References on the Administration of Epinephrine Using ALZET® Osmotic Pumps

Q8158: P. Alvarez, et al. Unpredictable stress delays recovery from exercise-induced muscle pain: contribution of the sympathoadrenal axis. Pain Rep 2019;4(5):e782

Agents: Epinephrine Vehicle: Saline; Route: SC; Species: Rat; Pump: 2004; Duration: 2 weeks;

ALZET Comments: Dose (5.4 mg/0.25 mL/h); Controls received mp w/ vehicle; animal info (adult male Sprague-Dawley rats, weighing 250 to 400 g (approximatet 8-12 weeks old)); antisense (intrathecal b2-adrenergic receptor antisense);

Q4766: Mohan R Dasu, et al. Crosstalk Between Adrenergic and Toll-Like Receptors in Human Mesenchymal Stem Cells and Keratinocytes: A Recipe for Impaired Wound Healing. STEM CELLS TRANSLATIONAL MEDICINE 2014;3):745 -759

Agents: epinephrine, macrophage-activating lipopeptide-2; ICI-118,551 Vehicle: Not Stated; Route: SC; Species: mice;
Pump: 1002; Duration: 7 days; 11 days;

ALZET Comments: animal info (Jax Mice, male, 8-10 weeks of age); peptides; macrophage-activating lipopeptide-2 aka MALP-2; Dose (7mg/kg body weight/day EPI; .7 mg/kg body weight/day ICI);

Q3234: M. H. Kim, et al. Catecholamine Stress Alters Neutrophil Trafficking and Impairs Wound Healing by beta(2)-Adrenergic Receptor-Mediated Upregulation of IL-6. Journal of Investigative Dermatology 2014;134(3):809-817

Agents: Epinephrine; antagonist, beta adrenergic receptor Vehicle: Saline; Route: SC; Species: Mice (transgenic); Pump: 1002; Duration: 8 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (female, EGFP-lys); functionality of mp verified by plasma levels; dose-response (pg. 810); immunology;

Q4819: M. R. DASU, et al. Crosstalk Between Adrenergic and Toll-Like Receptors in Human Mesenchymal Stem Cells and Keratinocytes: A Recipe for Impaired Wound Healing. STEM CELLS TRANSLATIONAL MEDICINE 2014;3):745 -759

Agents: Epinephrine; macrophage-activating lipopeptide-2; ICI-118,551 Vehicle: Not Stated; Route: SC; Species: mice;
Pump: 1002; Duration: 7 days; 11 days;

ALZET Comments: animal info (Jax Mice, male, 8-10 weeks of age); peptides; macrophage-activating lipopeptide-2 aka MALP-2; Dose (7mg/kg body weight/day EPI; .7 mg/kg body weight/day ICI);

Q1759: F. C. Beasley, et al. Staphylococcus aureus Transporters Hts, Sir, and Sst Capture Iron Liberated from Human Transferrin by Staphyloferrin A, Staphyloferrin B, and Catecholamine Stress Hormones, Respectively, and Contribute to Virulence. Infection and Immunity 2011;79(6):2345-2355

Agents: Epinephrine Vehicle: Saline, buffered; Route: SC; Species: Mice; Pump: 2001; Duration: 4 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (BALB/c)

Q0775: S. G. Khasar, et al. Sound Stress-Induced Long-Term Enhancement of Mechanical Hyperalgesia in Rats Is Maintained by Sympathoadrenal Catecholamines. JOURNAL OF PAIN 2009;10(10):1073-1077

Agents: Epinephrine Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2004; Duration: 14 days;

ALZET Comments: Animal info (adrenal medullectomy, adult, male, Sprague Dawley, 300-400 g); functionality of mp verified by plasma drug levels

P8857: C. von Montfort, et al. Contribution of the sympathetic hormone epinephrine to the sensitizing effect of ethanol on LPS-induced liver damage in mice. American Journal of Physiology Gastrointestinal and Liver Physiology 2008;294(5):G1227-G1234

Agents: Epinephrine Vehicle: Saline; Route: SC; Species: Mice; Pump: Not Stated; Duration: 5 days;

ALZET Comments: Half-life (p. G1227) "very short"; animal info (male, C57BL/6, 4-6 wks old); "Owing to the very short half-life of epinephrine, the hormone was infused instead of injected to maintain a low-grade elevated plasma level over a prolonged period which better mimics the effect of ethanol." pg. G1227

P8832: O. A. Dina, et al. Alcohol-induced stress in painful alcoholic neuropathy. European Journal of Neuroscience 2008;27(1):83-92
Agents: Epinephrine  Vehicle: Saline; Ascorbic acid;  Route: SC;  Species: Rat;  Pump: 2004;  Duration: 3 weeks;
ALZET Comments: Replacement therapy (adrenal medullectomy); animal info (male, Sprague Dawley, 250-450g.)

