

# Protocols

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## Delivery Modes

- Oral - first hepatic pass increases hypercoagulability for estrogen, but not progesterone.
- Progesterone is safe orally.
- Estrogen is not.
- Troche – partially first hepatic pass increases hypercoagulability
- Sublingual – first hepatic pass increases hypercoagulability
- Topical – base matters, rotate sites, rub in well, avoid transference.
- First vaginal pass – creams, vaginal soft pellets or pearls newest easiest way
- Labial vs vaginal – one month labial gets saturated
- Hormone Holidays
- Detox Weekends

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## Vaginal Delivery of Hormones First Vaginal Pass – if any uterine abnormalities

- **Abstract**

- Vaginal progesterone is an effective alternative to systemic administration by oral or intramuscular use. The first-pass effect is reviewed, as are the most common uses for this route of delivery. This includes use in hormone replacement therapy, luteal support particularly in assisted reproduction, and avoidance of side-effects of oral progestins and progesterone. Vaginal progesterone represents a unique therapeutic solution to a number of clinical problems.
- Vaginal progesterone and the vaginal first-pass effect. Climacteric. 2018 Aug;21(4):355-357. doi: 10.1080/13697137.2018.1450856. Epub 2018 Mar 27. PMID: 29583019.

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## Normal

- Estriol – 1/8<sup>th</sup> signaler of ER Alpha as E2
- Usually start with 0.25 mg E2 and can add estriol equal or .75 mg
- If woman is over 60 start with 0.1 mg go slowly as receptors have been quiet and become hyperactive the first year.

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## PMS

- Receptor Detox
- Hormone Balance and Protect
- Progesterone double during luteal phase
- Magnesium 300 mg BID to TID
- Treat constipation
- Back up B complex or multi
- Pregnenolone 25 mg before bed
- Fish oil with dinner helps body use hormones better if above is not helping

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## Overactive Bladder syndrome

- Magnesium
- Receptor Detox
- Hormone Balance and Protect
- BHRT
- **The Estrogen Impact on Overactive Bladder Syndrome: Female Pelvic Floor Microbiomes and Antimicrobial Peptides**
- Study presently ongoing

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## Overactive Bladder

- Vaginal Pellets of BHRT including DHEA often up to 5 mg
- Oxytocin cream
- Magnesium 200-600 mg BID unless get loose stools then back off
- Initial management includes behavioral modification with attention to total daily fluid intake, avoidance of bladder irritants like caffeine, treatment of constipation, weight loss, timed voiding, urge-suppression techniques, and pelvic floor physical therapy.
- Evaluation and Treatment of Overactive Bladder in Women. Mayo Clin Proc. 2020 Feb;95(2):370-377. doi: 10.1016/j.mayocp.2019.11.024. PMID: 32029089.

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## Fibroids

- Progesterone first vaginal pass
- Receptor Detox two twice a day
- Hormone Balance and Protect three twice a day
- Must get them when small but have a few patients starting to decrease fibroids based on this

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## Bases

- Versa Base
- Hypo-allergenic
- If in pellet or pearl and they have to be heated cannot add oxytocin

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## Dosing

- Topical given as dosage/ML
- 4 clicks = one ML
- Usually start with 2 clicks and increase if well tolerated
- The MBK holds 50 mg of hormones
- Pellets hold 80 mg of hormones
- But cannot use these due to heating with oxytocin

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## Early perimenopause Early Low T in males

- Menorrhagia, brain fog, hot flashes
- Receptor Detox, Hormone Balance and Protect, Progesterone, DHEA
- Low T in males – Receptor Detox, Hormone Balance and Protect, DHEA if these don't help, also can add progesterone if anxiety has not yet improved
- 3 mg of boron increases T in males and E in females
- 3 mg between both products of iodine protects breasts
- May also add pregnanolone



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## Gynecomastia

- Receptor Detox
- Hormone Balance and Protect
- Check estrogen levels may need higher dose melatonin but grape seed extract in Hormone Balance & Protect lowers aromatase
- Progesterone to oppose extra estrogen
- Palmetto-Plus to reduce aromatization if Hormone B and P is not enough
- Need the grape seed extract, need the boron, need receptors working, need the iodine

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## Pregnenolone

- Memory hormone 25 mg
- For pain may go to 75 mg



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## Oxytocin




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## Vaginal Atrophy – Dyspareunia non-responsive to basic BHRT

- Objective During and after menopause, the symptoms of vaginal atrophy cause great discomfort and necessitate effective treatment options. Currently, vaginally applied oxytocin is being investigated as a treatment for the symptoms of vaginal atrophy in postmenopausal women. To clarify the mechanisms behind oxytocins effects on vaginal atrophy, the present study investigated the effects of oxytocin on cell proliferation in the cells of the Vk2E6E7 line, a non-tumour vaginal cell line.
- The study also compared the effects of oxytocin with those of estradiol (E2). Study design The effects of both oxytocin and E2 on the proliferation of Vk2E6E7 cells were investigated using Cell Proliferation ELISA BrdU Colorimetric Assay. The expression of both oxytocin and oxytocin receptor was studied in Vk2E6E7 cells using quantitative real-time polymerase chain reaction and immunofluorescent staining. Main outcome measures Cell proliferation and gene expression. Results Oxytocin increased cell proliferation both time dependently and dose dependently. This differed from the effect pattern observed in cells treated with E2. In addition, in oxytocin-treated cells, the oxytocin receptor was found to be co-localized with caveolin-1, indicating pro-proliferative signalling within the cell.
- Conclusions Oxytocin stimulates cell proliferation and the co-localization of oxytocin receptor with caveolin-1 in oxytocin-treated cells, supporting the role of oxytocin signalling in cell proliferation.
- In addition, these findings suggest that increased cell proliferation is one mechanism by which local vaginal oxytocin treatment increases vaginal thickness and relieves vaginal symptoms in postmenopausal women with vaginal atrophy.
- Oxytocin stimulates cell proliferation in vaginal cell line Vk2E6E7. Post Reprod Health. 2017 Mar;23(1):6-12. doi: 10.1177/2053369117693148. Epub 2017 Mar 8. PMID: 28381099.

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- **Objective:** To investigate if topical oxytocin can reverse vaginal atrophy, as assessed by cytological and histological examination of the vaginal mucosal epithelium, in postmenopausal women after 12 weeks of treatment as compared to placebo.
- **Study design:** Sixty-eight postmenopausal women diagnosed with vaginal atrophy were randomized for this multicenter, double-blinded, placebo-controlled trial.
- Thirty-three women received 600 IU vagitocin, an oxytocin containing gel, and 35 women received a placebo gel intravaginally.
- The dose was 600 IU daily for the first two weeks and thereafter 600 IU twice a week for 10 weeks. All participant women underwent four visits and a subgroup of 20 women had a further fifth visit. Vaginal smears for cytological evaluation were collected at all visits. Vaginal biopsies were taken in 20 women before and after 12 weeks of treatment for histological analysis. In these women a vaginal smear was also collected after 14 weeks.
- **Results:** The increase in the percentage of superficial cells between 0 and 2 weeks was significantly greater after treatment with vagitocin in comparison with placebo ( $p = 0.04$ ). The difference in the maturation value between 0 and 12 weeks was significantly higher in the vagitocin than in the placebo group ( $p = 0.01$ ). The reduction in the scores of atrophy was according to the histological investigation significantly greater in the vagitocin group than in the placebo group at 12 weeks ( $p < 0.04$ ).
- **Conclusion:** Daily intravaginal treatment with vagitocin 600 IU improves expressions of vaginal atrophy as recorded by cytological investigation of vaginal smears and histological analysis of vaginal biopsies. Treatment twice weekly seems to be less effective regarding the increase in superficial cells.
- Karolinska Institute
- Oxytocin improves cytological and histological profiles of vaginal atrophy in postmenopausal women. Post Reprod Health. 2016 Mar;22(1):25-33. doi: 10.1177/2053369116629042. Epub 2016 Feb 15. PMID: 26883689.

