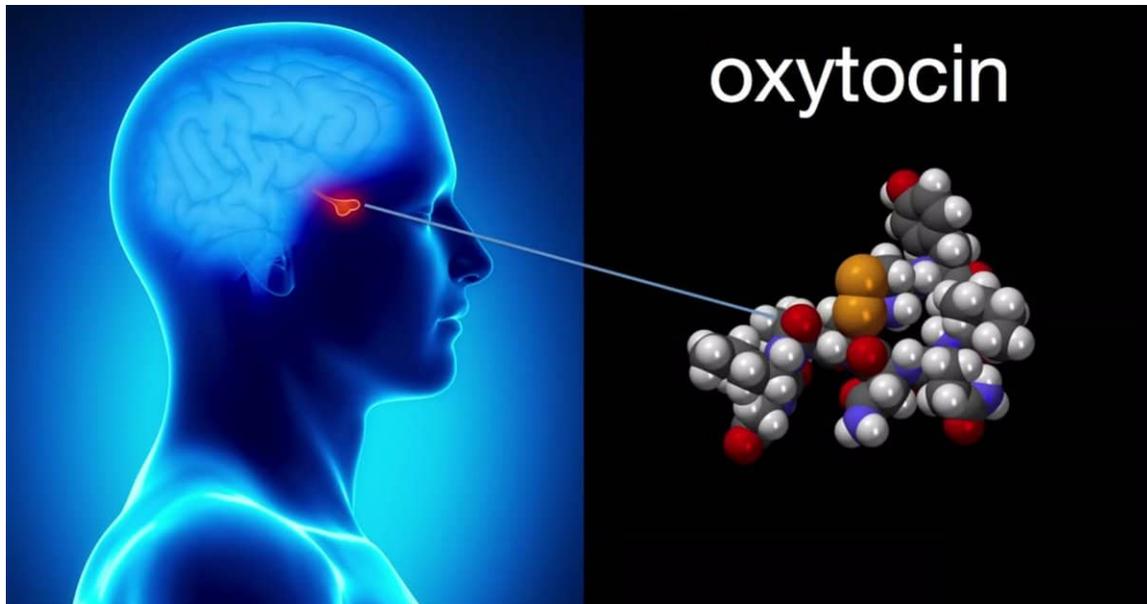


— Oxytocin —

Historically regarded as a pregnancy and lactation hormone, now shown to have many health actions & clinical applications from increasing empathy and human connection to protecting gut transit time, and more!

By Dr. Lindsey Berkson



Modern Dilemma.

In America today, marital relationships and personal moods seem pretty hard to hold together. Fifty percent of marriages end in divorce¹. Studies say 20 to 72% of husbands commit adultery and 10 to 54% of wives do likewise².

Try as we may to achieve happy relationships³, many fail.

Moods are murky. Anxiety disorders affect 40 million adults⁴ and cost one-third of all monies spent on mental health. The National Center for Health Statistics shows that one in ten Americans (and one out of four women in their 40s and 50s) take antidepressants.

What if there was a safe nasal spray (of all things) that could enhance relationship harmony and loyalty^{5 6 7 8}, heighten desire and orgasms, stabilize moods and make us feel more right with our world?

What if it wasn't addictive?

And didn't have rebound issues?

Enter Oxytocin.

In science this hormone is referred to as the official neuropeptide of "attachment." This article brings you up to snuff (the bulk of research on oxytocin is on the *intranasal* delivery mode) on the clinical applications of oxytocin replacement. You will learn it is a team player with our sex steroid hormones, our ability to be lean and *not* mean, and as part of the Buddha (Vagal) pathway between our brain and gut⁹.

Oxytocin is a peptide hormone. Peptide hormones are made of amino acids. A peptide is a link of two or more amino acids. As far as peptide hormones go, oxytocin is a small thing, with only nine amino acids. In comparison, thyroid-stimulating hormone (TSH) contains 201. Sometimes oxytocin is referred to as a *nonapeptide*, since *nona* means "nine."