P9158: O. A. Dina, et al. Neurotoxic catecholamine metabolite in nociceptors contributes to painful peripheral neuropathy. European Journal of Neuroscience 2008;28(6):1180-1190

Agents: Epinephrine  Vehicle: Saline; Ascorbic acid;  Route: Not Stated;  Species: Rat;  Pump: Not Stated;  Duration: Not Stated;
ALZET Comments: Animal info (male, Sprague Dawley, 270-450 g.)

P7594: S. G. Khasar, et al. Repeated sound stress enhances inflammatory pain in the rat. Pain 2005;116(1-2):79-86

Agents: Epinephrine bitartrate  Vehicle: Saline; Ascorbic acid;  Route: SC;  Species: Rat;  Pump: Not Stated;  Duration: Not Stated;
ALZET Comments: Controls received no treatment; animal info (male, Sprague-Dawley 250-380 g); pain

P7253: S. G. Khasar, et al. Estrogen regulates adrenal medullary function producing sexual dimorphism in nociceptive threshold and beta2-adrenergic receptor-mediated hyperalgesia in the rat. European Journal of Neuroscience 2005;21(12):3379-3386

Agents: Epinephrine  Vehicle: Saline; Ascorbic acid;  Route: SC;  Species: Rat;  Pump: 1007D;  Duration: 7, 14 days;
ALZET Comments: Functionality of mp verified by plasma epinephrine levels; replacement therapy (adrenal medullectomy, adrenal gland denervation); dose-response (Fig 3)

P5984: Y. Kitano, et al. Epinephrine inhibits tracheal occlusion induced lung growth in fetal sheep. Fetal Diagnosis and Therapy 2003;18(5):333-337

Agents: Epinephrine  Vehicle: Saline; Ascorbic acid;  Route: SC;  Species: Sheep (fetus);  Pump: 2ML1;  Duration: 4 days;
ALZET Comments: Teratology

P5711: S. G. Khasar, et al. Vagal modulation of nociception is mediated by adrenomedullary epinephrine in the rat. European Journal of Neuroscience 2003;17(4):909-915

Agents: ICI-118,551; epinephrine  Vehicle: Saline; Ascorbic acid; ethanol;  Route: SC;  Species: Rat;  Pump: 1007D;  Duration: 3, 7, 14 days;
ALZET Comments: Controls received mp w/ vehicle; dose-response (p. 911); ICI-118, 55 dissolved in ethanol and saline and infused for 7 days via 1007D pumps; epinephrine dissolved in saline and ascorbic acid and delivered for 3, 7, or 14 days via 2004 pumps.

P5744: G. V. R. Born, et al. Factors influencing the uptake of atherogenic plasma proteins by artery walls. Biorheology 2003;40(1-3):13-22

Agents: Epinephrine; Angiotensin II  Vehicle: Not Stated;  Route: SC;  Species: Rat;  Pump: Not Stated;  Duration: 6 days;
ALZET Comments: Controls received mp w/ saline; plasma levels reported; cardiovascular; pump rate 0.5 ul hr (p.15)

R0161: G. V. Born, et al. Endothelial factors in the flux of atherogenic plasma proteins into artery walls. Clinical Hemorheology and Microcirculation 2002;26(2):107-116

Agents: Epinephrine; Angiotensin II  Vehicle: Saline;  Route: SC;  Species: Rat;  Pump: 1007D;  Duration: 6 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by epinephrine plasma levels; cardiovascular; peptides; various methods of inducing hypertension explored

P4994: S. K. Juhn, et al. Effect of stress-related hormones on inner ear fluid homeostasis and function. American Journal of Otology 1999;20(800-806

