

The Jackson Laboratory's Mission

Performing Research

Investigating genetics and biology of human disease

Providing Resources

JAX Mice Clinical & Research Services, bioinformatics data, technical publications and more...

Educating Scientists

World-class courses, internships and other programs



Benefits of enrichment for laboratory mice

- Encourage natural instincts to produce or seek shelter
- Provide a degree of control over their environment
- Can improve brain & neuronal development
- Reduce undesirable traits (stereotypies, barbering)



Toth, et al. 2011 *Comp Med*. 61(4): 314-321
Wurbel. 2001. *Trends Neurosci*. 24(4):207-11

Enrichment breeding study

- Five groups of trio-mated C57BL/6J inbred mice were studied throughout a typical breeding period of 30 weeks
- All groups received same husbandry & autoclaved diet, water, & bedding (aspen chips & shavings) but differed in the type of supplemental enrichment
- Technicians were rotated among groups



Cardboard
tunnel



Aspen shavings
only



Cardboard hut



Cotton square



Twisted paper

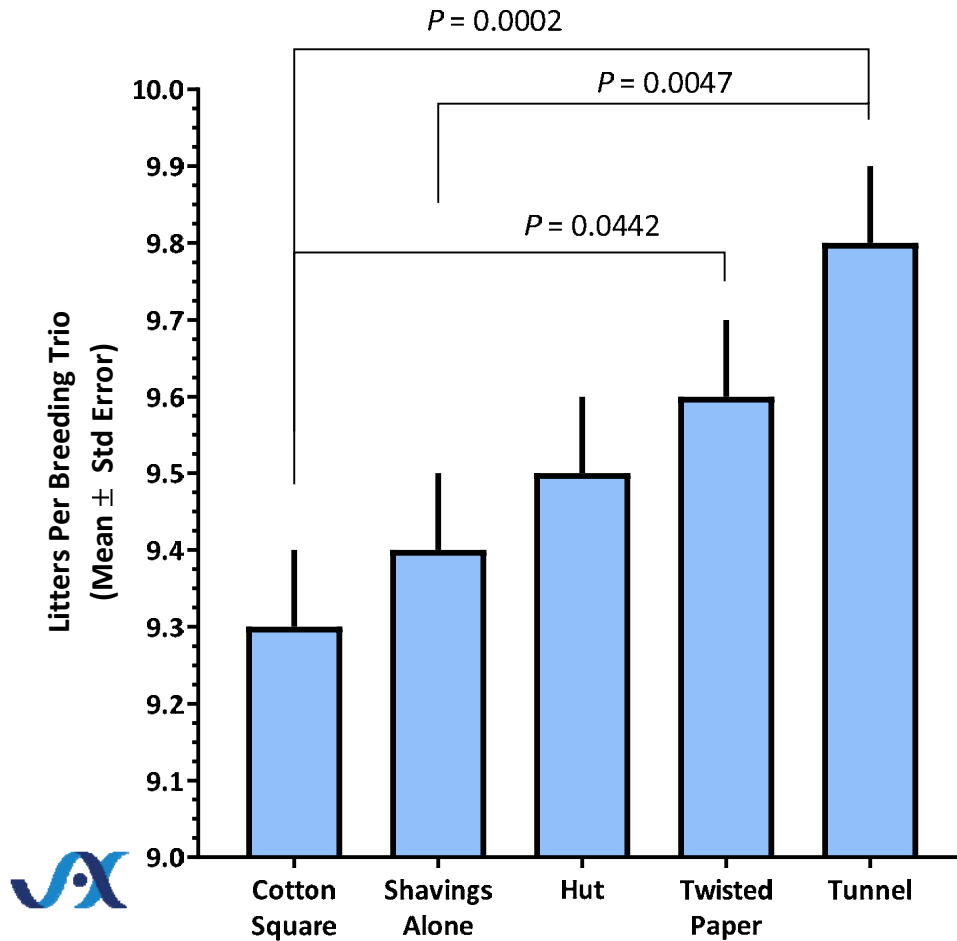
Enrichment breeding study

- Parameters measured for each cage:
 - Number of litters
 - Pups born
 - Pups weaned
 - Percent survival
 - Pup mortalities
 - Pups euthanized
 - Number of runts
 - Number of barbered pups
 - Number of flooded cages
- Each group contained ~600 cages

Enrichment	Total Cages (% Productive)
Shavings Only	600 (85%)
Twisted Paper	602 (91%)
Hut	598 (89%)
Cotton Square	603 (86%)
Tunnel	598 (91%)



Enrichment had marginal effects on litter counts



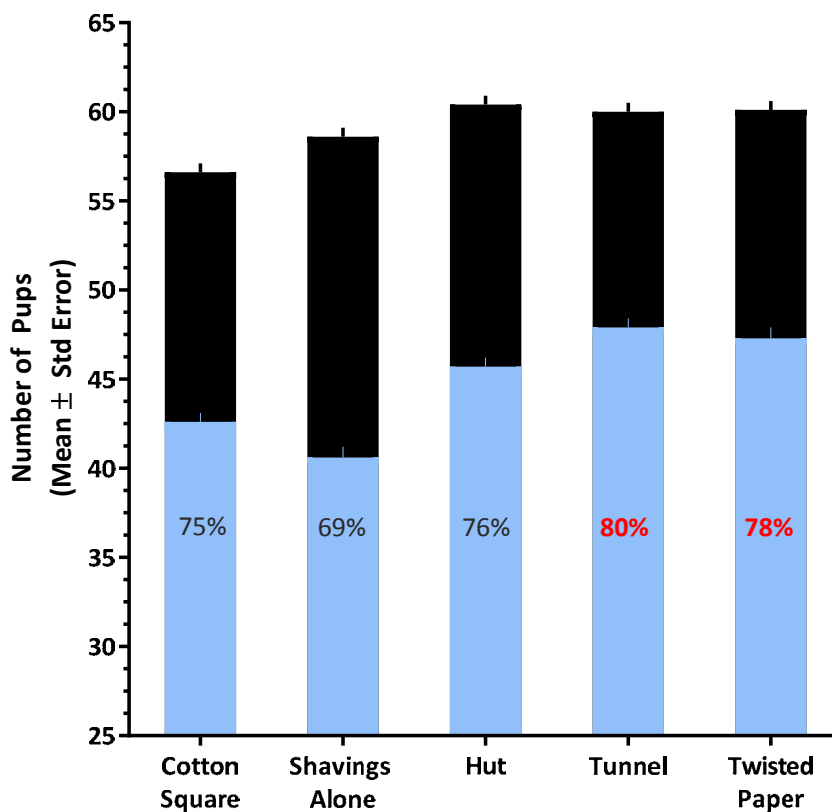
A tunnel offered improvements over a cotton square or aspen shavings alone

Twisted paper led to an increase over a cotton square

Statistical model: linear regression (ANOVA)

Twisted paper, tunnels improved survival to weaning

Bar graphs are overlaid
% indicates survival to weaning



■ Born
■ Weaned

Significant pairwise differences:

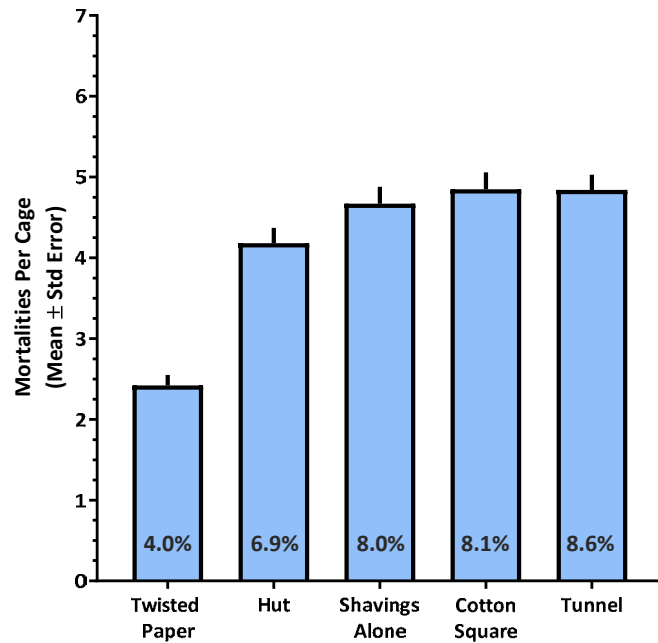
Born
Cotton square vs paper, hut, or tunnel

