References on the Administration of Glucocorticoids Using ALZET® Osmotic Pumps

1. Corticosterone

   **Agents:** Corticosterone  **Vehicle:** Saline;  **Route:** SC;  **Species:** Mice;  **Pump:** 1003D;  **Duration:** 3 days;
   **ALZET Comments:** Dose (15 ug/hr); Controls received mp w/ vehicle; animal info (Male, C57BL/6); dependence;

   **Agents:** Chenodeoxycholic acid, progesterone, 11b-hydroxy-, corticosterone, deoxy-, corticosterone, 3α,5α-TH-, progesterone, 3α,5α-TH-11β-hydroxy  **Vehicle:** Not Stated;  **Route:** SC;  **Species:** Rat;  **Pump:** Not Stated;  **Duration:** Not Stated;
   **ALZET Comments:** steroidal derivatives of corticosterone; Review presents the role of gut microbial metabolism of endogenous adrenocorticosteroids as a contributing factor in the etiology of essential hypertension.

   **Agents:** Corticosterone  **Vehicle:** DMSO; Propylene glycol;  **Route:** Not Stated;  **Species:** Mice;  **Pump:** Not Stated;  **Duration:** Not Stated;
   **ALZET Comments:** Dose (100 ug/day); 50% DMSO, 50% Propylene glycol used; animal info (Female 3-4 month old 5αR1-KO and wild-type mice); replacement therapy (glucocorticoid);

   **Agents:** Corticosterone; 2-hydroxypropyl-B-cyclodextrin; TDZD-8TDZD-8,  **Vehicle:** Saline;  **Route:** CSF/CNS (hippocampus);  **Species:** Mice;  **Pump:** Not Stated;  **Duration:** 2 weeks;
   **ALZET Comments:** animal info (5 weeks); functionality of mp verified by ELISA; bilateral cannula; behavioral testing (Y-maze, novel object preference task); TDZD-8 is a non-ATP-competitive selective inhibitor of GSK3b; Dose (2 uM/day);

   **Agents:** Corticosterone; Cortisol  **Vehicle:** DMSO; Propylene glycol; PEG400;  **Route:** SC;  **Species:** Mice (knockout);  **Pump:** 2001;  **Duration:** 7 days;
   **ALZET Comments:** Dose (corticosterone (250 ug/day) and cortisol (250 ug/day); Controls received mp w/ vehicle; animal info Female nu/nu nude mice (6 –8 weeks); Vehicle solution DMSO and ethanol at 2:1 ratio; functionality of mp verified by plasma levels, pg 979; functionality of mp verified by plasma

Q5320: M. Benlloch, et al. Pterostilbene Decreases the Antioxidant Defenses of Aggressive Cancer Cells In Vivo: A Physiological Glucocorticoids- and Nrf2-Dependent Mechanism. Antioxidants & Redox Signaling 2016;24(17):974-90
   **Agents:** Pterostilbene, Corticosterone  **Vehicle:** DMSO, Ethanol; PEG400;  **Route:** IV (jugular);  **Species:** mice;  **Pump:** Not Stated;  **Duration:** 35 days;
   **ALZET Comments:** Controls received mp w/ vehicle; animal info Female nu/nu nude mice (6–8 weeks); Vehicle solution DMSO and ethanol at 2:1 ratio; functionality of mp verified by plasma levels, pg 979; functionality of mp verified by plasma
levels, pg 979; Pterostilbene is a natural dimethoxylated analog of resveratrol; Mice xenograft models; Dose (50 mg/ml Pter; 0.3 ug/hr corticosterone); Resultant plasma level (pg. 979);


**Agents**: Corticosterone  
**Vehicle**: PEG 400;  
**Route**: SC;  
**Species**: Bird (kittiwake);  
**Pump**: 2002;  
**Duration**: 8 days;

**ALZET Comments**: Controls received mp w/ vehicle; animal info (late incubation, 380g); functionality of mp verified by serum levels; Multiple pumps per animal (2);


**Agents**: Corticosterone; progesterone, hydroxy-

**Vehicle**: Not Stated;  
**Route**: SC;  
**Species**: Rat;  
**Pump**: Not Stated;  
**Duration**: Not Stated;

**ALZET Comments**: These infused steroids produce glucocorticoid induced mineralcorticoid receptor mediated Na+ retention


