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**Oxytocin** (**Oxt**) is a [hormone](/wiki/Hormone), [neuropeptide](/wiki/Neuropeptide), and medication.<ref name=AHFS2015/>[[1]](#cite_note-1) As a medication, it is used to cause contraction of the [uterus](/wiki/Uterus) in order to [start labor](/wiki/Labor_induction) or [increase the speed of labor](/wiki/Augmentation_(obstetrics)), and to stop [bleeding following delivery](/wiki/Postpartum_bleeding).<ref name=AHFS2015/> For this purpose, it is given either by [injection into a muscle](/wiki/Intramuscular) or [into a vein](/wiki/Intravenously).<ref name=AHFS2015>[Template:Cite web](/wiki/Template:Cite_web)</ref>

The use of oxytocin as a medication can result in excessive contraction of the uterus that can cause distress in an unborn baby. Common side effects in the mother include nausea and a [slow heart rate](/wiki/Bradycardia). Serious side effects include [water intoxication](/wiki/Water_intoxication) with an excessive dose and [uterus rupture](/wiki/Uterus_rupture). Allergic reactions may also occur.<ref name=AHFS2015/>

Oxytocin is normally produced by the [paraventricular nucleus](/wiki/Paraventricular_nucleus) of the [hypothalamus](/wiki/Hypothalamus) and released by the [posterior pituitary](/wiki/Posterior_pituitary).[[2]](#cite_note-2) It plays a role in social bonding, [sexual reproduction](/wiki/Sexual_reproduction) in both sexes, and during and after [childbirth](/wiki/Childbirth).[[3]](#cite_note-3) Oxytocin is released into the bloodstream as a hormone in response to stretching of the [cervix](/wiki/Cervix) and [uterus](/wiki/Uterus) during labor and with stimulation of the nipples from [breastfeeding](/wiki/Breastfeeding).<ref name=Chi2012>[Template:Cite book](/wiki/Template:Cite_book)</ref> This helps with birth, [bonding with the baby](/wiki/Maternal_bonding), and [milk production](/wiki/Lactation).<ref name=Chi2012/>[[4]](#cite_note-4) Oxytocin was discovered in 1952.[[5]](#cite_note-5) It is on the [World Health Organization's List of Essential Medicines](/wiki/World_Health_Organization's_List_of_Essential_Medicines), the most important medications needed in a basic [health system](/wiki/Health_system).[[6]](#cite_note-6) [Template:As of](/wiki/Template:As_of), the wholesale cost in the [developing world](/wiki/Developing_world) is [Template:Currency](/wiki/Template:Currency)–0.56 per dose.[[7]](#cite_note-7)[Template:TOC limit](/wiki/Template:TOC_limit)

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## Physiological effects {{anchor|Actions within the brain}}[[edit](/index.php?title=(none)&action=edit&section=1)]

[Template:Primary sources](/wiki/Template:Primary_sources) Oxytocin has peripheral (hormonal) actions, and also has actions in the brain. Its actions are mediated by specific, [oxytocin receptors](/wiki/Oxytocin_receptor). The oxytocin receptor is a [G-protein-coupled receptor](/wiki/G-protein-coupled_receptor) that requires [magnesium](/wiki/Magnesium) and [cholesterol](/wiki/Cholesterol). It belongs to the [rhodopsin](/wiki/Rhodopsin)-type (class I) group of G-protein-coupled receptors.

Studies have looked at oxytocin's role in various behaviors, including [orgasm](/wiki/Orgasm), [social recognition](/wiki/Social_recognition), [pair bonding](/wiki/Pair_bond), [anxiety](/wiki/Anxiety), and maternal behaviors.[[8]](#cite_note-8) The peripheral actions of oxytocin mainly reflect secretion from the [pituitary gland](/wiki/Pituitary_gland). 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.[[9]](#cite_note-9) Oxytocin receptors are expressed by neurons in many parts of the brain and spinal cord, including the [amygdala](/wiki/Amygdala), [ventromedial hypothalamus](/wiki/Ventromedial_hypothalamus), [septum](/wiki/Septum), [nucleus accumbens](/wiki/Nucleus_accumbens), and [brainstem](/wiki/Brainstem).