Agents: Epinephrine  Vehicle: Saline;  Route: SC;  Species: Chinchilla;  Pump: Not Stated;  Duration: 1,2,3, or 4 weeks;
ALZET Comments: controls received mp w/ vehicle;

P3714: E.-L. Sainio. The role of adrenal hormones in the activation of tryptophan 2,3-dioxygenase by nicotinic acid in rat liver. Meth. Find Exp. Clin. Pharmacol 1997;19(7):465-470

Agents: Epinephrine; Corticosterone  Vehicle: Ethanol; NaCl;  Route: SC;  Species: Rat;  Pump: 2ML1;  Duration: 6 days;
ALZET Comments: controls received mp w/vehicle; replacement therapy (adrenalectomy)

P3530: L. E. Cardona-Sanclemente, et al. Increase by adrenaline or angiotensin II of the accumulation of low density lipoprotein and fibrinogen by aortic walls in unrestrained conscious rats. British Journal of Pharmacology 1996;117(1089-1094
Agents: Epinephrine; Angiotensin II Vehicle: Ascorbic acid; Route: SC; IA (carotid); Species: Rat; Pump: 2ML4; 1007D; Duration: 6 days;
ALZET Comments: controls received saline infusion; functionality of mp verified by plasma levels; stability verified by analyzing residual solution

P3704: F. Brandao, et al. Homogeneous or heterogeneous distribution of systemically administered adrenaline: organ dependence. Naunyn-Schmiedeberg's Arch. Pharmacol 1996;353(579-583
Agents: Epinephrine Vehicle: Water, distilled; Route: IP; Species: Rat; Pump: Not Stated; Duration: 6 days;
ALZET Comments: comparison of short-term iv infusion vs. mp

P3221: L. T. Jablonskis, et al. Lack of influence of circulating adrenaline on blood pressure in normotensive and hypertensive rats. Blood 1994;3(112-119
Agents: Epinephrine bitartrate Vehicle: Saline; Ascorbic acid; Route: SC; Species: Rat; Pump: 2002; Duration: 5-6 weeks;
ALZET Comments: long-term study, pumps replaced every 2 weeks; mp implanted in flank region

P2640: S. C. Birnbaum, et al. Nicotine- or epinephrine-induced uteroplacental vasoconstriction and fetal growth in the rat. Toxicology 1994;94(69-80
Agents: Nicotine free base; Epinephrine acid tartrate Vehicle: Saline; Ascorbic acid; Water, distilled; Route: SC; Species: Rat (pregnant); Pump: 2ML1; Duration: no duration posted;
ALZET Comments: controls received mp w/ saline; toxicology; teratology

P2391: T. A. Deisher, et al. Protective effect of clentiazem against epinephrine-induced cardiac injury in rats. J. Pharmacol. Exp. Ther 1993;266(1):262-269
Agents: Epinephrine bitartrate; Clentiazem Vehicle: Saline; Ethanol; DMSO; Route: SC; Species: Rat; Pump: 2ML2; Duration: 2 weeks;
ALZET Comments: no comment posted

P2425: H. M. Sadeghi, et al. Chronic epinephrine treatment fails to alter prejunctional adrenoceptor modulation of sympathetic neurotransmission in the rat mesentery. J. Pharmacol. Exp. Ther 1992;261(3):924-930
Agents: Epinephrine Vehicle: Saline; Ascorbic acid; Route: SC; Species: Rat; Pump: Not Stated; Duration: 6 days;
ALZET Comments: no comment posted

P1979: R. Dehner, et al. Adrenaline in cardiovascular diseases - effect of B-adrenoceptor antagonists. Z. Kardiol 1990;79(3):79-88
Agents: Epinephrine Vehicle: Ascorbic acid; Route: Not Stated; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: English with German summary

P1486: S. G. Trend, et al. Resistance of the rat embryo to elevated maternal epinephrine concentrations. American Journal of Obstetrics & Gynecology 1989;160(498-501
Agents: Epinephrine Vehicle: Ascorbic acid; Saline; Water; Route: IV (jugular); Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: dose-response; functionality of mp verified by plasma levels; no stress