Weaned
Every pair except twisted paper vs hut or tunnel

Percent Survival
Every pair except twisted paper vs tunnel, hut vs. cotton square

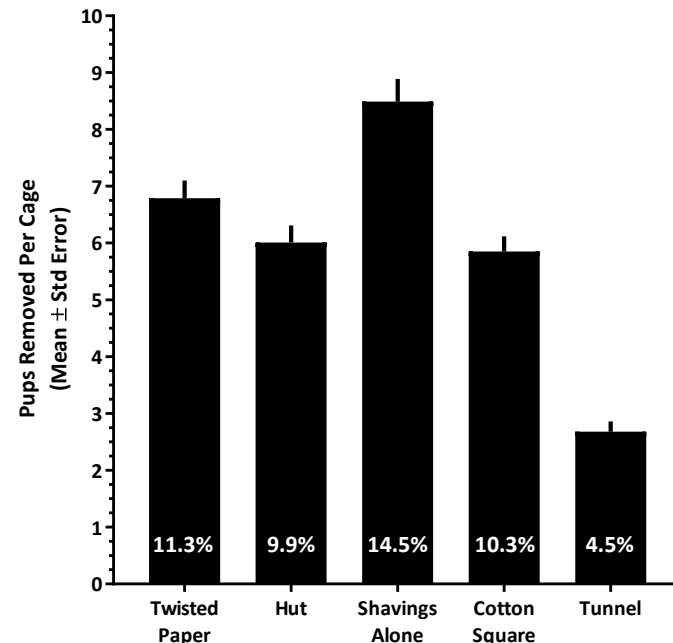
Statistical models: linear regressions (ANOVA)

Twisted paper reduced the number of pup mortalities



Each pairwise difference was significant for twisted paper ($P < 0.0001$)

Tunnels had the fewest pups euthanized for abnormalities



Each pairwise difference was significant for tunnel ($P < 0.0001$)

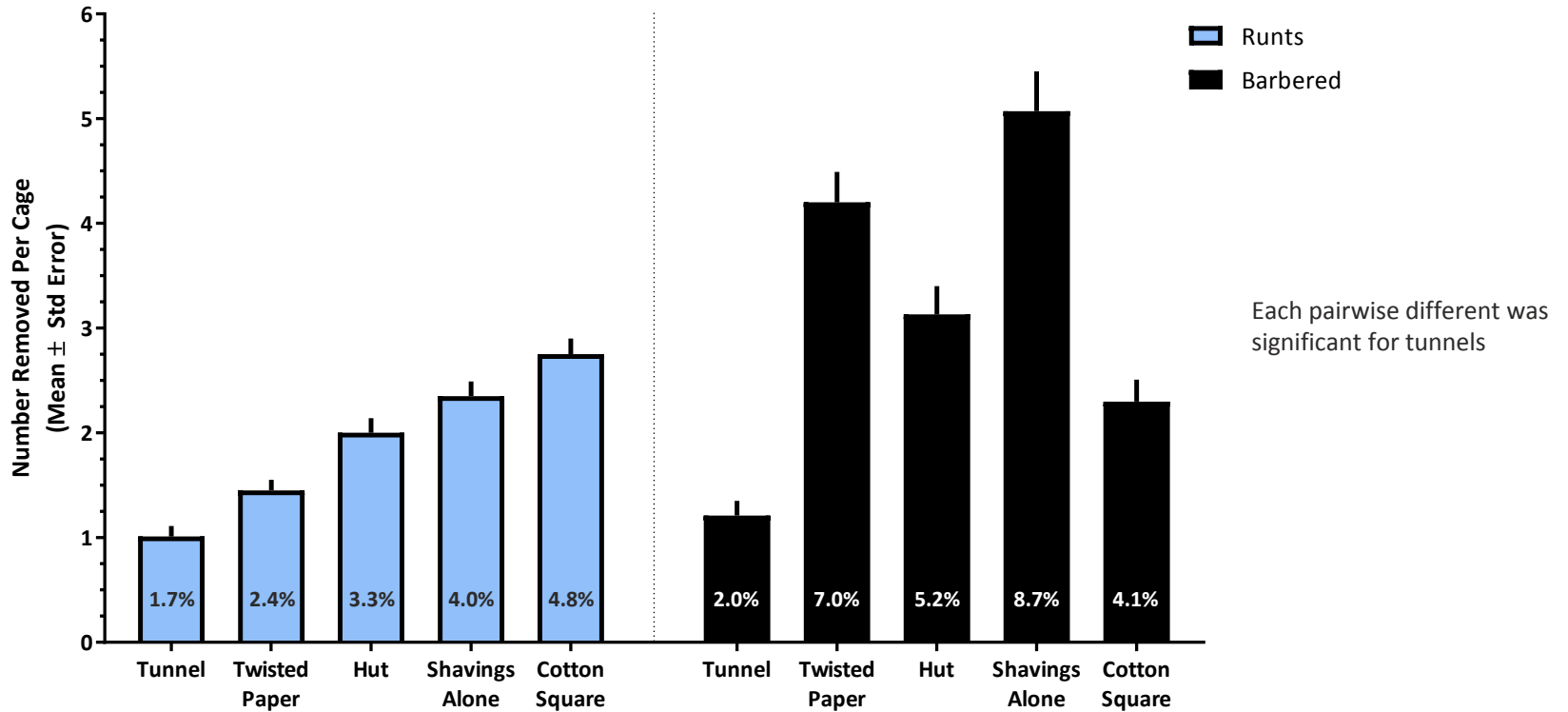


% indicates the portion of number born

Statistical models: zero-inflated negative binomial regressions

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Tunnel cages had fewest runts and barbered pups



% indicates the portion of number born

Statistical models: zero-inflated negative binomial regressions

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The tunnel group had the fewest wet cages

Enrichment	Wet Cages / Total Cages (%)
Tunnel	5/598 (0.8%) ^{abc}
Hut	16/598 (2.7%)
Shavings Only	21/600 (3.5%) ^a
Cotton Square	24/603 (4.0%) ^b
Twisted Paper	32/602 (5.3%) ^c

^a $P = 0.0295$, ^b $P = 0.0113$, ^c $P = 0.0009$



Statistical model: binomial (logistic regression)

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Breeder Enrichment discussion

- Environmental enrichment improved wellbeing and productivity in a C57BL/6J breeding colony
- Enrichment trials and comparisons help to determine the best type for each strain
- Combinations of cage enrichments should reveal additional benefits



Solving Strain-Specific Challenges Using Enrichment

C57BL/6J

- Most widely used inbred strain
- Prone to eye defects, hair loss, hydrocephalus, dermatitis