Oxytocin is historically appreciated for its role in pregnancy. It does this by its role in contraction. Oxytocin signals initiate and sustain uterine contractions, lets down milk for lactation by creating contraction in milk ducts, and deepens bonding between mother and child^{10 11}. But there's more. As the new mom and new baby's body are flushed with oxytocin, it travels through the blood stream in the brand new infant, and protects the gut wall from the trauma and shock of birth. Oxytocin is so gut protective, that presently we are performing early pilot studies using oxytocin and other

tools in gut patients, in collaboration with the LA Gastroenterology and Nutrition Clinic in California!

Emergent research and clinical evidence reveal ever-expanding possibilities for oxytocin replacement for diverse issues. For example, oxytocin therapy is being used to treat autism spectrum disorder, schizophrenia, obesity, addiction¹², erectile dysfunction¹³, orgasm disorders, pain from back pain to pelvic pain to emotional pain, and as a libido, orgasm, and emotional “bonding” enhancer¹⁴.

Viagra has become a household word. It’s an effective, best-selling sexual medication. Viagra has also been looked at for treating depression and other mental disorders^{15 16}. Why? It boosts oxytocin production¹⁷.

Oxytocin Receptors.

Hormones are signaling molecules, or “e-mailers” in the body’s physiologic Internet system. Hormones are made in various organs throughout the body. For example, oxytocin is made in the brain. These hormones are then secreted into the watery highways of the blood, where they swim to specific tissues in search of perfectly fitting receptors. Receptors are proteins shaped like malleable satellite dishes. Hormones swim into their exact receptor. Once inside, the hormone docks into specific binding domains. Marching orders are delivered to genes. Based on these directives, cells take action.

Much of the cross-talk communication that takes place to nudge life to unfold is due to hormonal (ligand to receptor) and genomic (delivering to genes) signaling. There are other forms of signaling, such as receptor-free and non-genomic signaling, but they are beyond the scope of this article.

Oxytocin (OT) delivers messages to specific oxytocin receptors (OTR). We have oxytocin receptors globally throughout human biologic real estate, not just in reproductive tissues. Oxytocin receptors line our gut from our mouths to our anus; they are robust in the pancreas, in your liver and all throughout your nervous system.

I have been using oxytocin replacement in practice for almost ten years and have some startling case histories as well as some duds. Five summaries are presented later in this article.

Brain.

Oxytocin is produced in the hypothalamus¹⁸. It is made by the neurons of the paraventricular and supraoptic nuclei of the hypothalamus¹⁹ (the same areas of the brain turned on by orgasm; the bigger the orgasm, the more these cells are “turned on”²⁰). These hypothalamic neurons have axons that deliver OT both locally and peripherally.

The brain has high levels of OTRs to receive a wide array of signals. Oxytocin acts as a neurotransmitter signaling the amygdala (seat of faith vs. fear), the nucleus accumbens (sense of well-being), and the hippocampus (home of short-term memory and confidence)²¹. Oxytocin traverses cerebral regions by diffusing across neural tissue, like you would cut across lanes to get to an off-ramp on a freeway.²² There are OTR receptors throughout the entire spinal cord.²³

Connection.

Animal model research emphasizes a strong relationship between the expression of OT in the brain and the ability to have socially monogamous *attachment* behavior. These investigations began with the vole. It's amazing research.

Two closely-related species of voles have exact opposite relationship styles: one is monogamous, mating for life, while the other is promiscuous, choosing to be a forever player. What's the biological difference? The monogamous prairie vole has many more oxytocin and vasopressin (a playmate with oxytocin) receptors and activity in the brain. In comparison, the polygamous vole has much less such bonding receptors, and thus, more sleuthing mating behaviors.

Researchers have gone to the trouble of reversing these mating behaviors. They accomplished this by re-engineering Mother Nature. By altering OT genes, they could morph typically promiscuous male voles into becoming devoted monogamous voles, and typically philandering male voles into acting less promiscuous. How? They altered the numbers of oxytocin genes. By reducing or increasing oxytocin signals (and its cohort, vasopressin) in the brain, they could reproducibly alter biologic desire for either monogamy or bigamy^{24 25} (though some say this should be dubbed “pig-amy”).

Moving forward from these findings, Young and Wang manipulated three attachment hormone musketeers (oxytocin, vasopressin and dopamine) and influenced preference of one beloved over another. They “gene-jerry-rigged”

whom the animals would choose to mate. They named this the neuro-biological model of pair bonding²⁶. A number of researchers have pleaded the case that this is how humans basically meet, mingle and mate, too^{27 28}.