* [Milk ejection reflex](/wiki/Lactation#Milk_ejection_reflex)/Letdown reflex: In [lactating](/wiki/Lactation) ([breastfeeding](/wiki/Breastfeeding)) mothers, oxytocin acts at the [mammary glands](/wiki/Mammary_gland), causing milk to be 'let down' into [subareolar](/wiki/Areola) [sinuses](/wiki/Sinuses), from where it can be excreted via the [nipple](/wiki/Nipple).[[10]](#cite_note-10) Suckling by the [infant](/wiki/Infant) at the nipple is relayed by spinal nerves to the [hypothalamus](/wiki/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](/wiki/Uterine_contraction): Important for [cervical dilation](/wiki/Cervical_dilation) before birth, oxytocin causes contractions during the second and third stages of [labor](/wiki/Labor_(childbirth)). 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](/wiki/Knockout_mouse) lacking the oxytocin receptor, reproductive behavior and [parturition](/wiki/Parturition) are normal.[[11]](#cite_note-11)\* [Social behavior](/wiki/Social_behavior)[[12]](#cite_note-12)[[13]](#cite_note-13) and [wound healing](/wiki/Wound_healing): Oxytocin is also thought to modulate [inflammation](/wiki/Inflammation) by decreasing certain [cytokines](/wiki/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 investigate this possibility. They found increases in plasma oxytocin following a social interaction were correlated with faster wound healing. They hypothesized this was due to oxytocin reducing inflammation, thus allowing the wound to heal more quickly. This study provides preliminary evidence that positive social interactions may directly influence aspects of health.[[14]](#cite_note-14) According to a study published in 2014, silencing of oxytocin receptor interneurons in the medial prefrontal cortex (mPFC) of female mice resulted in loss of social interest in male mice during the sexually receptive phase of the estrous cycle.[[15]](#cite_note-15):Oxytocin evokes feelings of contentment, reductions in anxiety, and feelings of calmness and security when in the company of the mate.[[16]](#cite_note-16) This suggests oxytocin may be important for the inhibition of the brain regions associated with behavioral control, fear, and anxiety, thus allowing orgasm to occur. Research has also demonstrated that oxytocin can decrease anxiety and protect against stress, particularly in combination with social support.[[17]](#cite_note-17)\* Due to its similarity to [vasopressin](/wiki/Vasopressin), it can reduce the excretion of [urine](/wiki/Urine) slightly. In several species, oxytocin can stimulate sodium excretion from the kidneys (natriuresis), and, in humans, high doses can result in [hyponatremia](/wiki/Hyponatremia).
* Oxytocin and oxytocin receptors are also found in the [heart](/wiki/Heart) in some rodents, and the hormone may play a role in the embryonal development of the heart by promoting [cardiomyocyte](/wiki/Cardiomyocyte) differentiation.[[18]](#cite_note-18)[[19]](#cite_note-19) However, the absence of either oxytocin or its receptor in knockout mice has not been reported to produce cardiac insufficiencies.[[11]](#cite_note-11)\* Modulation of [hypothalamic-pituitary-adrenal axis](/wiki/Hypothalamic-pituitary-adrenal_axis) activity: Oxytocin, under certain circumstances, indirectly inhibits release of [adrenocorticotropic hormone](/wiki/Adrenocorticotropic_hormone) and [cortisol](/wiki/Cortisol) and, in those situations, may be considered an antagonist of vasopressin.[[20]](#cite_note-20)\* [Autism](/wiki/Autism_spectrum): Oxytocin may play a role in autism and may be an effective [treatment for autism's](/wiki/Autism_therapies#Prescription_medication) repetitive and affiliative behaviors.[[21]](#cite_note-21) Oxytocin treatments also resulted in an increased retention of affective speech in adults with autism.[[22]](#cite_note-22) Two related studies in adults, in 2003 and 2007, found 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.[[23]](#cite_note-23) Oxytocin has also been implicated in the etiology of autism, with one report suggesting autism is correlated with genomic deletion of the gene containing the oxytocin receptor gene ([*OXTR*](/wiki/Oxytocin_receptor)). Studies involving Caucasian and Finnish samples and Chinese Han families provide support for the relationship of *OXTR* with autism.[[22]](#cite_note-22)[[24]](#cite_note-24) Autism may also be associated with an aberrant methylation of *OXTR*.[[22]](#cite_note-22) After treatment with inhaled oxytocin, autistic patients exhibit more appropriate social behavior.[[25]](#cite_note-25) 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.[[26]](#cite_note-26)\* Nasally administered oxytocin has also been reported to reduce [fear](/wiki/Fear), possibly by inhibiting the [amygdala](/wiki/Amygdala) (which is thought to be responsible for fear responses).[[27]](#cite_note-27) Indeed, studies in rodents have shown oxytocin can efficiently inhibit fear responses by activating an inhibitory circuit within the amygdala.[[28]](#cite_note-28)[[29]](#cite_note-29) Some researchers have argued oxytocin has a general enhancing effect on all social emotions, since intranasal administration of oxytocin also increases [envy](/wiki/Envy) and [*Schadenfreude*](/wiki/Schadenfreude).[[30]](#cite_note-30)\* [Trust](/wiki/Trust_(social_sciences)) is increased by oxytocin.[[31]](#cite_note-31)[[32]](#cite_note-32)[[33]](#cite_note-33) Disclosure of emotional events is a sign of trust in humans. When recounting a negative event, humans who receive [intranasal](/wiki/Intranasal) oxytocin share more emotional details and stories with more emotional significance.