SJL/J

- Used to make F1s, multiple sclerosis models
- Aggressive



Barbering in C57BL/6J

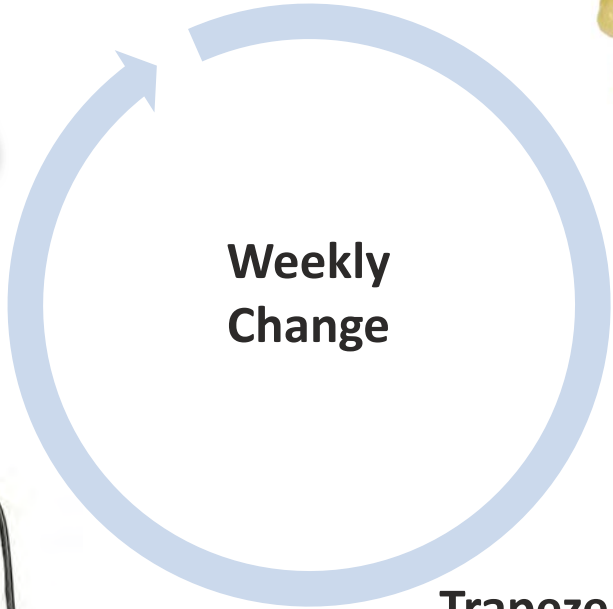
- Female bias
- Often involves whisker-picking, hair loss (alopecia)
- Increases with age, cage density
- Proposed explanations include social dominance, stress responses, obsessive-compulsive disorder



Rotational Enrichment



**Cardboard
Tube & Shack**



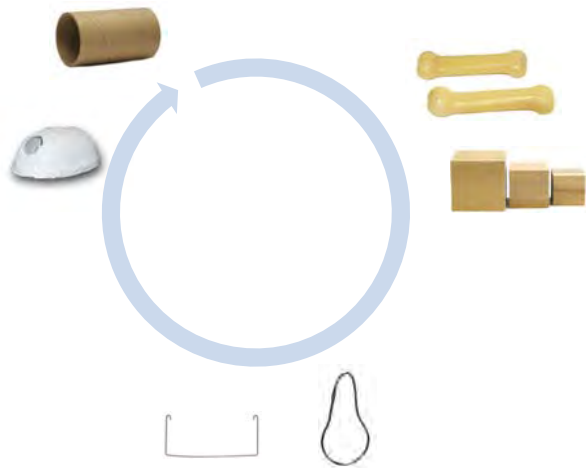
**Gumabone, Nylabone
& Gnawing Block**



**Trapeze & shower
curtain rings**



Rotational Enrichment Study in B6



Two sets of 120 female C57BL/6J mice were assigned at weaning to enrichment groups:

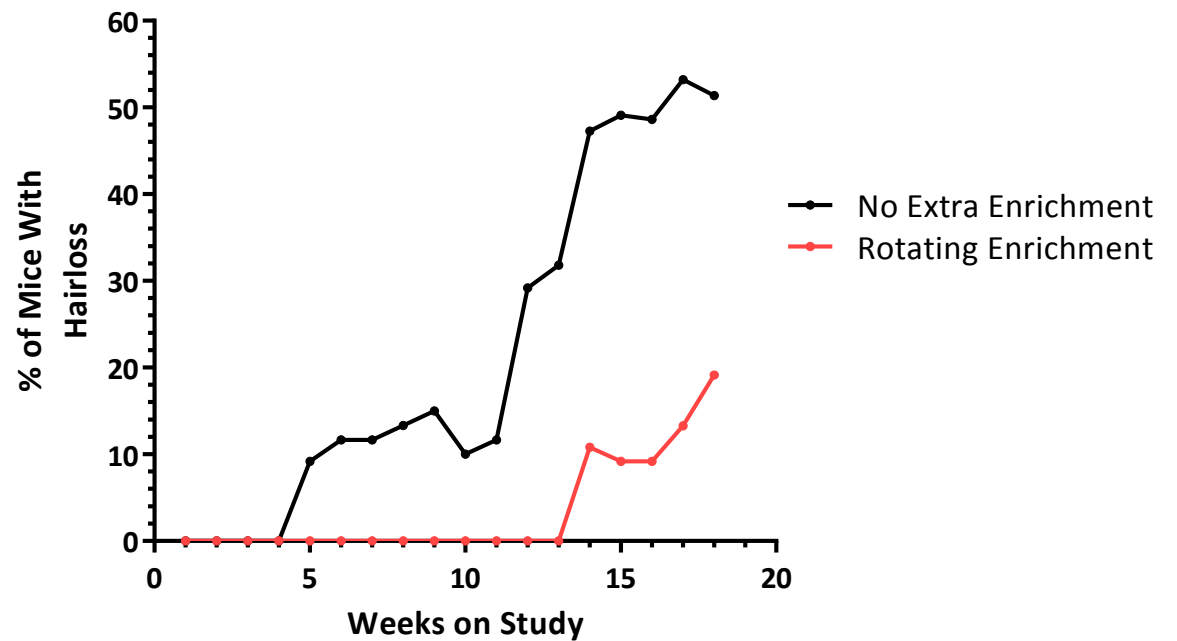
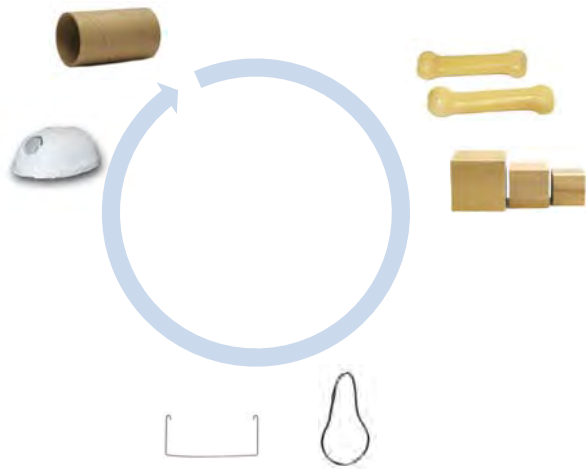
- Rotating enrichment
- No extra enrichment

Typical husbandry practices were followed

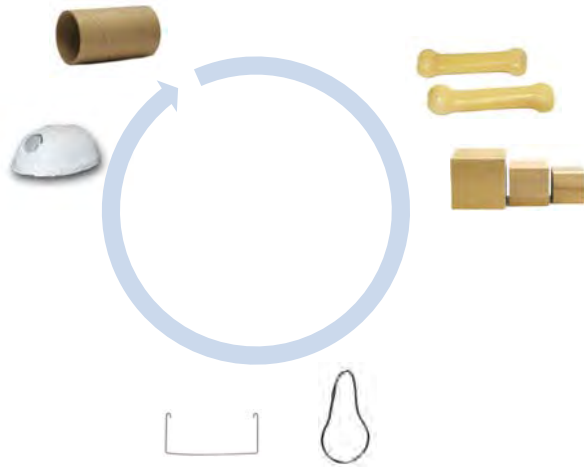
Mice were monitored weekly for hairloss or any other adverse conditions for 18 weeks



Rotational Enrichment Delays & Reduces Hairloss in B6 Females



Rotational Enrichment Delays & Reduces Hairloss in B6 Females



Pros

- Novelty & diversity
- Effective at reducing hairloss

Cons

- Cost
- Operational challenges



Comparing Enrichment: Shelter vs Activity

3 groups were created, each with 1080 female mice:

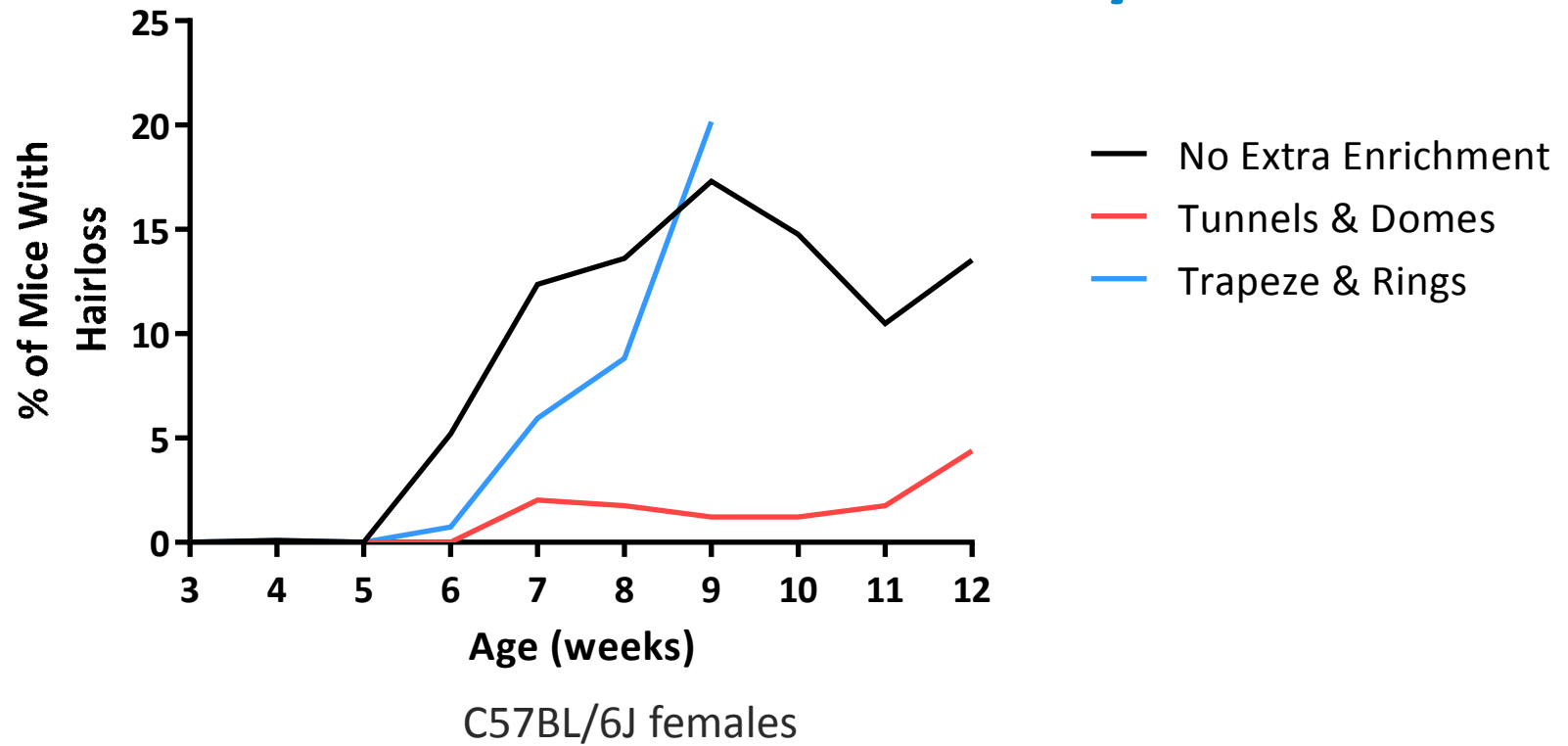
- No extra enrichment
- Cardboard tunnel and dome
- Trapeze and rings

Typical husbandry practices were followed

Mice were monitored between the ages of 3 & 12 weeks for hairloss and other adverse signs



Comparing Shelter & Activity Enrichment in C57BL/6J



Can Different Nesting Materials Reduce Aggressive Tendencies in SJL/J?

- Male bias
- Can affect pups, mates, same-sex cagemates
- Increases with age, cage density



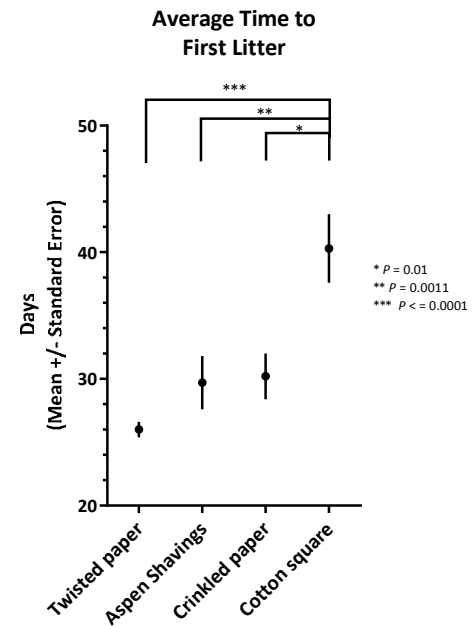
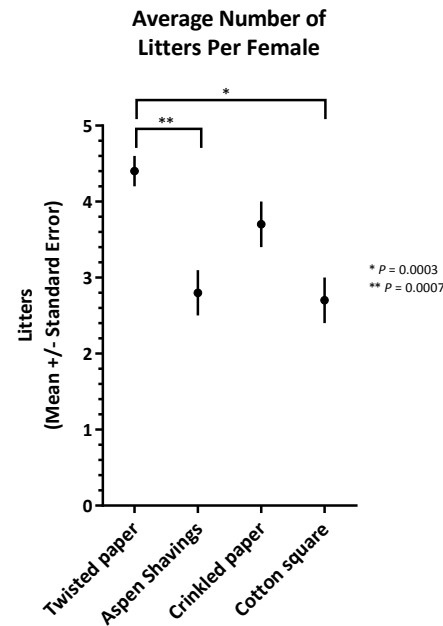
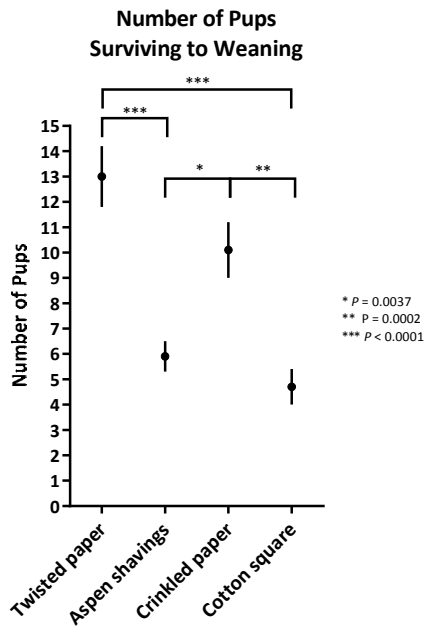
Can Different Nesting Materials Reduce Aggressive Tendencies in SJL/J?

- Supplement aspen chip bedding with one of four different nesting materials
 - Twisted paper
 - Aspen Shavings
 - Crinkled paper
 - Cotton square
- Productivity, welfare parameters measured throughout a standard breeding period (22 weeks)
- Standard husbandry practices were followed



Impacts of Nesting Material on SJL/J

- Productivity advantages for twisted paper, crinkled paper



Impacts of Nesting Material on SJL/J

- Many factors did not depend on nesting material
 - Born/Wean Ratio
 - Weight of pups at weaning
 - Female breeder mortality
 - Male breeder mortality
 - Pups removed for defects (bite wounds, runts, etc.)
 - Pup mortality



Solving Strain-Specific Challenges Using Enrichment

C57BL/6J

- Hair loss lessened when females were provided extra enrichment
- Shelter enrichment offered similar benefits as rotating enrichment



SJL/J

- Twisted paper greatly improved productivity
- No obvious effect on pup survival



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Group-Housed Animals

Common reasons for post-wean loss:

- Barbering
 - Hair Loss
 - Whisker Picking
- Aggression
- Eye defects
- Malocclusion



