



References on the Administration of Progesterone Using ALZET® Osmotic Pumps

Q8558: V. Joseph, *et al.* Progesterone decreases apnoea and reduces oxidative stress induced by chronic intermittent hypoxia in ovariectomized female rats. *Exp Physiol* 2020;105(6):1025-1034

Agents: Progesterone **Vehicle:** Cyclodextrin, 2-β-Hydroxypropyl-; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 28 days; **ALZET Comments:** Dose (4 mg/kg/day); Controls received mp w/ vehicle; animal info (Sprague-Dawley female rats (220-250g/57-70 days old)); post op. care (buprenorphine); Blood pressure measured via tail cuff method; 93.3 mmHg - 105.2 mmHg; Progesterone aka prog; dependence;

Q6232: S. F. Rosen, *et al.* T-Cell Mediation of Pregnancy Analgesia Affecting Chronic Pain in Mice. *J Neurosci* 2017;37(41):9819-9827

ALZET Comments: Estradiol, 17β-; Progesterone sulfate; SC; Mice; 2002; 14 days; Dose (17β-estradiol : 0.1 mg/kg/d, progesterone sulfate: 0.25 mg/kg/d, 0.1 mg/kg/d estradiol + 0.25 mg/kg/d progesterone); Controls received mp w/ vehicle; animal info (7-12 week old female C57BL/6J mice); replacement therapy (estradiol, ovariectomy); Therapeutic indication.

Q6066: D. J. Morris, *et al.* Glucocorticoids and gut bacteria: "The GALF Hypothesis" in the metagenomic era. *Steroids* 2017;125(1-13)

ALZET Comments: Chenodeoxycholic acid, progesterone, 11β-hydroxy-, corticosterone, deoxy-, corticosterone, 3α,5α-TH-, progesterone, 3α,5α-TH-11β-hydroxy-; SC; Rat; 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.

Q6204: S. McIlvride, *et al.* A progesterone-brown fat axis is involved in regulating fetal growth. *Sci Rep* 2017;7(1):10671

ALZET Comments: Progesterone; Prolactin; Cyclodextrin, 2-hydroxypropyl-β; SC; Mice; 2002; 14 days; Dose (progesterone 250 µg/day; prolactin 7 µg/day); 20% (w/v) 2-hydroxypropyl-β-cyclodextrin used; Controls received mp w/ vehicle; animal info (7–8 week old female mice with bilateral oophorectomy); replacement therapy (oophorectomy);

R0351: D. J. Morris. Why do humans have two glucocorticoids: A question of intestinal fortitude. *Steroids* 2015;102(32-8)

ALZET Comments: Corticosterone; progesterone, hydroxy-; SC; Rat; These infused steroids produce glucocorticoid induced mineralocorticoid receptor mediated Na⁺ retention.

Q4180: R. Wong, *et al.* Evaluating the translational potential of progesterone treatment following transient cerebral ischaemia in male mice. *BMC NEUROSCIENCE* 2014;15(U1-U10)

ALZET Comments: Progesterone; DMSO; SC; Mice; 1003D; 7 days; Controls received mp w/ vehicle; animal info (male, C57BL6 or BPH2/2, 15-25 weeks old, 25.9-41.2g); 100% DMSO used; ischemia (cerebral); behavioral testing (Foot fault test, t-maze test); "...mini-pump delivery could offer a more suitable dosing method with the advantages of reducing peaks and troughs in drug levels, the stress associated with repeated injections, and diminishing levels of release over time as seen with pellet implants. Infusion methods are commonly used clinically to maintain drug concentrations and osmotic mini-pump release of agents at a constant rate mimics this approach." pg 2; "Our previous pharmacokinetic study demonstrated that progesterone delivered via i.p. injection has a very short half-life in both plasma and brain but high progesterone concentrations in the brain can be achieved via mini pump infusion." pg 6; pumps primed overnight in 37C saline;

Q4468: D. J. Morris, *et al.* An alternative explanation of hypertension associated with 17α-hydroxylase deficiency syndrome. *Steroids* 2014;79(44-8)

ALZET Comments: corticosterone; progesterone, hydroxy-; Propylene glycol; sc; Rat; 14 days; 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 µg/hr of both agents.

