Oxytocin

From Wikipedia, the free encyclopedia

Not to be confused with OxyContin.

Oxytocin

Systematic (IUPAC) name

1-((4R,7S,10S,13S,16S,19R)-19-amino-7-(2-amino-2-oxoethyl)-10-(3-amino-3-oxopropyl)-16-(4-hydroxybenzoyl)-13-[(1S)-1-methylpropyl]--pentaoco-1,2-dithia-5,8,11,14,17-pentaazacycloicosan-4-yl]carbonyl)-,17-penL-prolyl-L-leucylglycinamide

Clinical data

**Trade names**  Pitocin
### AHFS/Drugs.com monograph

**Pregnancy cat.**  A (AU)

**Legal status**  POM (UK) R-only (US)

**Routes**  Intranasal, IV, IM

### Pharmacokinetic data

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<td><strong>Excretion</strong></td>
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### Identifiers

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### Chemical data

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**SMILES** eMolecules & PubChem

**InChI** show

[× (what is this?) (verify)]

Oxytocin (Oxt) (/ˈɒkstəˌtɪn/) is a mammalian hormone that acts primarily as a neuromodulator in the brain.

Oxytocin is best known for its roles in sexual reproduction, in particular during and after childbirth. It is released in large amounts after distension of the cervix and uterus during labor, facilitating birth, and after stimulation of the nipples, facilitating breastfeeding.

Recent studies have begun to investigate oxytocin's role in various behaviors, including *orgasm*, social recognition, *pair bonding*, *anxiety*, and maternal behaviors.[1] For this reason, it is sometimes referred to as the "love hormone." The inability to secrete oxytocin and feel empathy is linked to *sociopathy*, *psychopathy*, *narcissism* and general *manipulativeness*. [2]

The word oxytocin was derived from the Greek ὄκυτοκίνη, *ōkytokinē*, meaning "quick birth", after its uterine-contracting properties were discovered by British pharmacologist Sir Henry Hallett Dale in 1906.[3] The milk ejection property of oxytocin was described by Ott and Scott in 1910[4] and by Schafer and Mackenzie in 1911.[5] The nine amino acid sequence of oxytocin was elucidated by Vincent du Vigneaud et al. and by Tuppy in 1953.[6] and synthesized biochemically soon after by du Vigneaud et al. in 1953.[7] Oxytocin was the very first polypeptide hormone to be sequenced and synthesized. Du Vigneaud states in his publication of 1954 "This synthesis thus constitutes the first synthesis of a polypeptide hormone".[8]
Structure and relation to vasopressin

Oxytocin is a peptide of nine amino acids (a nonapeptide). Its systematic name is cysteine-tyrosine-isoleucine-glutamine-asparagine-cysteine-proline-leucine-glycine-amine (cys – tyr – ile – gln – asn – cys – pro – leu – gly - NH₂, or CYIQNCPLG-NH₂). The cysteine residues form a disulfide bond. Oxytocin has a molecular mass of 1007 daltons. One international unit (IU) of oxytocin is the equivalent of about 2 micrograms of pure peptide.

The biologically active form of oxytocin, commonly measured by RIA and/or HPLC techniques, is also known as the octapeptide "oxytocin disulfide" (oxidized form), but oxytocin also exists as a reduced dithiol nonapeptide called oxytoceine. It has been theorized that open chain oxytoceine (the reduced form of oxytocin) may also act as a free radical scavenger (by donating an electron to a free radical); oxytoceine may then be oxidized back to oxytocin via the redox potential of dehydroascorbate <--> ascorbate.
Oxytocin (ball-and-stick) bound to its carrier protein neurophysin (ribbons)

The structure of oxytocin is very similar to that of vasopressin (cys–tyr–phe–gln–asn–cys–pro–arg–gly–NH₂), also a nonapeptide with a sulfur bridge, whose sequence differs from oxytocin by 2 amino acids. A table showing the sequences of members of the vasopressin/oxytocin superfamily and the species expressing them is present in the vasopressin article. Oxytocin and vasopressin were isolated and synthesized by Vincent du Vigneaud in 1953, work for which he received the Nobel Prize in Chemistry in 1955.

Oxytocin and vasopressin are the only known hormones released by the human posterior pituitary gland to act at a distance. However, oxytocin neurons make other peptides, including corticotropin-releasing hormone (CRH) and dynorphin, for example, that act locally. The magnocellular neurons that make oxytocin are adjacent to magnocellular neurons that make vasopressin, and are similar in many respects.

**Actions**

Oxytocin has peripheral (hormonal) actions, and also has actions in the brain. The actions of oxytocin are mediated by specific, high-affinity oxytocin receptors. The oxytocin receptor is a G-protein-coupled receptor that requires Mg²⁺ and cholesterol. It belongs to the rhodopsin-type (class I) group of G-protein-coupled receptors.