**Agents**: Corticosterone  
**Vehicle**: DMSO;  
**Route**: SC;  
**Species**: Rat;  
**Pump**: Not Stated;  
**Duration**: 14 days;

**ALZET Comments**: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 250-350g); functionality of mp verified by plasma levels; behavioral testing (lever pressing); dependence; Dose (15 mg/kg);


**Agents**: Dexamethasone sodium phosphate; corticosterone  
**Vehicle**: Saline;  
**Route**: SC;  
**Species**: Mice (pregnant);  
**Pump**: 1003D;  
**Duration**: 60 hours;

**ALZET Comments**: Controls received mp w/ saline; animal info (female, E12.5, C57Bl6J, 8-10 weeks old); teratology; cardiovascular;

**Q3696**: M. Wosiski-Kuhn, et al. Glucocorticoid receptor activation impairs hippocampal plasticity by suppressing BDNF expression in obese mice. Psychoneuroendocrinology 2014;42(165-177

**Agents**: Corticosterone  
**Vehicle**: Cyclodextrin, 2-hydroxypropyl-b-;  
**Route**: CSF/CNS (hippocampus);  
**Species**: Mice;  
**Pump**: Not Stated;  
**Duration**: 2 weeks;

**ALZET Comments**: Controls received mp w/ vehicle and aCSF; animal info (male, C57Bl6J or db/db, 5 weeks old); functionality of mp verified by hippocampal corticosterone levels; Multiple pumps per animal (2); behavioral testing (y-maze apparatus); tissue perfusion (bilateral hippocampi); immunology; Cannula placement verified via histology; used Plastics One bilateral cannula; bilateral infusion;

**Q3573**: A. D. Mueller, et al. The inhibitory effect of sleep deprivation on cell proliferation in the hippocampus of adult mice is eliminated by corticosterone clamp combined with interleukin-1 receptor 1 knockout. Brain, Behavior, and Immunity 2014;35(4):182-188

**Agents**: Corticosterone  
**Vehicle**: PEG 400; ethanol;  
**Route**: SC;  
**Species**: Mice;  
**Pump**: 1002;  
**Duration**: Not Stated;

**ALZET Comments**: Animal info (male, homozygous IL1RI null, 7-8 weeks old); 5% ethanol used; post op. care (buprenorphine 0.1 mg/kg, metacam 1 mg/kg SQ, ADX rats given saline in water bottles); replacement therapy (adrenalectomy); immunology; sleep deprivation study;

**Q4468**: D. J. Morris, et al. An alternative explanation of hypertension associated with 17alpha-hydroxylase deficiency syndrome. Steroids 2014;79(44-48

**Agents**: corticosterone; progesterone, hydroxy-  
**Vehicle**: Propylene glycol;  
**Route**: sc;  
**Species**: Rat;  
**Pump**: Not Stated;  
**Duration**: 14 days;

**ALZET Comments**: Controls received mp w/ vehicle; animal info: adrenally intact rats; functionality of mp verified by measuring systolic blood pressure pg 46; replacement therapy (the agents infused); Dose: 5 ug/hr of both agents
ALZET Bibliography

Agents: Corticosterone Vehicle: PEG 400; Route: SC; Species: Rat; Pump: 1003D; Duration: 3 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (Long-Evans, PND15); functionality of mp verified by plasma levels pg22; no stress "Animals recovered quickly..." (see pg.20); post op. care (antibiotic ointment on wound, buprenorphine (0.052 mg/kg, heating pad until responsive and then returned to dam); "The corticosterone pellet was designed to produce a low, constant release of hormone over a 21-day period, but plasma assays showed otherwise. There was a large supraphysiological increase in circulating corticosterone levels (to \( \sim 80 \text{ ug/dl} \)) for about three days after implantation and a return to normal levels by the time testing occurred...In the present study, we administered corticosterone using an alternative, more reliable method that yielded the low level (within a normal physiological range) and constant rate of delivery we had originally expected. Furthermore, since the \( \sim 3 \)-day period of elevation in the previous study was sufficient to produce lasting effects on behavior, we chose to use an osmotic mini-pump that was designed to deliver corticosterone at a low and constant rate over a 3-day period only." pg 20; pumps primed for 24 hours in sterile saline;