### Topical oxytocin reverses vaginal atrophy in postmenopausal women: a double-blind randomized pilot study

- This double-blind, randomized study was performed at Huddinge Hospital of Karolinska Institutet, Stockholm in order to test the effectiveness of topical oxytocin gel in women with postmenopausal vaginal atrophy.
- **Methods:** Twenty postmenopausal women (at least two years after menopause) with symptoms of vaginal atrophy such as vaginal dryness, pain, itching, discomfort and bleeding during intercourse were enrolled in the study when visual inspection of the vagina had confirmed that their mucosa was atrophic. The participants were randomized to intravaginal treatment with either oxytocin or placebo gel for seven days. Before and after treatment, a gynaecological examination and a visual and colposcopic inspection of the vagina were performed, biopsies from the vaginal mucosa were taken and blood samples were collected for analysis of circulating levels of estradiol and oxytocin.
- **Results:** Prior to treatment, visual and colposcopic inspection showed that all of the 20 participants had an atrophic vaginal mucosa. After treatment with the oxytocin gel, the examination showed that the vaginal epithelium of seven of the 10 participants in the oxytocin group had become healthier and normalized. No change in these parameters was observed among the 10 participants in the placebo group. This difference between the oxytocin and placebo groups was significant ( $P = 0.003$ ). Seven participants in the active group and four in the placebo group reported relief of symptoms of vaginal atrophy after seven days of applying the gel.
- The effect of oxytocin to normalize the morphological appearance of the vaginal mucosa was almost significant when compared with the placebo group ( $P = 0.07$ ).
- There was no significant difference between the circulating levels of estradiol and oxytocin in both the oxytocin and placebo groups before and after treatment. None of the participants reported any side-effects.
- **Conclusion:** Topical treatment with oxytocin appears to improve vaginal atrophy in postmenopausal women. A limitation of this pilot study is that it was based on a small study population hence the results should be regarded with caution. Larger studies are in progress to establish the possibility of using oxytocin as a clinical treatment for vaginal atrophy.
- Karolinska Institute
- Topical oxytocin reverses vaginal atrophy in postmenopausal women: a double-blind randomized pilot study. Menopause Int. 2011 Dec;17(4):120-5. doi: 10.1258/mi.2011.011030. Epub 2011 Nov 25. PMID: 22120944.

## 400 IU randomized Swedish Trial – lowers Ph So treatment for chronic UTI? 400 was better than 100 IU.

- **Participants:** Sixty four post-menopausal women between February and June 2012 at the Karolinska University Hospital Huddinge/Sweden.
- **Main outcome measures:** The efficacy of oxytocin for treatment of vaginal atrophy after seven weeks and cytological evaluation.
- **Results:** The percentage of superficial cells in the vaginal smears and the maturation values were significantly increased after seven weeks of treatment with vagitocin 400 IU ( $p = 0.0288$  and  $p = 0.0002$ , respectively).
- The vaginal pH decreased significantly after seven weeks of treatment with vagitocin 100 IU ( $p = 0.02$ ).
- The scores of vaginal atrophy, according to the histological evaluation, were significantly reduced after administration of vagitocin 100 IU ( $p = 0.03$ ).
- The thickness of the endometrium did not differ between the treatment and placebo groups after seven weeks of treatment.
- The symptom experienced as the most bothersome was significantly reduced after seven weeks of treatment in the women receiving vagitocin 400 IU compared to women in the placebo group ( $p = 0.0089$ ).
- **Conclusions:** Treatment with intravaginally applied oxytocin could be an alternative to local estrogen treatment in women with post-menopausal vaginal atrophy.
- Intravaginally applied oxytocin improves post-menopausal vaginal atrophy. Post Reprod Health. 2015 Sep;21(3):88-97. doi: 10.1177/2053369115577328. Epub 2015 May 19. PMID: 25995333; PMCID: PMC4566058.


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## Fibrosis?

- Vaginal dosages 100 IU to 600 IU
- Human Transforming Growth Factor Beta 1 – elevated use taurine
- Gallectin-3 = over 15 use Modified Citrus Pectin

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# Nature Never Does Anything Without A Reason

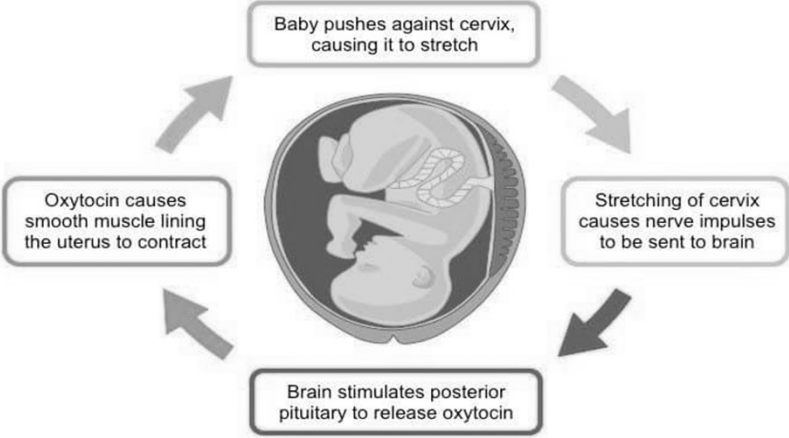


Text SEXY BRAIN 345345 To get free article on Oxytocin Published in Townsend Letter

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# Oxytocin - 1<sup>st</sup> Huge Hormonal Surge



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## Contractile Hormone

- **Uterus** (induces contraction in myometrium)
- **Breast**
- **To set up contractions in newborn gut**
- **And protect the gut from the shock of birth**
- Especially in the **crypts** where the gut continually renews itself
- And makes the baby feel “right with it’s new world” (**Berkson’s theory**)
- J Neuroendocrinol. 2014 Jun;26(6):356-69. doi: 10.1111/jne.12154.  
**Oxytocin: its mechanism of action and receptor signalling in the myometrium.**
- Sci Rep. 2018 Aug 30;8(1):13084. doi: 10.1038/s41598-018-31361-1.  
**Vasopressin and oxytocin in sensory neurones: expression, exocytotic release and regulation by lactation.**

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## Oxytocin Gastroparesis

- **Methods:** Nineteen patients with symptoms from the GI tract who had been examined with gastric emptying scintigraphy, oesophageal manometry, and deep-breathing test were included. They further received a fat-rich meal, after which blood samples were collected and plasma frozen until analysed for hormonal concentrations.
- **Results:** There was an increase in postprandial oxytocin plasma concentration in the group with normal gastric emptying ( $p = 0.015$ ) whereas subjects with delayed gastric emptying had no increased oxytocin secretion ( $p = 0.114$ ). Both CCK and gastrin levels increased after the meal, with no differences between subjects with normal respective delayed gastric emptying. The concentration of vasopressin did not increase after the meal. In patients with oesophageal dysmotility the basal level of CCK tended to be higher ( $p = 0.051$ ) and those with autonomic neuropathy had a higher area under the curve (AUC) of gastrin compared to normal subjects ( $p = 0.007$ ).
- **Conclusion:** Reduced postprandial secretion of oxytocin was found in patients with delayed gastric emptying, CCK secretion was increased in patients with oesophageal dysmotility, and gastrin secretion was increased in patients with autonomic neuropathy. The findings suggest that disturbed peptide secretion may be part of the pathophysiology of digestive complications in diabetics.
- Gastroparesis is associated with oxytocin deficiency, oesophageal dysmotility with hyperCCKemia, and autonomic neuropathy with hypergastrinemia. BMC Gastroenterol. 2009 Feb 25;9:17. doi: 10.1186/1471-230X-9-17. PMID: 19243587; PMCID: PMC2650701.