**Peripheral (hormonal) actions**

The peripheral actions of oxytocin mainly reflect secretion from the pituitary gland. (See oxytocin receptor for more detail on its action.)
- **Letdown reflex** – in lactating (breastfeeding) mothers, oxytocin acts at the mammary glands, causing milk to be 'let down' into subareolar sinuses, from where it can be excreted via the nipple. Sucking by the infant at the nipple is relayed by spinal nerves to the hypothalamus. The stimulation causes neurons that make oxytocin to fire action potentials in intermittent bursts; these bursts result in the secretion of pulses of oxytocin from the neurosecretory nerve terminals of the pituitary gland.

- **Uterine contraction** – important for cervical dilation before birth and causes contractions during the second and third stages of labor. Oxytocin release during breastfeeding causes mild but often painful contractions during the first few weeks of lactation. This also serves to assist the uterus in clotting the placental attachment point postpartum. However, in knockout mice lacking the oxytocin receptor, reproductive behavior and parturition are normal.

- **Social behavior** and **Wound healing** – Oxytocin is also thought to modulate inflammation by decreasing certain cytokines. Thus, the increased release in oxytocin following positive social interactions has the potential to improve wound healing. A study by Marazziti and colleagues used heterosexual couples to address this possibility. They found that increases in plasma oxytocin following a social interaction were correlated with faster wound healing. They hypothesized that this was due to oxytocin reducing inflammation, thus allowing the wound to heal faster. This study provides preliminary evidence that positive social interactions may directly impact aspects of health.

- The relationship between oxytocin and human sexual response is unclear. At least two non-controlled studies have found increases in plasma oxytocin at orgasm – in both men and women. Plasma oxytocin levels are notably increased around the time of self-stimulated orgasm and are still higher than baseline when measured 5 minutes after self arousal. The authors of one of these studies speculated that oxytocin's effects on muscle contractibility may facilitate sperm and egg transport. In a study that measured oxytocin serum levels in women before and after sexual stimulation, the author suggests that oxytocin serves an important role in sexual arousal. This study found that genital tract stimulation resulted in increased oxytocin immediately after orgasm. Another study that reports increases of oxytocin during sexual arousal states that it could be in response to nipple/areola, genital, and/or genital tract stimulation as confirmed in other mammals. Murphy et al. (1987), studying men, found that oxytocin levels were raised throughout sexual arousal and there was no acute increase at orgasm. A more recent study of men found an increase in plasma oxytocin immediately after orgasm, but only in a portion of their sample that did not reach statistical significance. The authors noted that these changes "may simply reflect contractile properties on reproductive tissue."

Oxytocin evokes feelings of contentment, reductions in anxiety, and feelings of calmness and security around the mate. Many studies have already shown a correlation of oxytocin with human bonding, increases in trust, and decreases in fear. One study confirmed that there is a positive correlation between oxytocin plasma levels
and an anxiety scale measuring the adult romantic attachment. This suggests that oxytocin may be important for the inhibition of brain regions that are associated with behavioral control, fear, and anxiety, thus allowing orgasm to occur.

- Due to its similarity to vasopressin, it can reduce the excretion of urine slightly. In several species, oxytocin can stimulate sodium excretion from the kidneys (natriuresis), and, in humans, high doses of oxytocin can result in hyponatremia.

- Oxytocin and oxytocin receptors are also found in the heart in some rodents, and the hormone may play a role in the embryonal development of the heart by promoting cardiomyocyte differentiation. However, the absence of either oxytocin or its receptor in knockout mice has not been reported to produce cardiac insufficiencies.

- Modulation of hypothalamic-pituitary-adrenal axis activity. Oxytocin, under certain circumstances, indirectly inhibits release of adrenocorticotropic hormone and cortisol and, in those situations, may be considered an antagonist of vasopressin.

- Autism. Oxytocin may play a role in autism and may be an effective treatment for autism's repetitive and affiliative behaviors. Oxytocin treatments also resulted in an increased retention of affective speech in adults with autism. Two related studies in adults, in 2003 and 2007, found that oxytocin decreased repetitive behaviors and improved interpretation of emotions. More recently, intranasal administration of oxytocin was found to increase emotion recognition in children as young as 12 who are diagnosed with autism spectrum disorders. Oxytocin has also been implicated in the etiology of autism, with one report suggesting that autism is correlated with genomic deletion of the gene containing the oxytocin receptor gene (OXTR). Studies involving Caucasian and Finnish samples and Chinese Han families provide support for the relationship of OXTR with autism. Autism may also be associated by an aberrant methylation of OXTR, as reported by Gregory and colleagues. After treatment with inhaled oxytocin, autistic patients exhibit more appropriate social behavior. While this research suggests some promise, further clinical trials of oxytocin are required to demonstrate potential benefit and side-effects in the treatment of autism. As such, researchers do not recommend use of oxytocin as a treatment for autism outside of clinical trials.

