

during the birth process. Vaccines or antibiotics given to mothers before delivery may be an effective treatment. The difference in outcome of animals given vaccines or antibiotics and those not treated is the focus of these studies.

3. Guinea pigs exposed to bacteria infection - 39 guinea pigs

Description of Procedures:

This protocol uses an otitis model in guinea pigs. Otitis externa is induced bilaterally in anesthetized guinea pigs by inoculation of both ears with suspensions of one of three microorganisms. Studies are conducted by singular infections using 1) *Staphylococcus aureus*; 2) *Pseudomonas aeruginosa*; and 3) *Malassezia pachydermatis*. The guinea pigs are examined daily. During establishment of the model, the animals are re-anesthetized and the ears examined on days 3, 7, 9, 13, 17 and 22. All ears are cultured, and examined and graded for 1) inflammation; 2) edema; and 3) debris accumulation. Experiments are concluded at 22 days after initiation of infection. All animals are then euthanized by an overdose of anesthetic.

Explanation of Reasons Why Pain- or Distress- Reliving Drugs Were Not Used:

The animals in this model, as reported, show mild lethargy and irritability at the height (6-7 days after inoculation) but this is a transient behavior which resolves as the otitis external resolves. Inflammation is one measured data point; therefore masking it with analgesics or anti-inflammatory agents is contraindicated.

4. Decapitation without prior anesthesia in guinea pigs – 53 guinea pigs

Description of Procedures:

Bradykinin affects many different tissues in the body. For effective drug development, new antagonists must be tested in a standard "classic" assay system. In this protocol, guinea pigs are euthanized by decapitation without prior anesthesia. Segments of the terminal ileum are then removed and hung in a tissue bath. Tissue responses are standardized with bradykinin, and then new potential antagonists are applied to the tissue to see if they block the action of the next standard ED₅₀ dose of bradykinin applied to the tissue.

Explanation of Reasons Why Pain- or Distress- Reliving Drugs Were Not Used:

Bradykinin is a peptide hormone involved in causing many serious kinds of inflammation, such as septic shock. The Investigators are developing new, more potent bradykinin antagonists as potential new drugs for these conditions. Isolated guinea pig ileum is the classical standard assay system for bradykinin. In order to compare results

with new compounds, they must first be tested in this system. No one has described a more humane procedure that doesn't require anesthesia. Anesthesia adversely affects the response of the tissue. This has been demonstrated in the Investigators' laboratory, as well as in other laboratories. Additionally, the Investigator has tried using carbon dioxide anesthesia and found that the stress caused by this process causes bradykinin to be released in the tissues, such that an adequate baseline cannot be obtained.

5. Maternal-Infant separation in non-human primates - 6 mothers and 6 infants (2 *M. nemistrima* + 2 infant, 4 *M. radiata* + 4 infants) (Total = 12 primates)

Description of Procedures:

When infants are 6 months old, mothers are removed from the social group for one separation period that lasts two weeks. During this time the infant is immunized with tetanus toxoid and blood is sampled biweekly. The infant remains with its social group during separation.

Explanation of Reasons Why Pain- or Distress- Reliving Drugs Were Not Used:

It is the effect of maternal-infant separation, which is being studied, so any psychoactive intervention to relieve the behavioral impact would negate the results of the study.

6. Parkinsonian Syndrome in non-human primates - 3 monkeys (*M. radiata*)

Description of Procedures:

The Parkinsonian syndrome is induced when MPTP-HCL is infused into the carotid artery to produce a stable unilateral lesion in the monkey. A dose of 0.8 mg/kg MPTP-HCL dissolved in 50 cc of sterile normal saline infused into the carotid artery over 20 minutes leads to unilateral dilation of the pupil and a weak arm and leg contralateral to the side of the lesion and sensory neglect on that side. The animals are infused at a rate of 2 ml/minute using a 30 gauge needle with the infusion in the direction opposite the normal arterial blood flow. Analgesics are given to all animals for any post-operative pain. The result of the surgical procedure is a weak arm and leg and sensory neglect on the side opposite the lesion. (Water bottles are adjusted for this disability.) Thus, once monkeys have been lesioned, abilities such as locomotion, visual fields, grasping, climbing, etc. are impaired. In addition, the lesioned animals are sensitive to sound and have an enhanced startle response. After the lesioning procedure has produced the hemiparkinsonian effect, each animal is assessed daily for any pain. L-dopa is given as needed to assist the animal in daily routine procedures. In addition, monkey's food intake is carefully assessed and animals are hand fed if necessary until they have learned to adapt to their limitations. Daily fruit, sunflower seed, pomegranate seeds, peanuts, etc., are