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- Conclusion
- We have shown that patients with diabetes mellitus and normal gastric emptying have a postprandial increase in oxytocin secretion, whereas oxytocin secretion is impaired in subjects with delayed gastric emptying. We could not find a difference in postprandial CCK or gastrin secretion in patients with and without delayed gastric emptying. However, in patients with oesophageal dysmotility the basal concentration of CCK tended to be higher, and in patients with autonomic neuropathy the gastrin concentrations were increased compared to normal subjects. In the light of our earlier research on oxytocin and its role for a normal GI function [11,12,33-37], the role of oxytocin treatment in gastroparesis has to be further evaluated.

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## Oxytocin GERD

- Oxytocin 50 IU/5ML
- Mucolox 25% solution
- Take 1 tsp 5 ML by mouth three times a day for a week 15 minutes away from liquids and meals
- And then reduce to twice a day for three bottle's worth
- Then do follow-up endoscopic exam

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## Oxytocin Barrett's – Case Report

- Treatment of two bottles worth
- In two year long standing patient on PPIs for Barrett's
- Added 25,000 units of betacarotene
- Cannot be a smoker
- Follow up endoscopic exam showed normal esophagus and Zline

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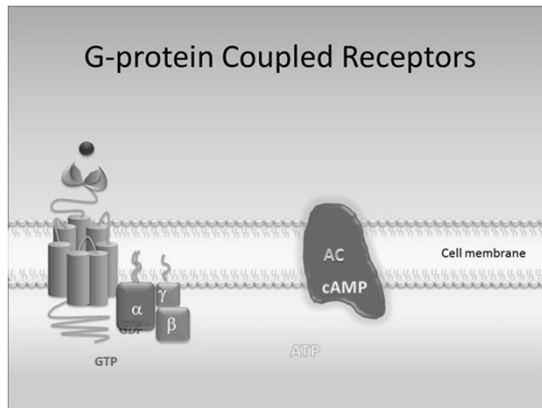
## Karen

- Was on PPIs for 4-5 years
- Then did mucolox and oxytocin and beta carotene and PPIs
- Two years later endoscopy was normal no Barrett's
- Still had GERD tried coming off PPIs and would get burping and discomfort
- Then Famotidine (H2 Blocker Pepsid) 20 mg/once a day
- Still GERD – added chew 2 before meals
- Iberogast – liquid herbal product (Bitters) 15 drops
- No more GERD – no burping, no stomach pain,

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Receptors – wherever they are: critical signals are delivered to genes.  
Oxytocin receptors robust throughout entire body

- Instantaneous
- Transmembraneous
- Receptor
- Results should not take that long
- If give oxytocin and no response
- Within 2 weeks
- Something needs to change in protocol



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## Oxytocin Receptors

- |                               |  |
|-------------------------------|--|
| • Uterus                      | • Oro-nasal cavity   |
| • Breast                      | • Eye  |
| • Entire Gut, liver, pancreas | • Adrenal Gland  |
| • Bone                        | • Brown fat (highest metabolism to help maintain healthier weight) |
| • Muscle                      | • Hypothalamus   |
| • Vagus Nerve                 | • Prostate   |
| • Brain                       | • And counting   |
| • Heart & Arteries            |  |
| • Endothelium                 |  |

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## Well-being

- “I just feel more right with my world.”
- Studies were identified through Medline, Pubmed, and PsychINFO search of the English-language literature from the past sixty years (1959 to 2009) using the key word "oxytocin" in human studies. Of 287 articles, 102 used.
- **OT induces a general sense of well-being including calm, improved social interactions, increased trust, and reduced fear as well as endocrine and physiological changes.**
- Some long-term benefits including blood pressure reduction, calm and affiliative behavior.
- As OT release is augmented by touch and physiological support so the hormone is involved in both the **cause and benefits of social interactions.**
- Just as OT has widespread effects in factors encompassing well-being, **its dysfunction is associated with morbidity and decreased quality of life as observed neuropsychiatric conditions such as autism, schizophrenia and social phobias and increased emotional and physical pain.**

J Affect Disord. 2011 Apr;130(1-2):1-9. **Oxytocin role in enhancing well-being: a literature review.** Cedar Sinai. Psychoneuroendocrinology. 1998 Nov;23(8):779-818. **Neuroendocrine perspectives on social attachment and love.**

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## Oxytocin 101

- Small peptide pulsed out every 2 to 3 minutes in healthy adults.
- Depends on magnesium, and may be one reason magnesium is relaxing.
- Depends also on zinc and vitamin C.
- Promoted by estrogen and thyroid.
- Insufficient in post-menopause and hypothyroidism.
- Oxytocin Receptor— OXTR
- Oxytocin Hormone—OTX or OT

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## Oxytocin Basics Continued

- Women on HRT get better OXT replacement response (**Berkson**).
- ER upregulates oxytocin almost immediately.
- But need zinc, vitamin C, magnesium, and normal thyroid functioning.

Lowers ERAlpha; anti-mitogenic. Int J Oncol. 2002 Aug;21(2):375-8. **Oxytocin modulates estrogen receptor alpha expression and function in MCF7 human breast cancer cells.**  
J Mol Endocrinol. 2017 Oct;59(3):235-243. **The regulation of oxytocin and oxytocin receptor in human placenta according to gestational age.**

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## Transmembrane Hormone Signals

- Instantaneous
- You feel the effect fast.
- Oxytocin nasal delivery - results within seconds.
- That lasts for about an hour.
- Vaginal gel has response within minutes and lasts for several hours so best given BID or sometimes with several pain syndromes TID.
- Mol Pharm. 2018 Jan 16. **Delivery of oxytocin to the brain for the treatment of autism spectrum disorder by nasal application.**

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## It's Understanding Is Growing, Even In Males

- **OT stimulates contractility** of the seminiferous tubules, epididymis and the prostate gland for prostate health.
- Exogenous administration of OT has, in some cases, been shown to **increase the numbers of ejaculated sperm**, possibly by stimulating **contractions** of the reproductive tract and thus aiding sperm passage.

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## Infertility Males

- Receptor Detoc
- Hormone Balance and Protect
- Oxytocin
- Progesterone

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# Oxytocin's



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# Oxytocin

- **Emotional** (social cognition, EQ and/or empathy) animal and human studies
- **Relational angst** animal and human studies
- **Physical pain** (from migraines to PTSD to hemorrhaging after birth) animal and human studies
- **Gut protection/contractility** animal and human studies
- **Treatment for GERD and Barret's Esophagus** in vitro and clinical application
- **Sexuality & orgasm** – human studies
- **Vaginal Atrophy** - human studies
- **Reduces desire for sweets & carbs** (insulin receptor enhancer) human studies
- **Appetite control & Obesity management** –animal & human studies
- **Brain** – reduces cortisol's adverse effects on hippocampus animal and human trails so helps maintain hippocampal volume
- **Enhances GABA signals in brain** – animal studies
- **Metabolic syndrome fighter** – animal and human
- **Heart disease** – theoretical and animal trials
- **Contraindication** – animal and human trials
- Seems to good to be true but it's the first major hormone of life acting intimately with all the other hormones and the parasympathetic nervous system. A healthy gut is a parasympathetic gut.
- Reduce desire for alcohol
- Hypopituitarism