Q3762: F. Marcouiller, *et al.* The Nuclear Progesterone Receptor Reduces Post-Sigh Apneas during Sleep and Increases the Ventilatory Response to Hypercapnia in Adult Female Mice. *PLoS One* 2014;9(U765-U776)



ALZET Comments: Progesterone; SC; Mice; 1007D; 7 days; Control animals received mp w/ vehicle; animal info (PRKO, wt, adult, female, 3-5 mo old).

Q5064: I. D. Kim, *et al.* Effect of ovariectomy, 17-beta estradiol, and progesterone on histology and estrogen receptors of bladder in female partial bladder outlet obstruction rat model. *J Obstet Gynaecol Res* 2013;39(7):1259-67

ALZET Comments: estrogen; progesterone; dehydroepiandrosterone; DMSO; SC; Rat; animal info: Sprague-Dawley, bladder outlet obstruction model, ovariectomized model; functionality of mp verified by plasma measurement ; mp used to infuse estrogen, progesterone, and DHEA to examine their effect on angiogenesis of the bladder detrusor; dose: E2 (0.1 mg/kg/day); P4 (1mg/kg/day); P4 and DHEA (300 ug/kg/day);.

Q2386: R. Wong, *et al.* Progesterone pharmacokinetics in the mouse: implications for potential stroke therapy. *Journal of Pharmacy and Pharmacology* 2012;64(11):1614-1620

ALZET Comments: Progesterone; DMSO; SC; Mice; 1003D; animal info (C57BL/6, male, wks old); 100% DMSO used; "AUC shows that far higher progesterone concentrations were reached and maintained in both plasma and brain using osmotic minipump delivery with loading dose compared with a bolus dose alone." pg 1616; comparison of bolus dosing vs mp; "Osmotic minipumps were used as the method of infusion as they release progesterone at a constant rate, therefore avoiding diminishing release levels over time as is the case with pellet implants." pg 1617; pk study; comparison of mp vs pellet;

Q0641: P. S. Suresh, *et al.* The effect of progesterone replacement on gene expression in the corpus luteum during induced regression and late luteal phase in the bonnet monkey (*Macaca radiata*). *Reproductive Biology and Endocrinology* 2011;9(;):U1-U16

ALZET Comments: Progesterone; Ethanol; propylene glycol; Monkey (*macaca radiata*); 2ML1; 24 hours; Animal info (adult, female, bonnet, *macaca radiata*, 3.3-5.1 kg); multiple pumps per animal (3); replacement therapy (corpus leuteum); endocrinology.

Q1290: T. Quintela, *et al.* Progesterone Enhances Transthyretin Expression in the Rat Choroid Plexus In Vitro and In Vivo via Progesterone Receptor. *Journal of Molecular Neuroscience* 2011;44(3):152-158

ALZET Comments: Progesterone; Polypropylene glycol; ethanol; DMSO; SC; Rat; 1007D; 2 weeks; Controls received mp w/ vehicle; animal info (Wistar); 1% ethanol used; 1% DMSO used; replacement therapy (ovariectomy).

Q0987: B. B. Braden, *et al.* Medroxyprogesterone acetate impairs memory and alters the GABAergic system in aged surgically menopausal rats. *NEUROBIOLOGY OF LEARNING AND MEMORY* 2010;93(3):444-453

ALZET Comments: Progesterone; medroxyprogesterone acetate; Propylene glycol; SC; Rat; 2ML4; Controls received mp w/ vehicle; animal info (18 mo old, female, Fischer 344); functionality of mp verified by blood serum levels of MPA; pumps replaced every 31-32 days; behavioral testing (Morris maze test); replacement therapy (ovariectomy).

Q0372: P. Pallares, *et al.* A new method for induction and synchronization of oestrus and fertile ovulations in mice by using exogenous hormones. *Laboratory Animals* 2009;43(3):295-299

ALZET Comments: Progesterone; Saline; SC; Mice; 6 days; Animal info (adult, 6-8 wks old, BALB/cAnNCrI, C57BL/6, CD1(ICR)); pumps replaced after 3 days.

P9502: G. N. Armaiz-Pena, *et al.* Estrous Cycle Modulates Ovarian Carcinoma Growth. *Clinical Cancer Research* 2009;15(9):2971-2978

ALZET Comments: Estradiol, 17b-; progesterone; megestrol acetate; Cyclodextrin, b-; water; SC; Mice (nude); Replacement therapy (ovariectomy); animal info (female, athymic); cancer (ovarian).