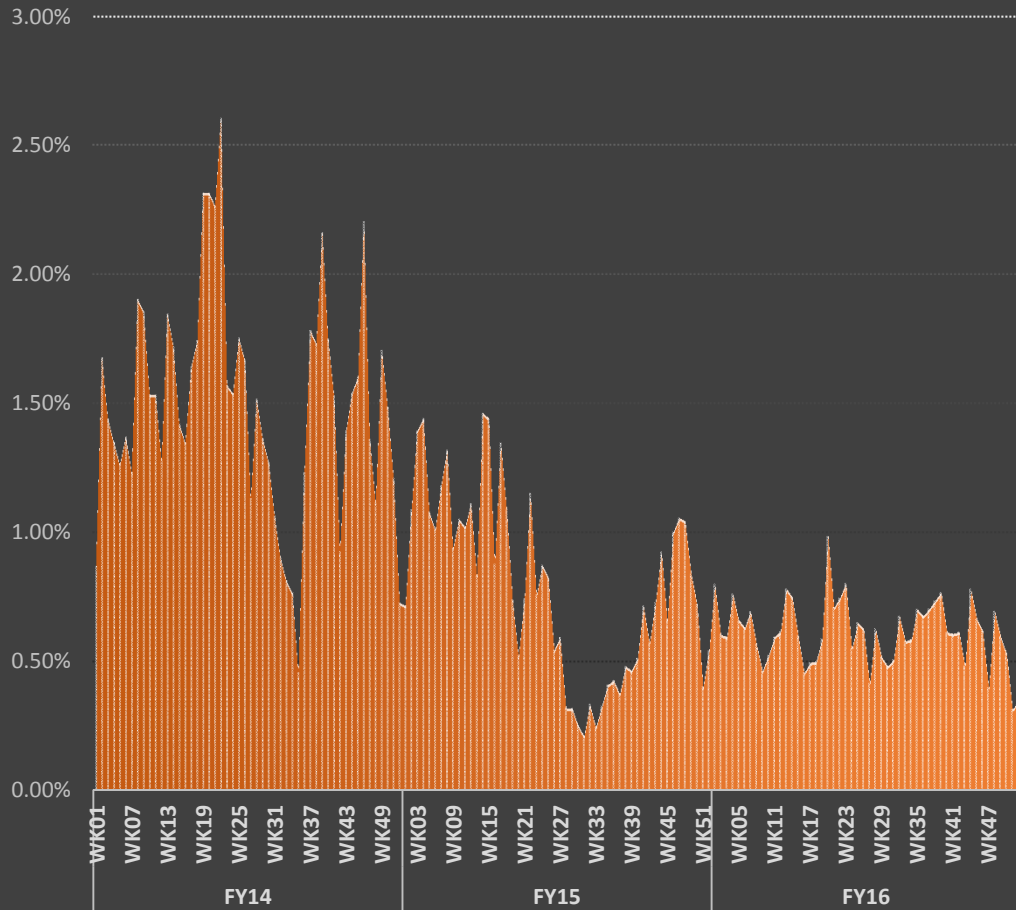


Tunnels & Huts reduced C57BL/6J female post-wean losses

- 50% decrease in loss



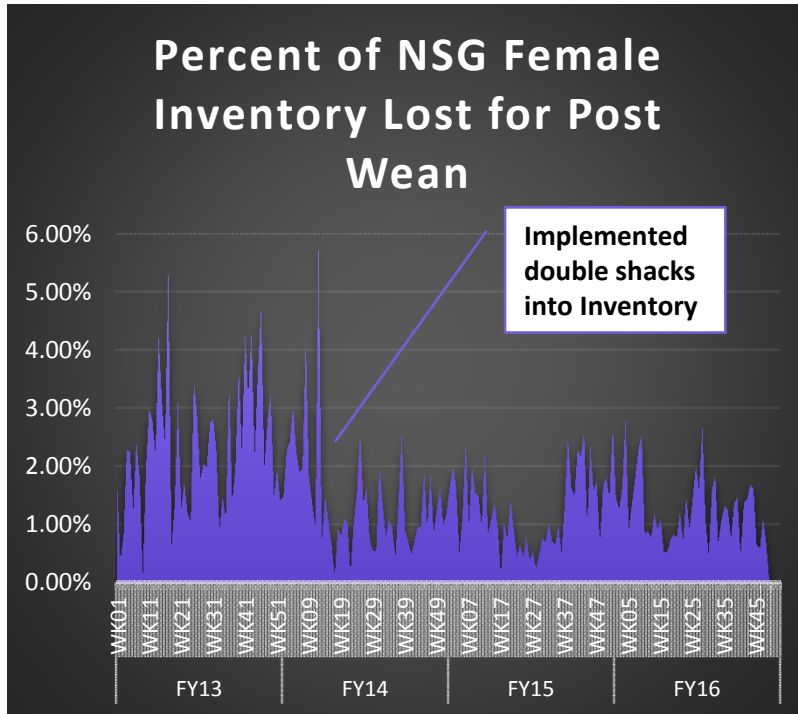
% of Male Inventory Lost to Hair Loss, Barbering, and Whisker Picking



Tunnels reduced C57BL/6J male post-wean losses

○ 50% decrease in loss

Enrichment in Immunodeficient NSG Mice



Huts reduced NSG female post-wean losses in inventory

NOD.Cg-Prkdc^{scid} Il2rg^{tm1Wjl}/SzJ



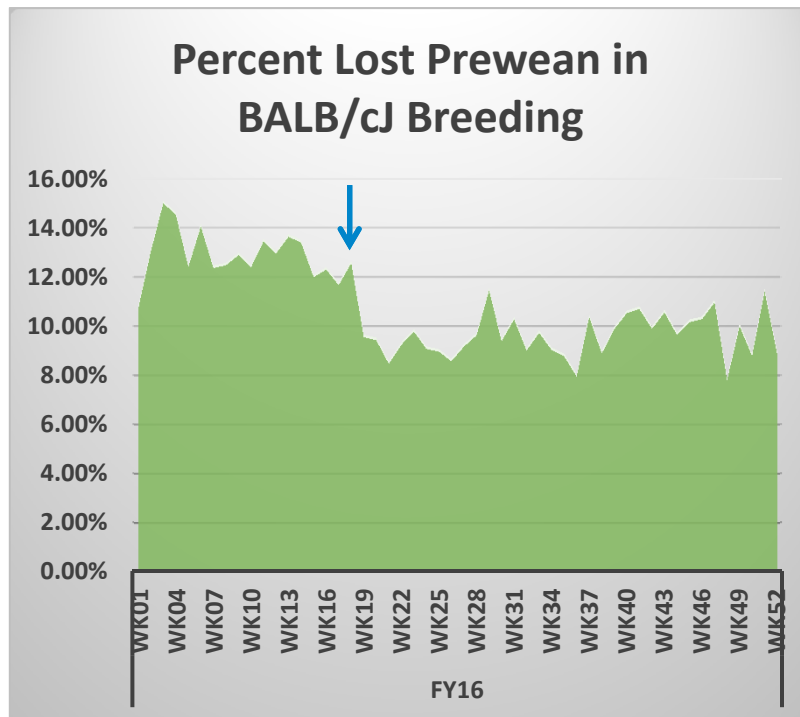
Losses in Breeding Colonies

Common reasons for pre-wean loss in breeding cages:

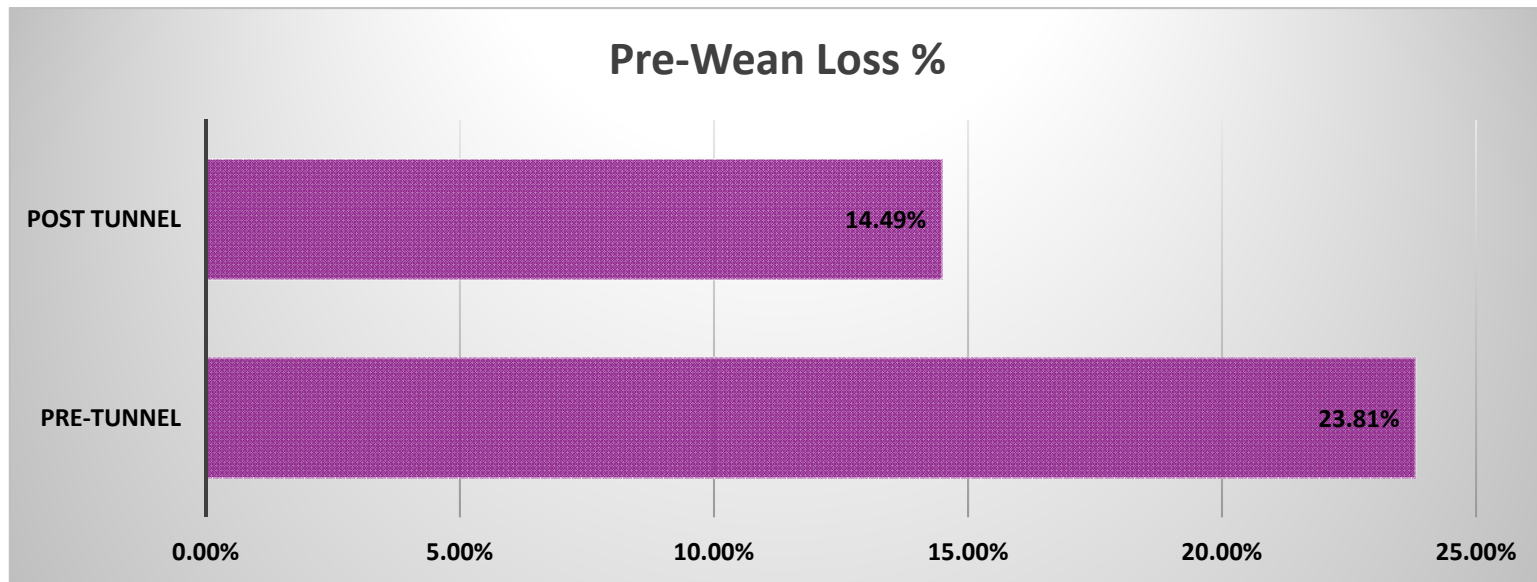
- Runts
- Missing Mice
- Barbering
 - Hair Loss
 - Whisker Picking



Huts Improved BALB/cJ Pup Survival



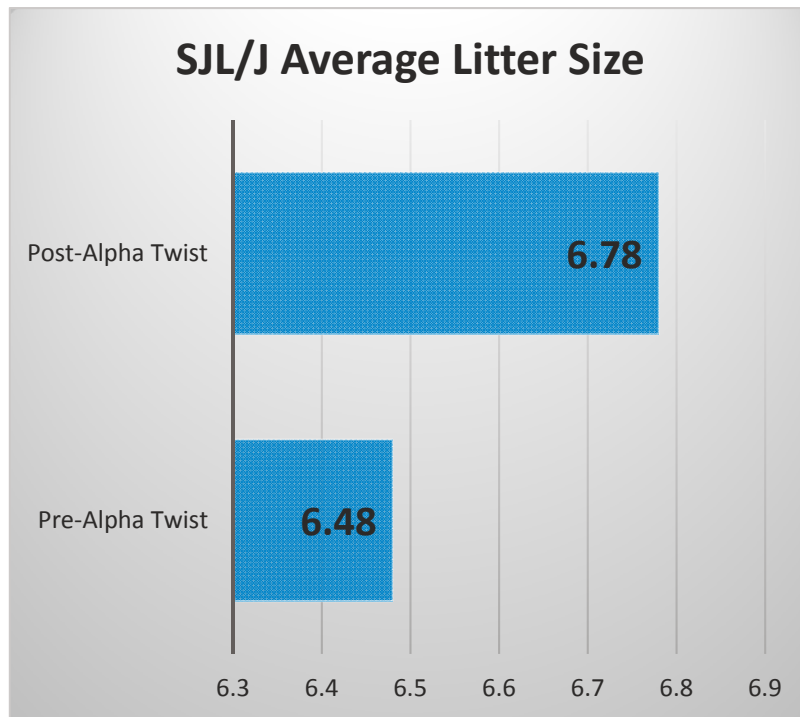
Tunnels Improved C57BLKS/J Pup Survival



Bio Tunnel enrichment supplied to breeders



Twisted Paper Enrichment Improves SJL/J Breeding

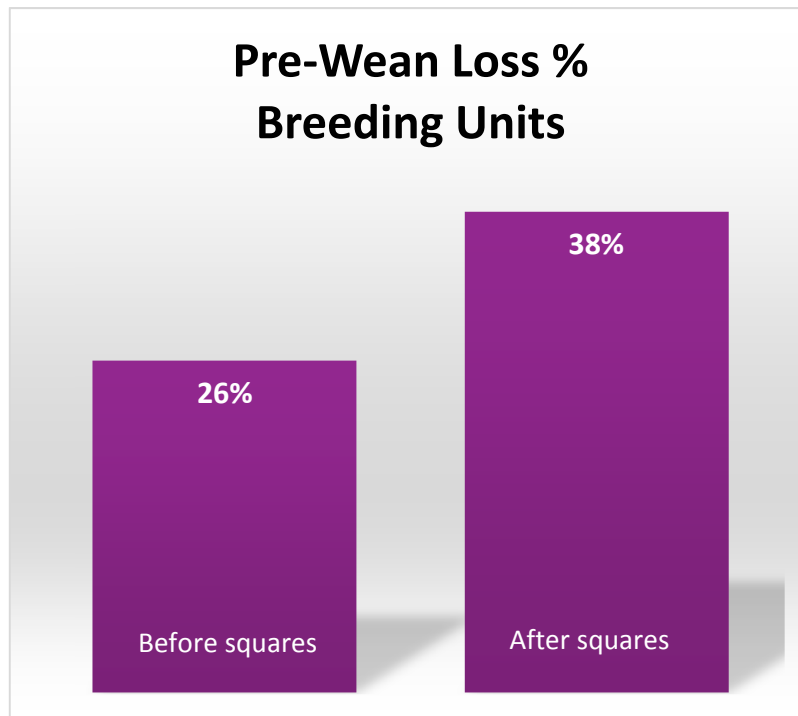


Twisted paper demonstrated a positive impact on the breeding performance for SJL/J Breeding Colonies.

Gains in productivity for both average litter size and wean output.