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## Hypopituitarism

- Patients with hypopituitarism display impaired quality of life and excess morbidity and mortality, despite apparently optimal pituitary hormone replacement.
- Recent studies have suggested that a deficiency of oxytocin may be evident in patients with hypopituitarism and that this may be associated with deficits in cognitive empathy.
- Preliminary data hint at potential benefits of oxytocin therapy in improving these deficits and the accompanying metabolic disturbances that are common in these conditions.
- Clin Endocrinol (Oxf). 2019 Feb;90(2):257-264. doi: 10.1111/cen.13909. Epub 2018 Dec 17. **Oxytocin therapy in hypopituitarism: Challenges and opportunities.**

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## Post Traumatic Stress Oxytocin, Zinc, Fish Oil

- **35 female PTSD patients who received oxytocin and placebo in a 2-week interval.**
- Small pilot study to get an idea of the relation of the stress-modulated endogenous oxytocin levels and heart rate - we correlated oxytocin serum levels with the heart rate of 10 healthy individuals before and after exposure to the Trier Social Stress Test (TSST).
- **Results:** Intranasal oxytocin treatment was followed by a reduction of provoked total PTSD symptoms.
- Furthermore, we found a positive correlation between endogenous oxytocin levels and heart rate both before and after TSST challenge in healthy control subjects.
- **Conclusions:** This study provides the first evidence that **oxytocin treatment reduces the intensity of provoked PTSD symptoms in female PTSD patients.**

Intranasal oxytocin reduces provoked symptoms in female patients with posttraumatic stress disorder despite exerting sympathomimetic and positive chronotropic effects in a randomized controlled trial. BMC Med. 2017 Feb 17;15(1):40.

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## Post Traumatic Stress

- In this multicenter double-blind randomized placebo-controlled trial we will recruit 220 Emergency Department patients at increased risk of PTSD.
- Trauma-exposed patients are screened for increased PTSD risk with questionnaires assessing peri-traumatic distress and acute PTSD symptoms within 7 days after trauma.
- Participants will be randomized to 7.5 days of intranasal oxytocin (40 IU) or placebo twice a day.
- Follow-up measurements at 1.5, 3 and 6 months post-trauma.
- **Conclusion:** We hypothesize that intranasal oxytocin administered early after trauma is an effective pharmacological strategy to prevent PTSD in individuals at increased risk, which is both safe and easily applicable.

**Efficacy of oxytocin administration early after psychotrauma in preventing the development of PTSD: study protocol of a randomized controlled trial. BMC Psychiatry. 2014 Mar 28;14:92.**

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## Addictive Behavior - N-acetylcysteine 1800 mg along with Oxytocin

- A substantial number of animal and recent clinical studies indicate that oxytocin is a particularly promising therapeutic agent for human addictions, **especially alcohol use disorders**.
- In preliminary trials, we found that oxytocin administered by the intranasal route, which produces some neuropeptide penetration into the CNS, potentially blocked withdrawal and reduced alcohol consumption in heavy drinkers.
- A considerable body of earlier animal studies demonstrated that oxytocin inhibits tolerance to alcohol, opioids, and stimulants as well as withdrawal from alcohol and opioids.
- Based on these preclinical findings and our clinical results, we hypothesize **that oxytocin may exert therapeutic effects in substance dependence by the novel mechanism of diminishing established tolerance**.
- A newer wave of studies has almost unanimously found that **oxytocin decreases self-administration of a number of addictive substances in several animal models of addiction**.
- Oxytocin efficacy in reducing anxiety and stress responses as well as established tolerance suggests it may be uniquely effective in **reducing negative reinforcement (Koob's "dark side" of addiction) that maintains chronic substance use**.
- Int Rev Neurobiol. 2017;136:239-274. doi: 10.1016/bs.irn.2017.08.003. **Oxytocin, Tolerance, and the Dark Side of Addiction**

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## Anorexia 24 IU in each nostril before meals and if necessary depending on mood Am/Pm

- 30 women with anorexia and 29 healthy comparison women took part in the current study.
- The study used double blind, placebo controlled, crossover design to investigate the effects of a single dose of intranasal oxytocin (40 IU) on a standard laboratory smoothie challenge, and on salivary cortisol, anxiety, and attentional bias towards food images.
- **OXT lowered cortisol, lowered anxiety and promoted better food consumption.**

**Relative to placebo intranasal oxytocin reduced salivary cortisol** and altered anomalies in attentional bias towards food images in the AN group only. Psychoneuroendocrinology. 2017 May;79:167-174.

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## Emotional Bonding with Others

- 2 weeks of daily OT double-blind between-subjects randomized placebo-controlled design.
- **40 healthy young adult men state** and trait attachment were assessed before and after 2 weeks of **daily intranasal OT (24 IU)** or placebo using the State Adult Attachment Scale and the Inventory of Parent and Peer Attachment.
- Mood, social responsiveness and quality of life were additionally assessed as 2ndry outcomes.
- **Reductions in attachment avoidance and increases in reports of attachment toward peers** were reported after two weeks of OT treatment.

Psychoneuroendocrinology Volume 78, April 2017, Pages 1-9 **Long-term oxytocin administration enhances the experience of attachment.**

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## Oxytocin

- Lowers cortisol
- One way to protect against our 24/7 sympathetic driven culture.

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## Case study

- 55 year old female
- On BHRT
- Continual hip pain at an 8
- Kept at a 1 or 2 on inhaled OTX at 24 IU TID.

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## Orgasm

### Orgasm



### Orgasm

- Measuring oxytocin serum levels before and after sexual intercourse in women affected by anorgasmia.
- The sample was constituted of 15 anorgasmic women and 16 orgasmic women.
- Anorgasmic women had an unpleasant sexual and were stressed, whereas orgasmic women were fully satisfied with their sexual activity.
- Anorgasmic women had lower levels of Oxt than orgasmic women,
- Oxt levels did not change in anorgasmic women after.
- Orgasmic women had higher levels of Oxt than anorgasmic women.

Gynecol Endocrinol. 2018 Jan;34(1):69-72. **Oxytocin plasma levels in orgasmic and anorgasmic women.**

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## Women With High Sex Drives

- 136 heterosexual ladies Greece.
- 20 to 25 years old.
- Assessed sexual drive.
- Wild type allele of ER alpha was correlated with increased oxytocin and sexual arousal levels.

Endocr Connect. 2017 Jan;6(1):44-52. **Impact of estrogen receptor  $\alpha$  gene and oxytocin receptor gene polymorphisms on female sexuality**

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## The Big O ➔ The Big O =



- During orgasm, female release of oxytocin activates the pituitary.
- Not near as much in the male.
- Self orgasm by clitoral stimulation, fake orgasm, and rest do not stimulate pituitary in females.
- But orgasm with a hetero partner did.
- Neuroimage. 2013 Aug 1;76:178-82. doi: 10.1016/j.neuroimage.2013.03.012. **Female orgasm but not male ejaculation activates the pituitary. A PET-neuro-imaging study.**

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## Oxytocin, Orgasm, Bonding

- In humans, concentrations of arousing and bonding neurotransmitters increase during orgasm in the cerebrospinal fluid and the bloodstream.
- The neurotransmitters (noradrenaline, oxytocin, prolactin) and others (e.g. dopamine, opioids, serotonin) modulate sexual behavior and reward.
- The higher the level, the more the bonding. These help dictate which partner you get bonded to.
- Socioaffect Neurosci Psychol. 2016 Oct 25;6:31815. doi: 10.3402/snp.v6.31815. eCollection 2016. **The role of orgasm in the development and shaping of partner preferences**