P1584: W. Terres, et al. Effects of chronic treatment with adrenaline or propranolol on platelet function and c-AMP levels in the rat. Cardiovascular Research 1989;23(112-116
Agents: Epinephrine Vehicle: Ascorbic acid; Saline; Route: SC; Species: Rat; Pump: 2002; Duration: 8 weeks;
ALZET Comments: long-term study, pump replaced every 14 days
P1176: D. D. Schwartz, et al. Enhanced endogenous neurotransmitter overflow in the isolated perfused rat kidney after chronic epinephrine administration: lack of a prejunctional beta adrenoceptor influence. J. Pharmacol. Exp. Ther 1988;244(1):11-18

**Agents:** Epinephrine **Vehicle:** Ascorbic acid; Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;

**ALZET Comments:** controls received mp w/ vehicle; propranolol used to examine influence of beta adrenoceptors and phentolamine for alpha adrenoceptors

P1554: N. M. Deighton, et al. The effects of chronic administration of adrenaline on the function and number of adrenoceptors in the rabbit. J. Cardiovasc. Pharmacol 1988;12(332-337)

**Agents:** Epinephrine **Vehicle:** Ascorbic acid; Water; **Route:** IV (femoral); **Species:** rabbit; **Pump:** 2002; **Duration:** 10 days;

**ALZET Comments:** dose-response; functionality of mp verified by plasma levels

P1412: B. F. Becker, et al. Blood platelet function after chronic treatment of rats and guinea pigs with nicotine. Klin. Wochenschr 1988;66(11):28-36

**Agents:** Nicotine base; Epinephrine bitartrate **Vehicle:** Ascorbic acid; Saline; **Route:** SC; **Species:** Guinea pig; Rat; **Pump:** 2002; **Duration:** 2, 8 weeks;

**ALZET Comments:** dose-response; functionality of mp verified by plasma levels; long-term study; pump replaced every 2 weeks

P0861: D. D. Schwartz, et al. Cardiovascular responsiveness to sympathetic activation after chronic epinephrine administration. J. Pharmacol. Exp. Ther 1986;238(1):148-154

**Agents:** Epinephrine bitartrate **Vehicle:** Ascorbic acid; Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 6 days;

**ALZET Comments:** controls received mp w/vehicle; hypertension

P0713: M. E. Upsher, et al. Beta-adrenergic receptors in rat myocardium during the development and reversal of hypertrophy and following chronic infusions of angiotensin II and epinephrine. Archives Internationales de Pharmacodynamie 1985;274(65-79)

**Agents:** Angiotensin II; Epinephrine **Vehicle:** Water; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 6 and 12 days;

**ALZET Comments:** mp primed in distilled water 24 hours prior to implant; peptides

P0651: G. Tsujimoto, et al. Desensitization of B-adrenergic receptor-mediated vascular smooth muscle relaxation. Mol. Pharmacol 1985;27(2):210-217

**Agents:** Epinephrine HCl, l- **Vehicle:** HCl; Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 1 week;

**ALZET Comments:** states in error that mp will deliver up to 10 days; mp primed 3 hr prior to implant; bioavailability of EPI determined by plasma level increase

P0607: W. B. Jeffries, et al. Withdrawal syndrome follows abrupt cessation of intracerebroventricular infusion of epinephrine in spontaneously hypertensive rats. Life Sci 1985;36(14):1331-1337

**Agents:** Epinephrine bitartrate **Vehicle:** Ascorbic acid; Saline; **Route:** CSF/CNS; **Species:** Rat; **Pump:** 2001; **Duration:** 5 days;

**ALZET Comments:** 2 day delay of mp Epi achieved by filling connecting tubing with vehicle; some tubing externalized to allow immediate cutoff of infusion; dose-response data; delayed delivery;

P0600: K. Kumano, et al. Adenylate cyclase activity in rat myocardium following chronic infusions of angiotensin II and epinephrine. J. Cardiovasc. Pharmacol 1984;6(5):756-761

**Agents:** Angiotensin II; Epinephrine, l- **Vehicle:** Ascorbic acid; HCl; Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; 2002; **Duration:** 6 or 13 days, or 4 weeks;

**ALZET Comments:** comparison of agents effects; 2002 mp replaced after 2 weeks; saline used as vehicle w/ AngII, HCl & ascorbic acid w/Epi; controls received vehicle; mp primed in saline before use; peptides