mycoplasma pulmonis*, *Pasteurella pneumotropica*, *Salmonella* spp., *Streptobacillus moniliformis*, ectromelia, hantavirus, K virus, lymphocytic choriomeningitis virus, mouse cytomegalovirus, pneumonia virus of mice; polyoma virus, and reovirus. In addition, spiny

mouse pelt swabs and pooled fecal samples can be used to conduct PCR screening (IDEXX RADIL) for the following rodent parasites: *Aspicularis tetraptera*, *Myocoptes* spp., *Radfordia/Myobia* spp., and *Syphacia obvelata*. We have not detected any of the listed infectious agents in our colony.

When new animals are obtained, quarantine is suggested to observe and monitor for signs of disease. Our program requires a minimum 7-d isolation period for quarantine of incoming animals. During this period, newly received spiny mice are observed for signs of disease that may affect other animals (for example, sneezing, skin lesions, ocular discharge). Animals with abnormalities are reported to the veterinarian for evaluation, additional testing, and treatment, up to and including euthanasia, if warranted, to protect the health of the colony. A necropsy is conducted when unanticipated and unexplained death, suspicion of an undiagnosed infectious disease, or increased morbidity or mortality in the colony occurs. A sentinel program for routine colony health surveillance should be established, similar to that used for laboratory mouse and rat colonies, and tailored to meet specific of the institutional animal program. Our sentinel program uses euthanized or culled spiny mice and laboratory mouse sentinels exposed to colony spiny mice via soiled bedding transfer. A minimum of 10 spiny mice from our colony may be tested approximately every 6 mo. In addition, 2 sentinel mice per room, which holds approximately 40 galvanized wire cages of spiny mice, may be tested every 6 mo. Sentinel mice are exposed to soiled bedding from spiny mice cages for 6 mo, and then samples are sent for pathogen screening as described earlier.

Research Uses

As previously noted, spiny mice have served as a model to examine physiologic adaptations to desert life, diet-induced type 2 diabetes, diel rhythmicity, late-gestation development, female aggression, and parental behavior. Recently, spiny mice have emerged as a new animal model for evolution, development, and regeneration research.[52,84] One group using a captive-bred colony of *A. dimidiatus* recently reported how spiny hairs develop as enlarged awl hairs.[52] In combination with other spiny mammals, *Acomys* offers an attractive opportunity to explore how diversity in skin appendages can evolve. In addition, *Acomys* species are emerging as important models of tissue regeneration.[84,85] For instance, *A. kempi* and *A. percivali* can regrow damaged skin tissue, including hair follicles, sebaceous glands, dermis, and adipose tissue, with little or no scarring.[84] This work demonstrated that the typical fibrotic response observed in laboratory mice and rats is muted in response to full-thickness skin wounding in *A. kempi* and *A. percivali*. Although the molecular mechanisms underlying this cellular response to injury are currently unknown, this is an ongoing area of research in several laboratories. In addition to skin wounding, our group showed that *A. kempi* and *A. percivali* can regenerate 4-mm punches through the ear pinna.[84] Our group is currently exploiting this model to investigate complex tissue regeneration as it relates to appendage regeneration in other vertebrates. Importantly, an active genome sequencing project is underway for *A. cahirinus*, which will facilitate genetic analysis of their regenerative ability. Therefore, in a comparative framework with other rodents, *A. cahirinus* will be a useful animal model to understand the cellular and molecular mechanisms that promote regeneration instead of scarring in mammals.

The precocial nature of *Acomys* spp. makes them interesting animals for studying the neural origins of behavior[79] and the in utero development of the brain.[6,8] In this regard, *Acomys* spp. are more similar to humans than are the laboratory mouse and rat, in which a major portion of organ maturation occurs during postnatal life. Given the precocial development of most organ systems in spiny mice, they are useful models to understand developmental defects that occur during late gestational development. Studies with *A. cahirinus* have shown that excess maternal glucocorticoid exposure (for example, dexamethasone) given in midgestation can have persisting effects on the placenta (and likely fetal development) and that the effect is dependent on fetal sex, placental region, and time after glucocorticoid exposure.[58,59] These studies also noted sex-dependent effects on placental glycogen stores with maternal glucocorticoid exposure.[58] Because elevated glucocorticoids during human pregnancy suppress fetal growth, especially in males, spiny mice will be useful to explore how natural hormones affect late gestational development. In addition, when a mother spiny mouse is exposed to the TLR3 agonist polyriboinosinic–polyribocytidylic acid to mimic a viral infection during midpregnancy, the offspring have reduced activity on several behavioral tests when compared with unexposed controls.[80,81]

Other studies have identified *Acomys* spp. as useful animal models for near-term birth asphyxia. In humans, birth asphyxia is associated with increased risk of cerebral palsy and impaired cognitive function (speech, hearing, vision, memory, and behavioral and emotional problems). A recent study compared spiny mice at gestational day 37 delivered by caesarean and immediately resuscitated with animals left in the uterus and placed in a 37 °C saline bath for 7.5 min (to mimic asphyxiation) and then delivered and resuscitated.[35] Behavior was tested in 28-d-old pups (open-field test, novel-object recognition test, rotarod). Brains examined histologically at 24 h and 1 wk after birth showed CNS inflammation in asphyxiated pups. In addition, asphyxiated pups showed impairment in nonspatial memory and learning tasks.[35] A follow-up study treated pregnant mothers with melatonin prior to asphyxiation and found a decrease in CNS inflammation, suggesting that melatonin may protect against hypoxic ischemic brain injury at birth.[34] A series of studies has shown creatine supplementation of the maternal diet (starting on day 20 of gestation) can reach the fetus and improve survival and postnatal growth after birth hypoxia.[38,39] Furthermore, creatine supplementation protects brain structure,[37] cognition,[19] and the structure and function of the diaphragm[9] and kidneys[24] but does not otherwise negatively affect the mother or fetus.[19] Together, these results pointed toward creatine as a potential therapy for birth hypoxia in humans.[18] The cited studies underscore that *Acomys* is a valuable model for testing how the in utero environment affects organogenesis and behavior. Importantly, these studies support the utility of *Acomys* as a viable model to test how exposure to toxicologic agents and environmental contaminants can lead to late-term developmental and behavioral defects.

Furthermore, *Acomys* is a model for type 2 diabetes mellitus because of their propensity to exhibit nutritionally induced diabetes.[87] *A. cahirinus* has been known to exhibit spontaneous diabetes with age. Researchers have noted that diabetes spontaneously occurs in about 15% of captive animals under laboratory conditions.[28,45,65] Diabetes occurs with hyperplasia of the endocrine pancreas, particularly the β cells.[28] In addition, spiny mice have increased pancreatic insulin content.[45] However, obesity does not always result in diabetes mellitus, and one study observed that 50% of spiny mice fed unrestrictedly in the laboratory developed obesity, whereas only 15% of these mice developed diabetes.[28] Some spiny mice will exhibit hyperglycemia, glucosuria, and ketosis, which is ultimately fatal.[45]

Nutritionally induced type 2 diabetes mellitus is significantly prevalent in humans, so the value and utility of a consistent rodent model is pertinent.

Conclusions

Acomys spp. are unique, precocial rodents originating from Africa, the Middle East, and Asia. These rodents have been useful animal models for physiologic and biomedical research and hold continued promise as models in studies of tissue regeneration, developmental defects in late-term pregnancy, fetal development, and type 2 diabetes mellitus. The standard of laboratory care we outlined here likely will prove useful for other groups wanting to establish breeding and research colonies of spiny mice.

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