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## Sexual Dysfunction

- Randomized, prospective, double-blind, placebo-controlled, crossover trial with duration of 22 weeks.
- 30 pre-and postmenopausal women with sexual dysfunction.
- **Over 8 weeks, intranasal oxytocin (32 IU)** or placebo self-administered by women **within 50 minutes before sexual intercourse**; after a washout period of 2 weeks, crossover with patients switched to the alternate group for another 8 weeks.
- Primary outcome parameter: **Female Sexual Function Index (FSFI)**; secondary outcome parameters: Female Sexual Distress Scale (FSDS), Sexual Quality of Life-Female (SQOL-F), Sexual Interest and Desire Inventory-Female (SIDI-F), and Hamilton depression scale (HDS).
- **After oxytocin and placebo, the FSFI score increased** by 26% and 31%, SQOL-F score by 144% and 125%, and SIDI-F score by 29% and 23%, respectively (repeated measures analysis of variance between groups).
- **Long-term intranasal oxytocin and placebo administration both improved sexual function and symptoms of depression in women over time.**

Fertil Steril. 2015 Sep;104(3):715-23.e4. **Effect of long-term intranasal oxytocin on sexual dysfunction in premenopausal and postmenopausal women: a randomized trial.**

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## Sexual Pleasure

- Oxytocin works as good as estrogen in lubrication and improvement of pain on intercourse.
- Eur J Obstet Gynecol Reprod Biol. 2018 Aug 6;229:45-56. doi: 10.1016/j.ejogrb.2018.08.008. **Efficacy of vaginal therapies alternative to vaginal estrogens on sexual function and orgasm of menopausal women: A systematic review and meta-analysis of randomized controlled trials.**

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## Case Study

- TV producer
- Painful intercourse, lack of enjoyment, dry, poor orgasms even on BHRT
- Referred by her gynecologist
- Vaginal cream 100 IU of oxytocin added to biest
- Within 2 days success.

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## Sexual Dysfunction

- Open prospective cohort study of 22 weeks. 30 male partners of premenopausal and postmenopausal women with HSDD being treated with OXT or placebo.
- Baseline, 3-month, and 5-month assessment of male response to female partner's use of oxytocin nasal spray (32 IE) and placebo within 50 minutes before sexual intercourse.
- Primary outcome parameters were Sexual Life Quality Questionnaire-Male.
- **Male Sexual Life Quality questionnaire improved significantly with female partners' treatment with oxytocin nasal spray and with placebo.**

Fertil Steril. 2017 Mar;107(3):781-787.e3. **Men's sexual response to female partner's intranasal oxytocin administration for hypoactive sexual desire disorder: an open prospective cohort study.**

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## Male Sexuality

- **Intranasal OT application (24I.U.) in 10 males.**
- Double-blind, placebo-controlled, balanced cross-over design, sexual arousal, and orgasm were induced by an erotic film and masturbation.
- **OT plasma levels were significantly elevated after intranasal OT throughout the whole experiment (>60 min).**
- **Higher levels of OT in blood stream linked to more sexual satisfaction.**

Psychoneuroendocrinology. 2008 Jun;33(5):591-600. **The acute effects of intranasal oxytocin administration on endocrine and sexual function in males.**

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## Oxytocin and Atrophic Vaginitis

- Pilot study: 20 post-menopausal women with atrophic vaginitis confirmed by visual and colposcopic exam
- 10 women were given 1mg/ml oxytocin gel
- 10 women were given placebo
- After 7 days, 7/10 women in the treatment group had normalized vaginal epithelium vs. none in the control group.
- Circulating oxytocin and estradiol were not different between the two groups. **It is NOT an estrogen agonist but has “estrogen-like actions” on mucous membranes.**

**Jonasson AF et al. Topical oxytocin reverses vaginal atrophy in postmenopausal women: a double-blind randomized pilot study. Menopause Int. 2011 Dec; 17(4):120-5.**

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## Vaginal Atrophy

- 68 postmenopausal women diagnosed with vaginal atrophy were randomized for this multicenter, double-blinded, placebo-controlled trial.
- Thirty-three women received 600 IU vagitocin, an oxytocin containing gel, and 35 women received a placebo gel intravaginally. The dose was **600 IU daily for the first two weeks and thereafter 600 IU twice a week for 10 weeks.**
- The increase in the percentage of superficial cells between 0 and 2 weeks was significantly greater after treatment with vagitocin in comparison with placebo .
- The difference in the maturation value between 0 and 12 weeks was significantly higher in the vagitocin than in the placebo group. The reduction in the scores of atrophy was according to the histological investigation significantly greater in the vagitocin group than in the placebo group at 12 weeks.
- Daily intravaginal treatment with vagitocin 600 IU improves expressions of vaginal atrophy as recorded by cytological investigation of vaginal smears and histological analysis of vaginal biopsies.
- Treatment twice weekly seems to be less effective regarding the increase in superficial cells.

Post Reprod Health. 2016 Mar;22(1):25-33. **Oxytocin improves cytological and histological profiles of vaginal atrophy in postmenopausal women.**

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## Post Partum Complications

- The more dates eaten in later pregnancy the shorter the labor.
- Dates increase number of oxytocin receptors.
- This randomized clinical trial was conducted among 182 nulliparous women 18-35 years who presented to OmAlBanin Hospital in Mashhad in 2013. The comparison has been made between 91 pregnant women who consumed 70-76 g dates daily from the 37th week of pregnancy and 91 pregnant women who did not consume dates.
- 3 dates/day
- According to the results of this study, consuming dates in late pregnancy was effective in decreasing length of labor processes and reduced the need of oxytocin for labor acceleration. Thus, it is recommended to consume dates in women without contraindications.
- To mother or child.
- Effect of Dates in Late Pregnancy on the Duration of Labor in Nulliparous Women.
- Iran J Nurs Midwifery Res. 2017 Sep-Oct;22(5):383-387. doi: 10.4103/ijnmr.IJNMR\_213\_15.
- Date fruit consumption at term: Effect on length of gestation, labour and delivery.
- J Obstet Gynaecol. 2017 Jul;37(5):595-600. doi: 10.1080/01443615.2017.1283304

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## Hippocampal Shrinkage (atrophy)

- Linked to Alzheimer's
- And use of anti-depressants
- Is oxytocin replacement going to be a tool to protect hippocampal volume?
- If HRT is not helping to slow down progression of MCI, add new products, receptor detox, hormone balance and protect and oxytocin.

Int J Geriatr Psychiatry. 2015 Mar;30(3):292-9. **Depression and antidepressant use moderate association between widowhood and Alzheimer's disease.**

Biol Psychiatry. 2000 Mar 15;47(6):557-61. **Hippocampus in Alzheimer's disease: a 3-year follow-up MRI study.**

Neuroimage Clin. 2015 Apr 29;8:230-7. doi: 10.1016/j.nicl.2015.04.016. eCollection 2015. **Hippocampal volume correlates with attenuated negative psychotic symptoms irrespective of antidepressant medication.**

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## ADHD/Conduct Disorder

- A total of 74 drug-naive children with ADHD combined presentation alone, 32 children with ADHD combined presentation + conduct disorder, and 42 healthy controls were included.
- **There was also a trend for lower oxytocin and DHEA in ADHD kids.**
- These findings suggest that oxytocin and DHEA may play a role in the pathophysiology of conduct disorder, at least in the presence of ADHD combined presentation.