- Increasing trust and reducing fear. In a risky investment game, experimental subjects given nasally administered oxytocin displayed "the highest level of trust" twice as often as the control group. Subjects who were told that they were interacting with a computer showed no such reaction, leading to the conclusion that oxytocin was not merely affecting risk-aversion. Nasally administered oxytocin has also been reported to reduce fear, possibly by inhibiting the amygdala (which is thought to be responsible for...
fear responses). Indeed, studies in rodents have shown that oxytocin can efficiently inhibit fear responses by activating an inhibitory circuit within the amygdala. Some researchers have argued that oxytocin has a general enhancing effect on all social emotions, since intranasal administration of oxytocin also increases envy and schadenfreude.

- Affecting generosity by increasing empathy during perspective taking. In a neuroeconomics experiment, intranasal oxytocin increased generosity in the Ultimatum Game by 80% but has no effect in the Dictator Game that measures altruism. Perspective-taking is not required in the Dictator Game, but the researchers in this experiment explicitly induced perspective-taking in the Ultimatum Game by not identifying to participants which role they would be in. Serious methodological questions have arisen, however, with regards to the role of oxytocin in trust and generosity.

- Certain learning and memory functions are impaired by centrally administered oxytocin. Also, systemic oxytocin administration can impair memory retrieval in certain aversive memory tasks. Interestingly, oxytocin does seem to facilitate learning and memory specifically for social information. Healthy males administered intranasal oxytocin show improved memory for human faces, in particular happy faces. They also show improved recognition for positive social cues over threatening social cues and improved recognition of fear.

- Empathy in healthy males has been shown to be increased after intranasal oxytocin. This is most likely due to the effect of oxytocin in enhancing eye gaze. There is some discussion about which aspect of empathy oxytocin might alter - for example, cognitive vs. emotional empathy.

**Actions within the brain**

Oxytocin secreted from the pituitary gland cannot re-enter the brain because of the blood-brain barrier. Instead, the behavioral effects of oxytocin are thought to reflect release from centrally projecting oxytocin neurons, different from those that project to the pituitary gland, or that are collaterals from them. Oxytocin receptors are expressed by neurons in many parts of the brain and spinal cord, including the amygdala, ventromedial hypothalamus, septum, nucleus accumbens, and brainstem.

- Sexual arousal. Oxytocin injected into the cerebrospinal fluid causes spontaneous erections in rats, reflecting actions in the hypothalamus and spinal cord. Centrally administrated oxytocin receptor antagonists can prevent non-contact erections, which is a measure of sexual arousal. Studies using oxytocin antagonists in female rats provide data that oxytocin increases lordosis behavior, indicating an increase in sexual receptivity.
Bonding. In the Prairie Vole, oxytocin released into the brain of the female during sexual activity is important for forming a monogamous pair bond with her sexual partner. Vasopressin appears to have a similar effect in males. Oxytocin has a role in social behaviors in many species, and so it seems likely that it also does in humans. In 2003, a study showed that in both humans and dogs oxytocin levels in the blood rose after five to twenty-four minutes of a petting session. It is possible that this plays a role in the emotional bonding between humans and dogs.

Maternal behavior. Female rats given oxytocin antagonists after giving birth do not exhibit typical maternal behavior. By contrast, virgin female sheep show maternal behavior toward foreign lambs upon cerebrospinal fluid infusion of oxytocin, which they would not do otherwise. Oxytocin is involved in the initiation of maternal behavior, not its maintenance; for example, it is higher in mothers after they interact with unfamiliar children rather than their own.

According to some studies in animals, oxytocin inhibits the development of tolerance to various addictive drugs (opiates, cocaine, alcohol) and reduces withdrawal symptoms.

Preparing fetal neurons for delivery. Crossing the placenta, maternal oxytocin reaches the fetal brain and induces a switch in the action of neurotransmitter GABA from excitatory to inhibitory on fetal cortical neurons. This silences the fetal brain for the period of delivery and reduces its vulnerability to hypoxic damage.

MDMA (ecstasy) may increase feelings of love, empathy, and connection to others by stimulating oxytocin activity via activation of serotonin 5-HT1A receptors, if initial studies in animals apply to humans. The anxiolytic Buspar (buspirone) also appears to produce some or all of its effect via 5-HT1A receptor-induced oxytocin stimulation.

Romantic Attachment – In some studies, high levels of plasma oxytocin have been correlated with romantic attachment. For example, if a couple is separated for a long period of time anxiety can increase due to the lack of physical affection. The authors of a recent study suggest that oxytocin may aid romantically attached couples by decreasing their feelings of anxiety when they are separated.