P9849: R. Lefter, *et al.* Contrasting effects of estradiol and progesterone on respiratory pattern and hypoxic ventilatory response in newborn male rats. *RESPIRATORY PHYSIOLOGY & NEUROBIOLOGY* 2008;164(3):312-318

ALZET Comments: Estradiol; progesterone; Propylene glycol; SC; Rat; 2ML2; 14 days; Controls received mp w/ vehicle; animal info (adult, female, male, multiparous, Sprague Dawley); estradiol and progesterone in same pump; replacement therapy (ovariectomy).



P8245: R. Lefter, *et al.* Progesterone increases hypoxic ventilatory response and reduces apneas in newborn rats. *RESPIRATORY PHYSIOLOGY & NEUROBIOLOGY* 2007;156(1):9-16

ALZET Comments: Progesterone; Propylene glycol; SC; Rat (lactating); 2ML2; 9 days; Controls received mp w/ vehicle; animal info (female, postnatal day 1, lactating); "This approach ensures adequate hormonal exposure in pups since steroids are excreted through the milk, and prevents the potential confounding influences of pup's manipulation on respiratory or metabolic variables." (p. 14).

P7200: M. Robichaud, *et al.* Oestrogen and testosterone modulate the firing activity of dorsal raphe nucleus serotonergic neurones in both male and female rats. *Journal of Neuroendocrinology* 2005;17(3):179-185

ALZET Comments: Estradiol, 17B-; testosterone; progesterone; pregnane-3, 20 dione, 5B-; pregnane-3a-ol, 20-one, 5a-; dehydroepiandrosterone; testosterone, 5a-dihydroxy; Ethanol; water, distilled; CSF/CNS; Rat; 2ML1; 3, 7 days; Controls received mp w/ vehicle; ALZET brain infusion kit used; 3% ethanol; animal info (Sprague-Dawley, 250-325 g).

P7097: M. Robichaud, *et al.* Modulation of the firing activity of female dorsal raphe nucleus serotonergic neurons by neuroactive steroids. *Journal of Endocrinology* 2004;182(1):11-21

ALZET Comments: NE-100; progesterone; pregnenolone; dehydroepiandrosterone; pregnane -3,20-dione, 5B; pregnane -3-ol,20-one, 5a; pregnane -3,20-dione, 5a; pregnane -5B-ol,20-one, 3a; pregnane -3B-ol,20-one, 5B; pregnane -3B-ol,20-one, 5a; Water, distilled; ethanol; SC; CSF/CNS; Rat; 7,14,21 days; Controls received mp w/ vehicle, or saline; replacement therapy (ovariectomy); NE-100 is N,N-dipropyl-2-(4-methoxy-3-(2-phenylethoxy) phenyl)-ethylamine; allopregnanolone; DHP and THP metabolite stereoisomers.

P6581: K. Pazol, *et al.* Medroxyprogesterone acetate antagonizes the effects of estrogen treatment on social and sexual behavior in female macaques. *Journal of Clinical Endocrinology and Metabolism* 2004;89(6):2998-3006

ALZET Comments: Progesterone acetate, medroxy-; progesterone; DMSO; SC; Monkey; 2ML1; 1 week; Controls received placebo; functionality of mp verified by serum hormone levels; replacement therapy (ovariectomy); pumps replaced animals received mp w/ agent 1 for 1 week, mp removed, 3 week washout period and then new mp w/ agent 2 for 1 week; peptides.

P6480: A. M. Traish, *et al.* Sex steroid hormones differentially regulate nitric oxide synthase and arginase activities in the proximal and distal rabbit vagina. *International Journal of Impotence Research* 2003;15(6):397-404

ALZET Comments: Testosterone; dehydroepiandrosterone; dihydrotestosterone, 5-alpha-; androstenediol, delta 5-3B, 17B; estradiol; progesterone; PEG; SC; Rabbit; 2002; 2 weeks; Controls received mp w/ vehicle; replacement therapy (ovariectomy); multiple pumps per animal (2).