Psychiatry Res. 2018 Jan 2;261:212-219. **Serum levels of cortisol, dehydroepiandrosterone, and oxytocin in children with attention-deficit/hyperactivity disorder combined presentation with and without comorbid conduct disorder.**

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## Depression

- Serum oxytocin levels were measured before and after treatment with antidepressant drugs or electroconvulsive therapy (ECT) in **40 inpatients (30 women, 10 men)** who met the DSM-IV criteria for major depressive disorder (n=29) or bipolar affective disorder depressive episode (n=11), and in 32 healthy controls (20 women, 12 men).
- **Serum oxytocin levels were decreased both pre-treatment and post-treatment in the patients compared with those in the controls.**
- Serum oxytocin levels were not affected by antidepressant drug treatment or ECT.
- **The female patients had significantly lower oxytocin levels than the control females**, whereas no difference was found between the male patients and the male controls.
- **Our result shows reduced oxytocin in depression and a gender difference in oxytocin levels.**
- Oxytocin for depression may be **more helpful for females than males.**

Psychiatry Res. 2009 Oct 30;169(3):249-52. **Serum oxytocin levels in patients with depression and the effects of gender and antidepressant treatment.**

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## Diabetes/Autoimmunity

- Cross-sectional study of premenopausal women with T1DM (n=88) from the Wisconsin Diabetes Registry Study, a population-based cohort of incident T1DM cases, and matched non-diabetic controls (n=74).
- Women with T1DM had lower OT levels than controls.
- **OT was negatively associated with hormonal contraceptive use** (quantified as lifetime contraceptive estrogen exposure) in women with T1DM.
- OT levels are lower in women with T1DM than matched controls..
- Diabetes Metab Res Rev. 2015 Jan; 31(1): 102–112. doi: 10.1002/dmrr.2577. **Oxytocin Levels are Lower in Premenopausal Women with Type 1 Diabetes Mellitus Compared to Matched Controls**

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## Gastroparesis

- **Oxytocin is released in response to a fatty meal.**
- Blockage of the oxytocin receptor led to slower gastric emptying.
- Patients with diabetes mellitus and gastroparesis lack oxytocin elevation
- 12 patients did not receive improvement.
- I added HCL and saw improvement in several clinical cases.

BMC Res Notes. 2012 Mar 16;5:148. **Oxytocin prolongs the gastric emptying time in patients with diabetes mellitus and gastroparesis, but does not affect satiety or volume intake in patients with functional dyspepsia.**

BMC Gastroenterol. 2009 Feb 25;9:17. **Gastroparesis is associated with oxytocin deficiency, oesophageal dysmotility with hyperCKemia, and autonomic neuropathy with hypergastrinemia.**

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## Oxytocin Vagal Nerve

- **Oxytocin up-regulates vagal/parasympathetic signaling.**
- Vagus nerve is massive internal feed back loop—part of optimal gut functioning, feeling right with the world and having a para-symphthetic dominant gut. Meditation boosts vagal tone and oxytocin release.

Am J Physiol Regul Integr Comp Physiol. 2015 Mar 1;308(5):R360-9. **Peripheral oxytocin activates vagal afferent neurons to suppress feeding in normal and leptin-resistant mice: a route for ameliorating hyperphagia and obesity.**

Devi, G. (2012) *A Calm Brain: How to relax into a stress-free, high-powered life.* NY, NY, Penguin Dutton.

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## Gabanergic

- Data demonstrate ante-stress treatments of Oxt inhibits stress activation of the HPA axis through **recruitment of GABAergic neurons**,
- Providing insights to the local circuitry and potential therapeutically-relevant mechanisms.

Psychoneuroendocrinology. 2016 Jan;63:50-8.

**Local oxytocin tempers anxiety by activating GABAA receptors in the hypothalamic paraventricular nucleus.**

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## Reduces Desire for Carbs

- Oxytocin within the brain is involved in food reward, food choice, and satiety.
- Oxytocin preferentially suppresses intake of sweet-tasting carbohydrates while improving glucose tolerance and supporting bone remodeling, making it an enticing translational target.
- Trends Endocrinol Metab. 2017 May;28(5):365-376. doi: 10.1016/j.tem.2017.02.007. **Oxytocin - The Sweet Hormone?**

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66

## Oxytocin and Bone Health

- Osteoblasts and osteoclasts express OTR.
- Genetically modified mice with null OT and OTR develop osteoporosis that progressively worsens with age in BOTH genders.
- OT stimulates the development and maturation of osteoblasts.
- Mice without OTR, did not experience bone enhancing effects of  $17\beta$ -estradiol. (OT + E)

Colaïanni G et al. The oxytocin-bone axis. J Neuroendocrinol. 2014 Feb;26(2):53-57.

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## Skeletal Muscles are Flush with OTRs

- Both OT and OTR decline in the aging process
- Researchers theorized OT may be linked with muscle health and preserving muscle mass in young and protecting against sarcopenia in aging.
- OT use to avoid or treat sarcopenia?

Elabd C et al. Oxytocin is an age specific circulating hormone that is necessary for muscle maintenance and regeneration. Nat Commun. 2014 Jun 10;5:4082.

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## Sarcopenia

- The regenerative capacity of skeletal muscle declines with age.
- Here we report that oxytocin is required for proper muscle tissue regeneration and homeostasis, and that plasma levels of oxytocin decline with age.
- Inhibition of oxytocin signaling in young animals reduces muscle regeneration, whereas systemic administration of oxytocin rapidly improves muscle regeneration by enhancing aged muscle stem cell activation.
- **Considering that oxytocin is an FDA-approved drug, this work reveals a potential novel and safe way to combat or prevent skeletal muscle ageing.**

Nat Commun. 2014 Jun 10;5:4082. **Oxytocin is an age-specific circulating hormone that is necessary for muscle maintenance and regeneration.**

Lab Anim (NY). 2014 Aug;43(8):260. **With oxytocin, old muscles act like new.**

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## Appetite Reducer

- Oxytocin regulates eating behaviour and metabolism.
- In rodents and nonhuman primates, **chronic oxytocin administration leads to sustained weight reduction by reducing food intake**, increasing energy expenditure and inducing lipolysis.
- Oxytocin might improve glucose homeostasis, independently of its effects on weight.
- Clinical studies are beginning to translate these important preclinical findings to humans.
- **For example, a single intranasal dose of oxytocin can reduce caloric intake, increase fat oxidation and improve insulin sensitivity in men.**
- Furthermore, a **pilot study of 8 weeks of oxytocin treatment in adults with obesity or overweight led to substantial weight loss.**
- **Being considered for use in obesity and Type 2D.**

Nat Rev Endocrinol. 2017 Dec;13(12):700-709. **The effects of oxytocin on eating behaviour and metabolism in humans.**

Obes Rev. 2019 Jan;20(1):22-40. doi: 10.1111/obr.12757. **Oxytocin in metabolic homeostasis: implications for obesity and diabetes management.**

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## Heart Disease

- In addition to elevated lipid levels, **oxidative stress and inflammation** are key factors driving atherogenesis and CVD.
- New strategies are required to mitigate risk and most urgently for statin-intolerant patients (numbers are growing)
- Oxytocin is worthy of consideration as a CVD ancillary treatment because it moderates factors directly linked to atherosclerotic CVD such as inflammation, weight gain, food intake and insulin resistance.
- Oxytocin has shown promise in animal models of atherosclerosis and in some human studies, too.
- Oxytocin not only lowers fat mass and cytokine levels, it improves glucose tolerance, lowers blood pressure and relieves anxiety.
- Further, it has an important role in communication in the gut-brain axis that makes it a promising treatment for obesity and type 2 diabetes.
- Oxytocin acts through its receptor which is a class I G-protein-coupled receptor present in cells of the vascular system including the heart and arteries.
- This review discusses the possible role for oxytocin in human CVD prevention and treatment.
- Peptides. 2019 May 18. pii: S0196-9781(19)30061-0. doi: 10.1016/j.peptides.2019.05.001. **Oxytocin: Potential to Mitigate Cardiovascular Risk.**

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## Bisphenol A – Oxytocin Endocrine Disruptor

- Sprague-Dawley dams.
- Consistent with prior observations, **BPA induced sex-specific effects on hypothalamic ER $\alpha$  and ER $\beta$  (Esr1 and Esr2) expression and hippocampal and hypothalamic oxytocin (Oxt) expression.**
- **These data demonstrate prenatal BPA exposure, even at doses below the current no-observed-adverse-effect level, can alter gene expression in the developing brain.**

Endocrinology. 2016 Oct;157(10):3856-3872 Impact of Low Dose Oral Exposure to Bisphenol A (BPA) on the Neonatal Rat Hypothalamic and Hippocampal Transcriptome: A CLARITY-BPA Consortium Study.

