Policy 7 – Experimental Allergic Encephalomyelitis (EAE) in Mice

Version 2.0
Approval Date: 1/22/07, 3/5/13

Purpose - The purpose of this policy is to describe the specialized care of EAE animals, in order to ensure their humane care and treatment.

Background - Experimental allergic encephalomyelitis (EAE) is an animal model for central nervous system autoimmune disease; it is widely used as a human Multiple Sclerosis (MS) model. Although clinical signs vary according to species and strain, they typically include visual, sensory, and motor deficits. This generally manifests as an ascending paralysis graded on a five-point scale ranging from the loss of tail tone in an otherwise normal animal (1) to one in a moribund condition (5). The course may vary from one or more episodes with short periods of remission of clinical signs, to a progressive, chronic state.

Policy -

Care of EAE mice:

1. Every animal to be injected with any substance to elicit EAE should be identified with a cage card with the letters “EAE”.
2. At the time of inoculation, post-procedural cage card (blue card) specifying “EAE mice” and date of inoculation should be placed in every applicable cage.
3. Once animals develop clinical signs, animals should be monitored at least daily, including weekends and holidays.
4. Food should be placed on the floor of the cage and a water bottle with a long sipper tube should be used. An alternative source of water should be provided (i.e. Napa nectar).
5. Monitoring will include the graded score of EAE development (see Table 1), hydration status, body condition score, general condition, and activity level of the animal(s). All observations and treatments must be recorded on the blue post-procedural cage card, dated and initialized.
6. All paralyzed mice should be monitored for skin irritation associated with urine scalding and, if male, observed for penile irritation secondary to flaccid paralysis.
7. Paralyzed animals should be removed from the cage if healthy mice compromise their health. Healthy animals may walk on paralyzed animals, causing discomfort and/or injuries, and may eat food intended for paralyzed animals.

Humane endpoints (euthanasia indicated):

- EAE grade 4 and 5 (see EAE clinical signs and interventions table for exceptions)
- BCS ≤1.5 or body weight loss ≥20%
- Veterinarian recommendation
<table>
<thead>
<tr>
<th>Onset</th>
<th>Clinical sign(s)</th>
<th>Intervention action</th>
</tr>
</thead>
</table>
| N/A                   | Normal                                                                          | 1. Baseline weight  
2. Write "EAE" on record cage card  
3. Write immunization date |
| early                 | Tail tone: Decreased tail tone                                                  | 1. Start record keeping (activity,  
EAE stage#)  
2. Monitor daily |
| early                 | Hind limb Paresis: Weakness in hind limbs, Animals have difficulty to move, appear ataxic or "clumsy" | 1. Monitor BW 1X a week and record  
2. Use long sipper tubes, soft food  
Or gel diets  
3. Provide moistened food pellets on cage floor |
| middle                | Hind limb paralysis: Inability to move one or both hind limbs  
Urinary Incontinence: Urine is leaking, urine scald around prepuce or vulva  
Dehydration: Decreased skin turgor  
Oral/Lingual paralysis: Inability to swallow | 1. Follow stage 2  
2. Palpate bladder 3X/week  
3. Monitor for skin lesions, urine scald, penile prolapse  
4. Use SC fluid for dehydration  
5. Use softer bedding materials (alpha dry)  
6. Provide food via oral gavage if animal unable to swallow |
| Late to end stage     | Weakness of fore limbs with paraparesis or quadriplegia  
Atonic bladder: Enlarged, unable to urinate  
Dehydration: Decreased skin turgor  
Oral/Lingual paralysis: Inability to swallow | 1. Follow stage 3  
2. For atonic bladder, express bladder at least 2X/day. |
| Late End stage        | Quadriplegia: Paralysis of all four limbs  
Atonic bladder: Enlarged, unable to urinate  
Dehydration: Decreased skin turgor  
Oral/Lingual paralysis: Inability to swallow  
Dyspnea: Difficulty or abnormal breathing  
Moribund: Animal is not moving, recumbent | 1. Follow stage 4  
2. Animals must be euthanized unless exempted by the IACUC  
3. All moribund, body weight loss≤20%, dyspenic animals must be euthanized |
Table 1- Clinical grading of EAE mice

<table>
<thead>
<tr>
<th>EAE GRADE</th>
<th>CLINICAL SIGNS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal mouse; no overt signs of disease</td>
</tr>
<tr>
<td>1</td>
<td>Decreased tail tone or weak tail only</td>
</tr>
<tr>
<td>2</td>
<td>Hind limb weakness (paraparesis)</td>
</tr>
<tr>
<td>3</td>
<td>Hind limb paralysis (paraplegia) and/or urinary incontinence</td>
</tr>
<tr>
<td>4</td>
<td>Weakness of fore limbs with paraparesis or paraplegia (quadriparesis) and/or atonic bladder</td>
</tr>
<tr>
<td>5</td>
<td>Paralysis of all limbs (quadriplegia), moribund state; death by EAE</td>
</tr>
</tbody>
</table>

Any exceptions to this policy must have IACUC approval

References -