Agents: Corticosterone Vehicle: Water, deionized; Route: SC; Species: Rat (neonate); Pump: 1007D; Duration: 7 days;
ALZET Comments: Control animals received mp w/ vehicle; animal info (naive, Sprague Dawley, P7). no stress pg 595-596. "The entire surgery took less than 5 min and the rats recovered well. The dorsal placement of the micropump was chosen because it does not interfere with the feeding position of pups." pg 595. "...dams in the current studies tolerated the pups well after both surgeries and there were no instances of cannibalism or obvious abuse (e.g., bite marks)" pg 596; pumps removed after 1 week;

2. Cortisol

Agents: Cortisol; radio-isotopes Vehicle: DMSO; propylene glycol; 2H tracer; Route: SC; Species: Mice; Pump: 1003D; Duration: 2 days;
ALZET Comments: Dose (1.75 mg/day); Controls received mp w/ vehicle; animal info (Male, C57Bl6, 12 weeks old); stable-isotope labelled [9,11,12,12-2H]4-cortisol; dependence;

Agents: Corticosterone; Cortisol Vehicle: DMSO; Propylene glycol; Route: SC; Species: Mice (knockout); Pump: 2001; Duration: 7 days;
ALZET Comments: Dose (corticosterone (250 ug/day) and cortisol (250 ug/day); Controls received mp w/ vehicle; animal info (Male(ABCC1−/−) mice);

Agents: Cortisol; propranediol Vehicle: Hydrocortisone; Route: IP; Species: Fish; Pump: Not Stated; Duration: 27.3 days;
ALZET Comments: Controls received mp w/ 80% 1.2-propanediol; animal info (cod, 1.8kg, female); 2ML pump used

Agents: Cortisol; potassium canrenoate; mifepristone Vehicle: Saline; Route: SC; Species: Sheep (ewe); Pump: 2ML2; Duration: 10 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, singleton pregnancies); teratology; cardiovascular; impact of maternal stress during late gestation

Agents: Cortisol; PF915275; meloxicam; interferon, tau, recomb. ovine Vehicle: Ethanol; Route: Intrauterine (uterine horn); Species: Sheep (ewe); Pump: 2ML1; Duration: Not Stated;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, singleton pregnancies); teratology; cardiovascular; impact of maternal stress during late gestation

Agents: Cortisol Vehicle: Cyclodextrin, 2-hydroxypropyl-b-; Route: Not Stated; Species: Fish (Eel); Pump: 1003D; Duration: 8 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by plasma levels; 30% 2-hydroxypropyl-b-cyclodextrin used; “The infusion of cortisol into FW eels using osmotic mini-pumps led to a 2.8-fold increase in the level of plasma cortisol as measured 8-days after the onset of the experiment (Fig. 1)” pg 311; Dose (15 ug/hr);

Agents: Cortisol Vehicle: Cyclodextrin, beta; Route: IP; Species: Fish (eel); Pump: 1003D; Duration: 8 days;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by cortisol plasma levels; pumps implanted IP per contact with author; 30% cyclodextrin used

Agents: Cortisol Vehicle: Cyclodextrin, beta; Route: IP; Species: Fish (eel); Pump: 1003D; Duration: 8 days;
ALZET Comments: Controls received mp w/ vehicle; cortisol plasma levels; yellow/silver eels with an ambient temp. of 5 -14 degrees celsius, 30 degrees celsius Cyclodextrin used; pumps implanted IP; per contact with author; 30% cyclodextrin used

Agents: Cortisol Vehicle: Cyclodextrin, beta; Route: IP; Species: Fish (carp); Pump: 1007D; Duration: Not Stated;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by cortisol plasma levels taken; “this approach was used instead of cortisol injection, which evokes stress responses due to repetitive handling...” (p. 2275); 30% cyclodextrin used

Agents: Cortisol Vehicle: Not Stated; Route: SC; Species: Rat; Pump: 2001; Duration: 7 days;
ALZET Comments: Controls received mp w/ saline

R0368: B. A. Teicher. The Combination of Antiangiogenic Therapy with Cytotoxic Therapy. Tumor Angiogenesis and Microcirculation 2001;506-548
Agents: Tetrahydrocortisol; Cyclodextrin-beta tetradecasulfate Vehicle: Not Stated; Route: SC; Species: Mice; Pump: Not Stated; Duration: 14 days;
ALZET Comments: Dose: β-Cyclodextrin tetradecasulfate (1000 mg/kg) and tetrahydrocortisol (125 mg/kg); cancer (Lewis lung carcinoma);