Cotton Squares Did Not Increase Pup Survival in B6.129S7-Ldlr^{tm1Her}/J

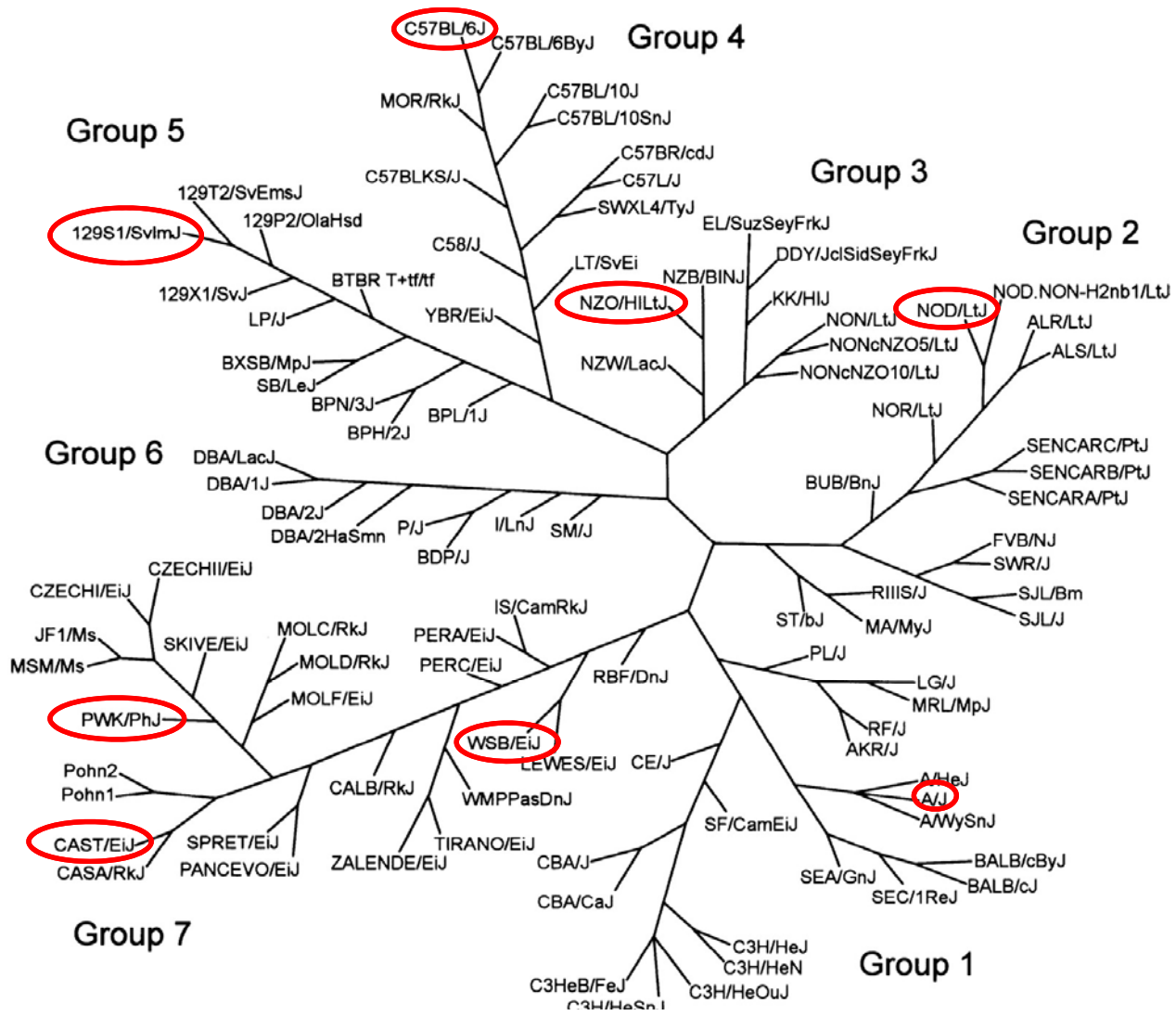


- A 12 week trial of cotton squares showed no improvement to breeding or prewean loss.
- Struggling with runty mice, missing mice, as well as hair loss in pups.



J:DO, A Highly Diverse Population of Mice





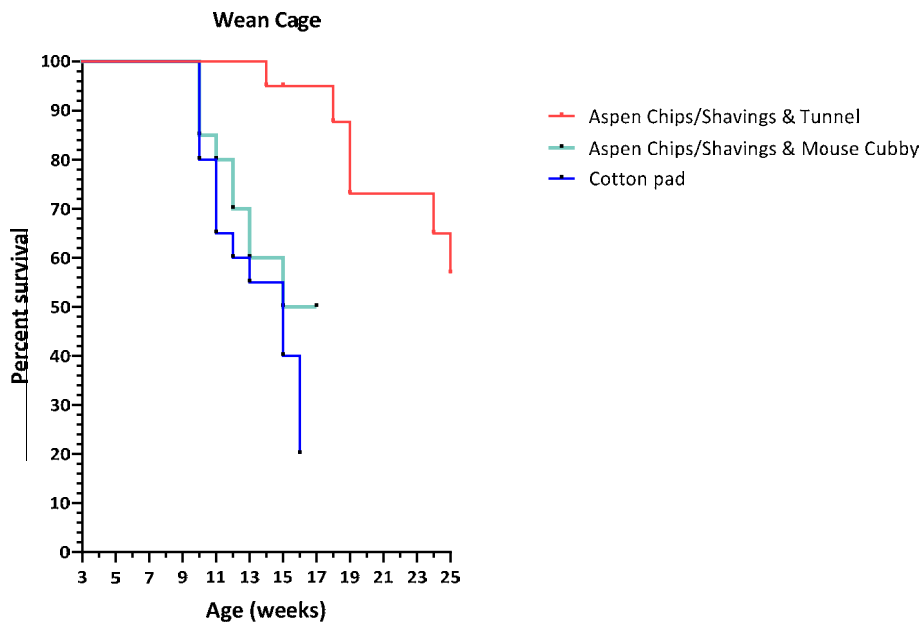
Study Design

To identify conditions leading to reduced aggression, J:DO males were assigned to one of 5 groups at 3 weeks of age:

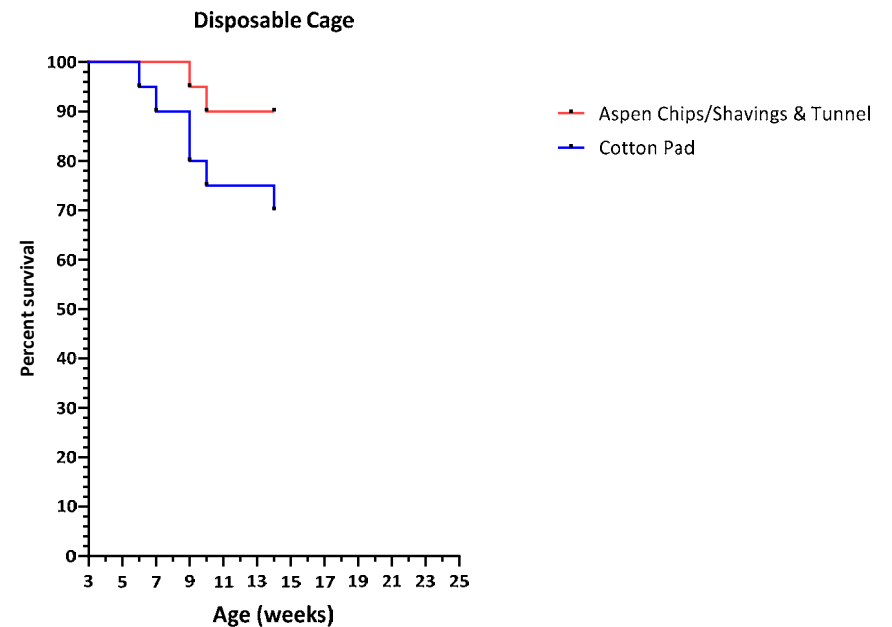
GROUP	CAGE	BEDDING/ENRICHMENT	MICE/CAGE	NUMBER OF CAGES
A	Disposable	Aspen chips/shavings, tunnel	4	5
B	Disposable	Cotton pad	4	5
C	Wean box	Aspen chips/shavings, tunnel	4	5
D	Wean box	Cotton pad	4	5
E	Wean box	Aspen chips/shavings, cardboard divider	4	5