P5927: T. C. Shao, *et al.* In vivo preservation of steroid specificity in CWR22 xenografts having a mutated androgen receptor. *PROSTATE* 2003;57(1):1-7

ALZET Comments: Testosterone; estradiol; progesterone; flutamide; Cylodextrin, 2-beta-hydroxypropyl; SC; Mice (nude); 2004; 4 weeks; Replacement therapy (castration); cancer (prostate); CWR22 xenograft used; flutamide is an anti-androgen; animal info (5-6 week old, nude ,ORX).

P4635: L. Zhang, *et al.* Estrogen mediates the protective effects of pregnancy and chorionic gonadotropin in a mouse model of vascular injury. *Arterioscler. Thromb. Vasc. Biol* 1999;19(2059-2065)

ALZET Comments: Estradiol, 17B-; Progesterone; Gonadotrophin, human chorionic; SC; Mice; 2002; 14 days; Controls received sham operation; functionality of mp verified by serum levels; replacement therapy (ovariectomy); vascular cuff injury; B human chorionic gonadotrophin used;

P5305: E. P. Gomez-Sanchez, *et al.* Maternal hypertension and progeny blood pressure: role of aldosterone and 11beta-HSD. *Hypertension* 1999;33(6):1369-1373

ALZET Comments: Aldosterone; Hydroxyprogesterone, 11a; Carbenolone; SC; CSF/CNS; Rat (pregnant); 2002; 2004; 14, 28 days; Controls received mp w/ vehicle; stress/adverse reaction (p.1370); seroma around pump assembly in systemic



carbenolone and hydroxyprogesterone high dose groups; some pumps became disconnected from cannula; glucocorticoids; comparison of sc vs. icv infusion.

P4144: G. W. Souness, *et al.* 11a- and 11b- hydroxyprogesterone, potent inhibitors of 11b-hydroxysteroid dehydrogenase, possess hypertensinogenic activity in the rat. *Hypertension* 1996;27(pt 1):421-425

ALZET Comments: Progesterone, 11a; Hydroxyprogesterone, 11b; RU-28318; Corticosterone; Propylene glycol; SC; Rat; 2002; 14 days; controls received mp w/vehicle; functionality of mp verified by residual volume; replacement therapy (adrenalectomy); agents infused singly and concomitantly in same pump; cardiovascular.

P3698: C. Nolan, *et al.* The effects of oophorectomy and female sex steroids on glucose kinetics in the rat. *Diabetes Res. Clin. Pract* 1995;30(181-188

ALZET Comments: Estradiol, 17B-; Progesterone; Propylene glycol; SC; Rat; 2ML1; 7 days; controls received sham oophorectomy and/or mp w/ vehicle; replacement therapy (oophorectomy).

P3238: M. J. Lobo, *et al.* Effect of chronic intravenous injection of steroid hormones on body weight and composition of female rats. *Biochem. Molec. Biol. Intl* 1993;29(2):349-358

ALZET Comments: Progesterone; Cortisol; Cortisone; Corticosterone; Dehydroepiandrosterone; Androstenedione, 4-; Androstendiol, 5-; Testosterone; Nortestosterone, 19-; Estradiol, B-; Estrone; Estriol; Deoxycorticosterone; PEG 400; IV (lower cava); Rat; 2002; 15 days; controls received mp with PEG; no stress (see pg. 351); pumps placed into peritoneal cavity and sutured to musculature; surgical wound sprinkled with sulphathiazol.

P3233: M.-Y. Lee, *et al.* Induction of flavin-containing monooxygenase (FMO B) in rabbit lung and kidney by sex steroids and glucocorticoids. *Archives Biochem. Biophys* 1993;302(2):332-336

ALZET Comments: Estradiol, B-; Progesterone; Propylene glycol; Ethanol; Ascorbic acid; IP; rabbit; 2001; 4-5 days; controls received mp w/pg; functionality of mp verified by plasma levels; comparison of injections vs. mp.

P1852: S. Dauvois, *et al.* Additive inhibitory effects of an androgen and the antiestrogen EM-170 on estradiol-stimulated growth of human ZR-75-1 breast tumors in athymic mice. *Cancer Res* 1991;51(3131-3135

ALZET Comments: EM-170; Progesterone acetate, medroxy-; DMSO; mice; 40 days; replacement therapy (ovariectomy); long-term study, pumps replaced every 20 days; cancer; antiestrogen.