We know moms and babes bond through oxytocin. Magnetic imaging of the brains of mothers who see photos of their own infants (compared to pics of matched control infants unknown to them), show the areas of the brain that “activate” are flush with oxytocin, vasopressin, and dopamine receptors²⁹.

It’s clear. Oxytocin deserves to be called “the cuddle hormone,” “the love hormone,” or “the cuddle chemical.”

Stress.

Oxytocin helps buffer stress. It has hormonal influence over the hypothalamus/pituitary/adrenal axis (HPA axis). At various levels OT helps the host cope with stress and promotes anti-anxious reactions³⁰. In other words, OT signaling reduces the font size of suffering caused by stress. In fact, oxytocin studies show that replacement reduces posttraumatic stress disorder symptoms.

Sex Hormones and Oxytocin.

Sex steroid hormones—estrogen, testosterone and progesterone—intimately interact with OTR and are part of sex hormonal influence over human emotions. Estrogens act synergistically with OT by enhancing its anxiolytic effects and increasing OTR levels. A single dose of estradiol increases plasma OT levels in women³¹ (one of the many reasons estrogen replacement makes many women enjoy happier moods and avoid anti-depressants) and a metabolite of testosterone (nicknamed 3beta-diol) has similar input in the brain and other critical areas, such as within the HPA axis.

Estrogen Receptor β .

Estrogen has two major receptors that receive estrogen signals: ER alpha and ER beta. ER beta is an oncogene suppressor (protects against cancer) and anti-inflammatory molecule balancing out the pro-growth signals of ER alpha. Areas in the brain with OTRs stunningly overlap with exactly where ER beta-receptors live³².

Activation of ER beta normalizes HPA axis activity and acts to buffer stress and anxiety. Approximately 85% of OT neurons in the pituitary “co-express” ER beta! There is grand crosstalk between OT and ER beta throughout the body.

There appears to be a “best-friendship” between oxytocin and estrogen receptor beta, in that they mutually protect diverse tissues.

The multiple interplays are just now being explored. I prophesize the “good” and “bad” roles of oxytocin and estrogen receptor beta will takes twists and turns because in some cellular places (like the breast, prostate and brain) *ER beta dominance* (having many of these receptors) is what we want for tissue protection, but in other conditions (like endometriotic implants and dysfunctional endothelium) this is not always the case.

There also appears to be a “threesome” between a metabolite of testosterone (3B-diol—itself a promoter of ER beta) and ER beta and OT. All three synergize, especially in the brain and the vagus nerve.

Vagal or Buddhist Nerve Highway.

In utero, when the fetus is developing, a mass of cells that are to become our brain and gut divide in half, and one cellular clump travels northerly to the brain and the other southerly to the gut. What connects the two throughout life is the vagus nerve. It’s the second largest nerve system after the spinal cord. It’s the longest cranial nerve, extending from the brain to the gut and other crucial organs. It starts in the brainstem behind the ears, travels down each side of the neck, across the chest and throughout the abdomen. It connects the brain to the stomach and digestive tract and many other organs like the lungs and the heart.

The vagus nerve is a bundle of multiple thousands of nerve fibers, of which 80% are sensory, meaning these nerves report and reinforce back to the brain what’s going on in the gut and the rest of the body. It’s *cellular Big Brother*. The vagus nerve is a crucial part of the parasympathetic nervous system (though some is sympathetic, too). It is mostly the *opposite* of flight and flight.

Healthy vagal tone creates calm. Everyone has his or her own *vagal footprint*. The better the vagal tone, the less ruffled we are by stress and the more cast iron stomachs we seem to enjoy. A healthy digestive tract is mostly para-sympathetically “vagal.”

The healthier your vagal tone, the lower your level of cellular inflammation, or the faster you bring inflamed tissues back to normal after infection, or the more peaceful your moods or the faster recovery back to calm after an emotional storm has hit³³.

Oxytocin appears to be a major hormone player traveling vagal highways, maintaining calm, hormonal satiety and peace³⁴, suppressing inflammation and more. Being a hormone of connectivity, oxytocin upregulation in the vagal nerve—this massive internal feed back loop— may be part of feeling well and right with the world. Meditation boosts vagal tone and oxytocin³⁵.