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## BPA

- BPA exposure affects OTR expression across the whole brain.
- Our results demonstrate prenatal exposure to BPA can eliminate sex differences in OTR expression in three hypothalamic regions, and that male OTR expression may be more susceptible.
- Our data also identify a sub-region of the brain with sexually dimorphic OTR expression not previously reported in juvenile rats that is also susceptible to BPA.
- Neurotoxicology. 2019 Jun 25;74:139-148. doi: 10.1016/j.neuro.2019.06.007. **Perinatal bisphenol A (BPA) exposure alters brain oxytocin receptor (OTR) expression in a sex- and region- specific manner: A CLARITY-BPA consortium follow-up study.**

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## BPA

- There is perhaps no endocrine disrupting chemical more controversial than bisphenol A (BPA).
- Comprising a high-volume production chemical used in a variety of applications, BPA has been linked to a litany of adverse health-related outcomes, including effects on brain sexual differentiation and behaviour.
- To address current controversies on the safety of BPA, the United States National Institute of Environmental Health Sciences, the National Toxicology Program (NTP), and the US Food and Drug Administration **established the Consortium Linking Academic and Regulatory Insights on BPA Toxicity (CLARITY-BPA)**.
- CLARITY-BPA performed a classical regulatory-style toxicology study (Core study) in conjunction with multiple behavioural, molecular and cellular studies conducted by academic laboratories (grantee studies) using a collaboratively devised experimental framework and the same animals and tissues.
- Evidence of altered neuroendocrine development, including age- and sex-specific expression of oestrogen receptor (ER) $\alpha$  and ER $\beta$ , and the abrogation of brain and behavioural sexual dimorphisms, supports the conclusion that developmental BPA exposure, even at doses below what regulatory agencies regard as "safe" for humans, contribute to brain and behavioural change.
- The consistency and the reproducibility of the effects across CLARITY-BPA and prior studies are compelling.
- Effects amygdala – anxiety, fear.
- J Neuroendocrinol. 2019 May 7:e12730. doi: 10.1111/jne.12730. **Achieving CLARITY on bisphenol A, brain and behaviour.**
- Neurotoxicology. 2018 Mar;65:207-220. doi: 10.1016/j.neuro.2017.10.005. **Prenatal bisphenol A (BPA) exposure alters the transcriptome of the neonate rat amygdala in a sex-specific manner: a CLARITY-BPA consortium study.**

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## Transgenerational Behavioral Issues

- Thus, exposure to a low dose of BPA, during gestation, has immediate and long-lasting, transgenerational effects on mRNA in brain and social behaviors.
- Brains from embryos exposed to BPA had lower gene transcript levels for several estrogen receptors, oxytocin, and vasopressin as compared with controls; decreased mRNA persisted into the F(4) generation, at which time oxytocin was also reduced (but only in males).
- BPA produces differences/insufficiencies in ER $\alpha$  in generations having long-term consequences for reproduction and social behavior.
- Endocrinology. 2012 Aug;153(8):3828-38. doi: 10.1210/en.2012-1195. Epub 2012 **Gestational exposure to bisphenol a produces transgenerational changes in behaviors and gene expression.**
- Endocrinology. 2017 Jan 1;158(1):21-30. doi: 10.1210/en.2016-1188. **Multi- and Transgenerational Consequences of Bisphenol A on Sexually Dimorphic Cell Populations in Mouse Brain.**

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## Phthalates

- Perinatal exposure to endocrine disrupting chemicals (EDCs) can induce promiscuous neurobehavioral disturbances.
- Social behaviors, such as communication, mate choice, pair bonding, social inquisitiveness and recognition, play behavior, social grooming, copulation, and aggression, are compromised in animal models exposed to BPA, phthalates, and other EDCs.
- Early contact to these chemicals is also correlated with maladaptive social behaviors in children.
- Concern also exists for transgenerational persistence of such neurobehavioral disruptions.
- Front Neurosci. 2015 Mar 3;9:57. doi: 10.3389/fnins.2015.00057. eCollection 2015. **Bisphenol A and phthalate endocrine disruption of parental and social behaviors.**
- Schizophr Bull. 2009 Jan;35(1):256-78. doi: 10.1093/schbul/sbm147. **Effects of bisphenol-A and other endocrine disruptors compared with abnormalities of schizophrenia: an endocrine-disruption theory of schizophrenia.**
- PLoS One. 2012;7(9):e43890. doi: 10.1371/journal.pone.0043890. **Anxiogenic effects of developmental bisphenol A exposure are associated with gene expression changes in the juvenile rat amygdala and mitigated by soy.**

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## Contraindications

- The aim of the present study was to evaluate oxytocin and benign prostatic hyperplasia (BPH).
- Oxytocin was significantly elevated in the serum and prostate tissue of patients with BPH, and a positive correlation with prostate volume indicated.
- In the animal experiments, prostate enlargement was observed in the oxytocin-treated group, whereas oxytocin antagonist reduced prostate hyperplasia.
- Oxytocin is highly expressed in the serum and prostate tissue of patients with BPH.
- Oxytocin aggravates BPH.
- Probably avoid in prostate cancer.
- Uterine cancer
- Manic episodes
- PREGNANCY!

Clin Sci (Lond). 2017 Apr 1;131(7):595-607. **Oxytocin: its role in benign prostatic hyperplasia via the ERK pathway.**

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## Nasal Delivery

- Rodent studies published this Jan.
- **Nasal bioavailability is approximately 2%.**
- **A rapid initial half-life of 3 min.**
- **Brain concentration of OXT after nasal application was much higher than that after intravenous application,** despite much lower concentrations in the plasma.
- More than 95% of OXT in the brain was directly transported from the nasal cavity.
- The in vivo stress-relief effect by OXT was observed only after intranasal administration.
- These results indicate that pharmacological active OXT was effectively delivered to the brain after intranasal administration.
- In conclusion, the nasal cavity is a promising route for the efficient delivery of OXT to the brain.

Mol Pharm. 2018 Jan 16. **Delivery of oxytocin to the brain for the treatment of autism spectrum disorder by nasal application.**

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## Inhaled OXT compared to IM

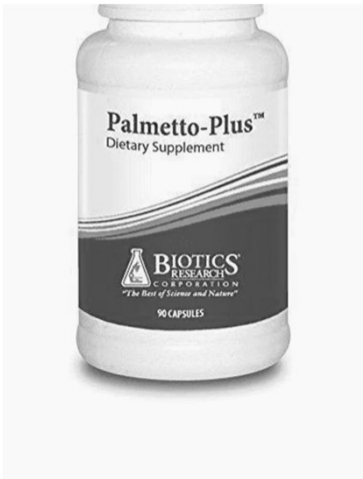
- Of the 16 subjects randomized following initial dosing, 15 (IH placebo  $n = 3$ ; IH oxytocin  $n = 12$ ) completed the study.
- **Systemic exposure with IH oxytocin 400 µg most closely matched IM oxytocin 10 IU.**
- Systemic exposure was approximately dose proportional for IH oxytocin.
- No serious AEs were reported.
- These data suggest that similar oxytocin systemic exposure can be achieved with IM and IH administration routes, and no safety concerns were identified with either route. The inhalation route may offer the opportunity to increase access to oxytocin for women giving birth in resource-poor settings.