P1697: S. Mukai, *et al.* Changes in plasma gonadotropins, ovarian steroids and inhibin concentrations in gilts following progesterone treatment with implantable osmotic pumps. *Anim. Reprod. Sci* 1989;20(287-297

ALZET Comments: Progesterone; Ethanol; propylene glycol; SC; Pig; 2ML1; 7 days; Multiple pumps per animal (12); "implanted pumps effectively suppressed follicular growth" (p. 296).

P1271: C. G. Hatjis, *et al.* Up-regulation of guinea pig myometrial b-adrenoreceptors by systemic estradiol and progesterone. *Endocrinology* 1988;122(4):1455-1459

ALZET Comments: Estradiol, 17B-; Progesterone; Propylene glycol; Guinea pig; 7 days; Pump model not stated; controls received mp w/vehicle; separate and simultaneous infusion of agents; replacement therapy (oophorectomy).

P0566: P. C. Will, *et al.* Regulation of amiloride-sensitive electrogenic sodium transport in the rat colon by steroid hormones. *Am. J. Physiol* 1985;248(1):G124-G132

ALZET Comments: Aldosterone; Corticosterone; Dexamethasone phosphate; Estradiol, 17B-; Progesterone; Testosterone; PEG 400; PEG 600; IP; Rat; 1701; 2001; 3-8 days; comparison of agents effects; replacement therapy (adrenalectomy & ovariectomy); controls received mp with solvent or glass rods of mp size; no stress implied G125, weight regained; functionality of mp verified.

P1224: L. A. Lavia, *et al.* Uterine growth responses of the mature castrate rat to estradiol-17B. *Steroids* 1984;43(6):663-675

ALZET Comments: Estradiol, 17B-; Progesterone; SC; Rat; 2001; 24 hours; separate and simultaneous infusion of agents; 2 doses of E2 infused; functionality of mp verified by radioimmunoassay.



P0498: R. Bochtskanl, *et al.* Progesterone dependent uptake of uteroglobin by rabbit endometrium. *Histochemistry* 1984;80(581-589

ALZET Comments: Progesterone; IP; rabbit; 2ML1; no duration posted; replacement therapy (ovariectomy).

P0238: P. H. Jellinck, *et al.* Differential effects of catechol estrogens, progestins and CI-628 administered by constant infusion on the central and peripheral action of estradiol. *Neuroendocrinology* 1982;35(73-78

ALZET Comments: CI-628; Progestins; R-5020; Catecholestrogens; Estradiol, 17B-; Progesterone; Ascorbic acid; PEG; SC; Rat; 2001; 2-3 days; organ replacement therapy (ovariectomy); agents used alone and/or in combination; CI-628 is an anti-estrogen; R-5020 is a progestin.

P0161: P. Komanicky, *et al.* Experimental hypertension induced by 19-nor-progesterone treatment in the rat. *Endocrinology* 1981;109(4):1164-1167

ALZET Comments: Aldosterone acetate; Progesterone, 19-nor-; Ethanol; Propylene glycol; Water; SC; Rat; 1701; no duration posted; pumps replaced after 7 and 14 days.

P0146: R. Bochtskanl, *et al.* Uteroglobin and the accumulation of progesterone in the uterine lumen of the rabbit. *Wilhelm Roux's Archives* 1981;190(127-131

ALZET Comments: Progesterone; Ethanol; Propylene glycol; IP; rabbit; 2001; 4 days; organ replacement therapy (ovariectomy); 1-2 pumps/animal.

P0061: P. C. Will, *et al.* Polyethylene glycols as solvents in implantable osmotic pumps. *J. Pharm. Sci* 1980;69(6):747-749

ALZET Comments: Aldosterone; Corticosterone; Deoxycorticosterone acetate; Dexamethasone acetate; Estradiol, 17B-; Hydrocortisone; Progesterone; Spironolactone; Testosterone; PEG; PEG 400; PEG 600; IP; Rat; 1701; no duration posted; 3-7 days aldosterone, 6 days PEG only; replacement therapy (adrenalectomy).

P0100: M. Cervantes, *et al.* Progesterone facilitation of EEG synchronization in response to milk drinking in female cats. *Psychoneuroendocrinology* 1979;4(3):245-251

ALZET Comments: Progesterone; Ethanol; Propylene glycol; SC; cat; 1701; 8 days; comparison of injections 2x/day vs. infusion; organ replacement therapy (ovariectomy).