Again, cross talk abounds. The vagus nerve is not only flush with oxytocin receptors, this large feed back nerve also influences the number of estrogen receptors in the nervous system and brain³⁶. Remarkable!

Romantic Love.

Adults shown photos of a romantic partner with whom they are “intensely in love” light up brain areas flush with oxytocin, vasopressin, and dopamine receptors³⁷.

A number of studies have looked at mating under experimental conditions, before and after orgasm, and when giving couples nasal administration of oxytocin, which delivers it directly to the brain. These have been done in both observational manners (not randomized controlled) and in double blind, placebo-controlled scientific experimental design. These studies are where the hormonal rubber meets the enhancement effectiveness road.

Oxytocin replacement has been shown to create more pleasurable orgasms and a stronger sense of empathy in both men and women. Men given OT intranasally report the biggest bang, perhaps since they naturally, during orgasm, make less oxytocin than women, so any bump *up* might be more noticed.

Since men produce less oxytocin, which is a bonding hormone, men are less vulnerable to intimacy attachment compared to women^{38 39}. The highest experimental recorded levels of oxytocin, by the way, were demonstrated in women who were multi-orgasmic⁴⁰. The more oxytocin, the more orgasms—if a woman is capable of having these types of releases. (My theory is that all women are capable but not all are hormonally replete, or in shape emotionally or physically, or they or their partner have simply not been taught how. This is discussed in detail with helpful to-dos in SEXY BRAIN see below.)

Orgasm.

When orgasming, oxytocin levels are significantly increased in the brains of both men and women. But, oh so much more in ladies. Oxytocin remains elevated for about five minutes and then levels rapidly decline. Much less is produced by masturbation or sex without orgasm^{41 42}. If you are solo, you can love the one you're with, but you won't get as much oxytocin signaling.

During orgasm, the woman wins out in that her brain, proven by PET-neuroimaging, activates the pituitary more than the guy⁴³. When she orgasms, her pituitary is tremendously *turned on* to secrete more oxytocin and prolactin. So, when she orgasms, she longs to bond and has deep satisfaction (from the prolactin, a satiety hormone in this scenario) with that sensation. The man's pituitary is less turned on. Produces less oxytocin. And less bonding sensation.

No matter how much a "friend with benefits" male lover might insist a liaison is only a friendly wham bang, if it's done repetitively enough, and she orgasms enough, she'll bond with him. Her brain and hormones make her do it. He will only bond if his emotions come along for the ride. But he does not bond based on orgasms alone.

Social Attachment.

If oxytocin helps bond, why not use it clinically when there are social bonding issues? Some forward-thinking neurologists and functional medicine docs are using oxytocin replacement therapy to treat specific conditions of "disrupted attachment," such as schizophrenia, eye contact disorders, social discomfort and phobias. It's even being used to boost decision-making processes when the lack of this ability is disabling.

Case Studies: Hormones Are Stranger Than Fiction

(I've had patients where oxytocin replacement therapy did not improve their problems, but the following are a few examples of effective responses, some rather startling.)

Patient One. Woman with an attachment disorder, that first started when she was pregnant with her first child, in her first marriage. At the end of the first trimester she had an episode that landed her in the ER. She felt that she had a mini-stroke and half of her body went numb. Nothing significant was found

on imaging or exams. Since that time, she claimed that she had a flat affect and was unable to bond. When her child was born, she could not bond. She no longer wanted intimacy or even to interact socially with her husband, who eventually left her. She was then in a second marriage and had the one daughter from the previous marriage. She couldn't seem to bond with either daughter or the new husband, who she said was a very good man. She now feared losing this marriage, too. She felt the fault was hers and she wanted to know if hormone therapy could help her.

She was put on a 200 IU oxytocin lozenge (at that time I was unaware of the better clinical responses with nasal applications). Within one month she returned and reported that both relationships with her daughter and husband were improved. She wanted sex and enjoyed it. She had good feelings during sex, which she hadn't experienced for years. She was now doing things with her daughter, like dance classes and hugging her. This was amazing to her. She cried in the office as she described feeling human for the first time in many years. She finally had hope.