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Benign Prostatic Hypertrophy give it 3 months



- Iodine – Receptor Detox and H B & P = 3 mg/iodine
- High dose flax seed 30 g/d or 3 TB decreased proliferation by 68%
- So give 2 TB/d
- Flaxseed muffin for free at resources at [drindseyberkson.com](http://drindseyberkson.com)
- Zinc 30 mg three times a day (back up copper 1-4mg)
- Saw Palmetto Biotic's Palmetto-Plus
- Glycine/alanine/glutamic acid amino acids
- Saw palmetto inhibits 5 alpha reductase in dose dependent manner 320 mg
- Beta-sitosterol
- Pilot study to explore effects of low-fat, flaxseed-supplemented diet on proliferation of benign prostatic epithelium and prostate-specific antigen. Urology. 2004 May;63(5):900-4. doi: 10.1016/j.urolgy.2003.12.010. PMID: 15134976.

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BPH – Receptor Detox, Hormone B & Protect, Flaxseed, Biotics Sawpalmetto Plus Forte

BIOTICS RESEARCH®

Supplement Facts		
Serving Size: 3 Capsules		
Servings Per Container: 30		
	Amount Per Serving	% Daily Value
Vitamin A (as natural mixed carotenoids and acetate) (IU ratio 1:1)	3,310 mcg RAE	368%
Vitamin B6 (as pyridoxal-5-phosphate)	6 mg	353%
Magnesium (as magnesium glycinate)	100 mg	24%
Zinc (as zinc citrate)	45 mg	409%
Selenium (as selenomethionine)	50 mcg	91%
Saw Palmetto (Serenoa repens) (berry) (4:1 extract)	500 mg	*
Glycine	200 mg	*
L-Alanine	200 mg	*
Glutamic Acid (as L-Glutamic acid HCl)	200 mg	*
Lycopene (as naturally isolated from tomatoes)	15 mg	*
Chlorophyllins (from Mulberry leaf)	2 mg	*
Superoxide Dismutase (from vegetable culture 1)	10 mcg	*
Catalase (from vegetable culture 1)	10 mcg	*
* Daily Value not established		
Other ingredients: Capsule shell (gelatin and water).		

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The two new products = 3 mg iodine

- **Background:** There is some evidence that Benign Prostatic Hyperplasia (BPH) may increase the risk of developing prostate cancer, so conducting research on effective BPH inhibitors is important.
- **Objective:** This research studied the inhibitory effect of Iodized Serum Milk Protein (ISMP) on BPH in rats. ISMP is a concentrate of lactic protein containing 2.2% iodine.
- **Methods:** Male Wistar rats, aged 18 months, were used. In the intact control group, sunflower oil was administered intragastrically by gavage. In 36 rats, BPH was induced by surgical castration, followed by subcutaneous injections of prolonged testosterone - omnadren, 25mg/kg every other day (7 administrations). One group of rats served as BPH-control. ISMP and finasteride (positive control), dissolved in sunflower oil, were administered to rats intragastrically daily at a dose of 200µg/kg and 5mg/kg, respectively, for 4 weeks starting immediately after castration.
- **Results:** ISMP inhibited the development of BPH in rats, significantly reducing the mass of the prostate and its parts (except for the anterior lobes) by 1.1-1.3 times and the prostatic index (the ratio of prostate weight to the body weight) - by 1.3-1.4 times. Finasteride inhibited the development of BPH, and its activity was higher (by 1.1-1.3 times) than in ISMP. Histological analysis of the prostate showed fewer pronounced morphological hyperplasia signs in animals treated with ISMP or finasteride.
- **Conclusion:** The iodine-containing preparation ISMP has the ability to inhibit the development of BPH in rats although its activity is somewhat lower than that of finasteride.
- Iodine Bonded with Milk Protein Inhibits Benign Prostatic Hyperplasia Development in Rats. Anticancer Agents Med Chem. 2019;19(13):1627-1632. doi: 10.2174/1871520619666190705143927. PMID: 31284874.

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BPH

- Benign prostatic hyperplasia (BPH) is a common chronic disease in ageing men. Synthetic inhibitors of 5α-reductase commonly used in BPH treatment have limited effectiveness and may cause side effects.
- Evaluation of iodised serum milk protein and lycopene therapeutic effect in rat BPH model was the aim of the present study. BPH was induced in male Wistar rats by surgical castration and subsequent testosterone administrations (25 mg/kg, 7 injections).
- Rats with induced BPH received lycopene (5 mg/kg), iodised serum milk protein (200 µg/kg) or their combination for 1 month daily. The efficacy of the treatment was evaluated by the prostate weight, prostatic index and ventral lobe epithelium thickness.
- In lycopene and iodised serum milk protein-treated rats, prostate weight and prostatic index were significantly reduced compared to control group; and lycopene and iodised serum milk protein used in combination yielded an additive effect. Thus, further investigation of combined supplementation with micronutrients and plant-derived substances in BPH models may help to find new opportunities or its safe and effective treatment.
- Receptor Detox and Hormone Balance and Protect for growth controllers and iodine and Palmetto Plus-Forte also adds in the lycopene.
- Therapeutic effect of iodised serum milk protein, lycopene and their combination on benign prostatic hyperplasia induced in rats. Andrologia. 2021 Oct;53(9):e14173. doi: 10.1111/and.14173. Epub 2021 Jun 29. PMID: 34185339.

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- Finasteride
- Saw palmetto
- Stop T going to DHT
- So can also use this with PCOS
- But it may worsen alopecia

85

## PCOS

- D-chiro inositol (stereoisomer of myo-inositol known as inositol) helps insulin resistance and so do Receptor Detox and Hormone Balance and Protect and lowers T several thousand mg/d 1200 to 3000 BID depending on body weight
- Myoinositol 2 grams BID
- Vitamin D track and treat
- 1000 mcg Chromium/d
- N-acetylcysteine 600 mg TID
- Spearmint tea 4 cups/day
- Fish oil
- Track thyroid function often need SR T3 often have high normal rT3
- Avoid Bisphenol A but new products help with this
- Saw Palmetto
- Ozempic
- Spearmint herbal tea has significant anti-androgen effects in polycystic ovarian syndrome. A randomized controlled trial. *Phytother Res.* 2010 Feb;24(2):186-8. doi: 10.1002/ptr.2900. PMID: 19585478.

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## Endometriosis

- Gluten free
- Higher dose melatonin
- New products
- HCG injections 1400 IU twice a week for three months subQ

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## Adenomyosis



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## Macular Degeneration

- Check stomach acid production
  - Often have hypochlorhydria
  - Check pancreatic and bile
  - MacuHealth 2/d with largest meal
  - Bilberry extract 80 mg BID
  - Selenium, zinc, taurine one gram BID, best even if IV
  - Vitamin E mixed tocopherols and Anatto-e 300
  - N-acetyl cysteine
  - BHRT
- 
- Home ozone insulfation with appropriate stethoscope

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## Eye Health

- 24 hour blood pressure cuff to know blood pressure while sleep

90

## Libido



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## Weight Loss

- Sensitize Insulin Receptor
- Receptor Detox
- Hormone Balance and Protect
- BHRT
- There are some plateaus that can last days to few weeks then do Receptor Detox 4 twice a day to burst through

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### Weight Loss –

- Case Report
- She was 295 lbs. 1+ years ago.
- Comes from a family where all are mostly in their mid 300's and had never gone below 30" waist or this low of weight for this long. For a year now.
- Hormones helped her lose first.
- Then Receptor Detox and Hormone Balance & Protect broke through her plateau's/