Aspen Chips/Shavings & Tunnel Group Survived Longest

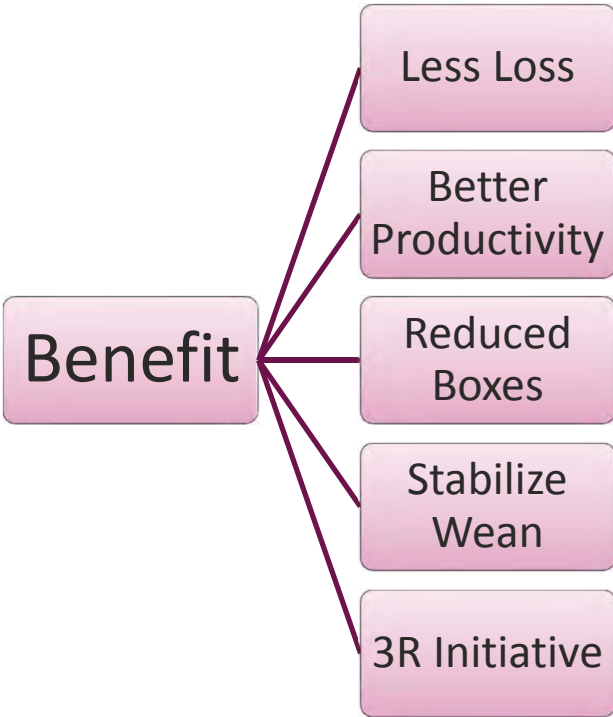
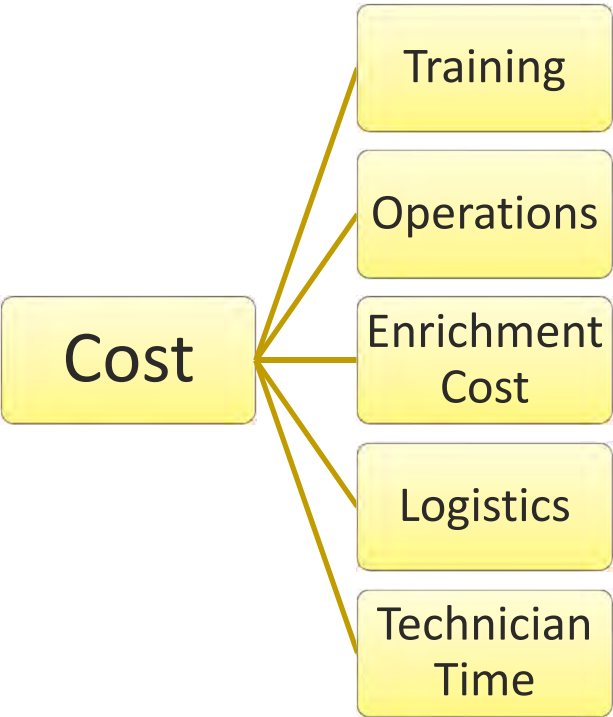


Aspen Chips/Shavings & Tunnel Losses:
 - 5 for bite wounds, 1 for barbering



Study discontinued at 14 weeks of age
 (chewing on disposable cages)

Cost Versus Benefit



Enrichment Discussion

- Environmental enrichment can improve mouse welfare and breeding productivity
- Benefits depend on the strain
- Enrichment trials and comparisons help to determine the best type for each strain

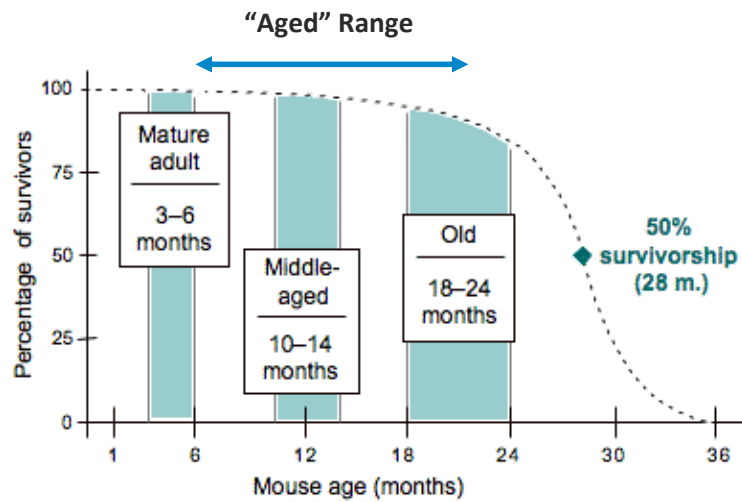


Aged C57BL/6J Mice

- Most studied inbred mouse strain
- Reference genome for mice
- Prone to eye defects, hair loss, malocclusion, dermatitis
- Males and females are offered up to 90 weeks (~22 months) of age



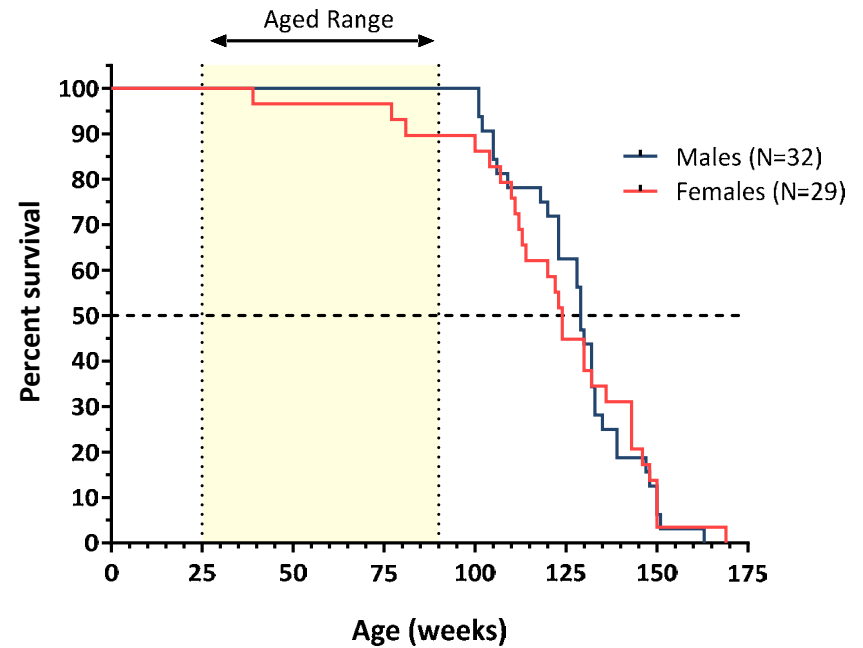
Human – Mouse Life Stage Equivalencies



Adapted from Figure 20-3: Flurkey, Curren, and Harrison, 2007. 'The mouse in biomedical research.' in James G. Fox (ed.), American College of Laboratory Animal Medicine series (Elsevier, AP: Amsterdam; Boston)



Survival of C57BL/6J



Data from the Nathan Shock Aging Center at The Jackson Laboratory (Yuan2 data set in the Mouse Phenome Database; phenome.jax.org)

Defining Tolerated Conditions for Aged B6 Colonies

Tolerated

- Weight variation
- Coat color changes
- Hair loss



Not Tolerated

- Dermatitis
- Bite wounds
- Malocclusion
- Hernias
- Other adverse clinical conditions



Husbandry & Housing Conditions

Diet: LabDiet 5K52 formulation (6% fat by weight)

Water: Filtered, acidified & autoclaved water in bottles

Change frequency: Weekly (ventilated) or 2X weekly (conventional)

Bedding: Aspen chips & aspen shavings

Extra enrichment: Cardboard shelters



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General Observations

Few mice are lost on a typical week

Age Range	Females	Males
6 mo – 1 yr	0.18%	0.16%
1 – 1.5 yrs	0.71%	0.14%
1.5 yrs +	TBD	1.0%

Common reasons for losses

Females

Aged 6 Mo – 1 Yr
Dermatitis (53%)
Bite Wounds (20%)

Aged 1 – 1.5 Yrs
Dermatitis (52%)
Mortality (16%)

Males

Aged 6 Mo – 1 Yr
Mortality (28%)
Dermatitis (18%)

Aged 1 – 1.5 Yrs
Mortality (44%)
Bite Wounds (14%)

Aged >1.5 Yr
Mortality (57%)
Dermatitis (12%)

number indicates % of losses due to the indicated reason



Jan 2017 – Aug 2019 data

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Additional Information

- Aged B6 Strain Data Sheet (jax.org/aged-b6)
- Mouse Phenome Database (phenome.jax.org)



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The End



Thank you!

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