Patient Two and Three. 39-year old woman was married to a 25-year old man who was a photographer in the model industry. She had gained weight and he had lost interest. He was used to looking at slim models all day long. They were religious, positive people, devoted to each other. In the office they spoke kindly and frankly in front of each other discussing their conundrum. He loved her but he no longer desired or enjoyed sex as much with her. She was on life-long antidepressants (which she felt had put on her weight) and couldn't get off due to fierce historical rebound issues. They wanted her to lose weight and him to gain interest, and perhaps even for her to get off antidepressants.

They both went on oxytocin (24 IU in one nostril TID) and also before and during any sexual encounter. They informed me that within several days their intimacy was better than it had been in years. They felt their marriage was back on track. It's half a year later and they are doing better than ever. She has still not tapered off the antidepressant.

Patient Four. I worked with this 36-year old intelligent woman for a year and got nowhere. She had a life-long history of severe constipation that severely reduced the quality of her life. She had numerous colonoscopies and the gastroenterologists had consistently reported to her that she had a "dead" area in her sigmoid colon. It could not be "revived" and surgery was

her only answer. She had tried hormone replacement, fermented foods, fiber and seeds, neurotransmitter balancing, exercise, colonic therapy, thyroid replacement, and still she was limited in what she could eat and prone to severe and constant flatulence and pain. She only eliminated once every two weeks. It took a lot to achieve that. She had tried numerous digestive enzymes, stomach acid replacement, and was down to only being able to eat a handful of foods without constant pain and bloat. I offered oxytocin as a last resort.

The first week she did 24 IU [twice a day] in one nostril, which changed nothing. I happened to ask her, after that first week, if the oxytocin by chance had made her feel any more intimate or sexy with her husband. It was then, for the first time in a year, she confided that she did not view herself as a very “connected” person. That even though she loved her husband and her kids and did right by them, she was not connected to them like she thought a true loving person would be. On the third week, her dosage was increased to one spray in each nostril (three times a day) and before sex and during sex, which she reported they did once a week. A follow-up phone call within a week found her feeling more at peace with life, and miraculously going easily to the bathroom twice daily for the first time in her life. She now had no gas or belly pain, and could consume a more diverse diet without issues.

The intestinal area is lined with oxytocin receptors. Studies have shown oxytocin to have anti-colitis action in rats. In-vitro studies have shown it to protect enterocytes and to have protective gut anti-inflammatory, motility, and gut wall enhancing permeability actions^{44 45}.

Patient Five. Woman in her late 20’s with trouble with portion control. She had a history of ulcerative colitis and would have flare-ups if she ate too much, which kept her in a flare-up loop, as she continuously ate too much. One week on 24 IU intranasal spray in one nostril BID accomplished nothing, but when we increased it to one spray in each nostril TID right before eating, she was able to eat less, lose weight, and avoid continuous flare-ups. Oxytocin has also been shown to act as an anti-inflammatory in the gut.

Future Applications.

Because oxytocin receptors are so global, stimulation of them by intranasal oxytocin replacement is being looked at for diverse disorders. Oxytocin cream lubricates the vaginal vault in similar ways to that of estrogens, healing, soothing and lubricating the mucosa, but without activating the estrogen receptor. Thus, OT (in a gel delivery system, NOT cream) is safe for high-risk women to reverse vaginal atrophy⁴⁶ and reduce pain on intercourse.

Oxytocin signaling is being investigated as an anti-aging tool to protect muscle mass as we age⁴⁷ (muscles are exceptionally flush with OTR and signaling helps maintain fiber mass), to reduce overeating by reducing caloric intake⁴⁸, may even be used to decrease leaky gut and systemic inflammation⁴⁹, and possibly as breast tissue protector⁵⁰.

Oxytocin might even be linked to stimulating the newly found *happiness epicenter* in the brain^{51 52}.

Up with oxytocin.

Or shall I say, up your nose with it.

Resources for You

Want to hear more about Oxytocin? Listen to “Episode 6: Oxytocin” on my podcast, Dr. Berkson's Best Health Radio.

Please visit DrLindseyBerkson.com for a wealth of cutting edge information on hormones, nutrition and healthy living. Receive a free eBook on how to sleuth hidden carbs out of your foods, read the latest blog, listen to my podcast, learn about my new courses or schedule a consultation with me.

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