[[32]](#cite_note-32) Humans also find faces more trustworthy after receiving intranasal oxytocin. In a study, participants who received intranasal oxytocin viewed photographs of human faces with neutral expressions and found them to be more trustworthy than those who did not receive oxytocin.[[31]](#cite_note-31) This may be because oxytocin reduces the fear of social betrayal in humans.[[34]](#cite_note-34) Even after experiencing social alienation by being excluded from a conversation, humans who received oxytocin scored higher in trust on the [Revised NEO Personality Inventory](/wiki/Revised_NEO_Personality_Inventory).[[33]](#cite_note-33) Moreover, 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 they were interacting with a computer showed no such reaction, leading to the conclusion that oxytocin was not merely affecting [risk aversion](/wiki/Risk_aversion).[[35]](#cite_note-35) When there is a reason to be distrustful, such as experiencing betrayal, differing reactions are associated with [oxytocin receptor](/wiki/Oxytocin_receptor) [gene](/wiki/Gene) ([OXTR](/wiki/OXTR)) differences. Those with the CT [haplotype](/wiki/Haplotype) experience a stronger reaction, in the form of anger, to betrayal.[[36]](#cite_note-36)\* Oxytocin affects [social](/wiki/Social_behavior) distance between adult males and females, and may be responsible at least in part for [romantic attraction](/wiki/Romance_(love)) and subsequent [monogamous](/wiki/Monogamy) pair bonding. An oxytocin nasal spray caused men in a monogamous relationship, but not single men, to increase the distance between themselves and an attractive woman during a first encounter by 10 to 15 centimeters. The researchers suggested that oxytocin may help promote fidelity within monogamous relationships.[[37]](#cite_note-37) For this reason, it is sometimes referred to as the "bonding hormone". There is some evidence that oxytocin promotes [ethnocentric](/wiki/Ethnocentric) behavior, incorporating the trust and empathy of [in-groups](/wiki/Ingroups_and_outgroups) with their suspicion and rejection of outsiders.[[12]](#cite_note-12) Furthermore, genetic differences in the [oxytocin receptor](/wiki/Oxytocin_receptor) gene (OXTR) have been associated with maladaptive social traits such as aggressive behaviour.[[38]](#cite_note-38)\* Affecting [generosity](/wiki/Generosity) by increasing empathy during perspective taking: In a [neuroeconomics](/wiki/Neuroeconomics) experiment, [intranasal](/wiki/Intranasal) oxytocin increased generosity in the [Ultimatum Game](/wiki/Ultimatum_Game) by 80%, but had no effect in the [Dictator Game](/wiki/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 into which role they would be placed.[[39]](#cite_note-39) Serious methodological questions have arisen, however, with regard to the role of oxytocin in trust and generosity.[[40]](#cite_note-40):Empathy in healthy males has been shown to be increased after intranasal oxytocin[[41]](#cite_note-41)[[42]](#cite_note-42) This is most likely due to the effect of oxytocin in enhancing eye gaze.[[43]](#cite_note-43) There is some discussion about which aspect of empathy oxytocin might alter – for example, cognitive vs. emotional empathy.[[44]](#cite_note-44)\* Certain learning and memory functions are impaired by centrally administered oxytocin.[[45]](#cite_note-45) Also, systemic oxytocin administration can impair memory retrieval in certain aversive memory tasks.[[46]](#cite_note-46) 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.[[47]](#cite_note-47)[[48]](#cite_note-48) They also show improved recognition for positive social cues over threatening social cues [[49]](#cite_note-49)[[50]](#cite_note-50) and improved recognition of fear.[[51]](#cite_note-51)\* Sexual activity: The relationship between oxytocin and human sexual response is unclear. At least two uncontrolled studies have found increases in [plasma](/wiki/Blood_plasma) oxytocin at orgasm – in both men and women.[[52]](#cite_note-52)[[53]](#cite_note-53) Plasma oxytocin levels are notably increased around the time of self-stimulated orgasm and are still higher than baseline when measured five minutes after self arousal.[[52]](#cite_note-52) The authors of one of these studies speculated that oxytocin's effects on muscle contractibility may facilitate sperm and egg transport.[[52]](#cite_note-52):In a study measuring oxytocin serum levels in women before and after [sexual stimulation](/wiki/Sexual_stimulation), the author suggests it serves an important role in [sexual arousal](/wiki/Sexual_arousal). This study found genital tract stimulation resulted in increased oxytocin immediately after orgasm.[[54]](#cite_note-54) Another study reported increases of oxytocin during sexual arousal could be in response to nipple/areola, genital, and/or genital tract stimulation as confirmed in other mammals.[[55]](#cite_note-55) Murphy et al. (1987), studying men, found oxytocin levels were raised throughout sexual arousal with no acute increase at orgasm.[[56]](#cite_note-56) 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 these changes "may simply reflect contractile properties on reproductive tissue".[[57]](#cite_note-57)\* Bonding: In the [prairie vole](/wiki/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.[[58]](#cite_note-58) Oxytocin has a role in social behaviors in many species, so it likely also does in humans. In a 2003 study, both humans and dog oxytocin levels in the blood rose after five to 24 minutes of a petting session. This possibly plays a role in the [emotional bonding between humans and dogs](/wiki/Human-canine_bond).[[59]](#cite_note-59)\* [Maternal behavior](/wiki/Maternal_bond): Female rats given oxytocin [antagonists](/wiki/Receptor_antagonist) after giving birth do not exhibit typical maternal behavior.[[60]](#cite_note-60) By contrast, virgin female sheep show maternal behavior toward foreign lambs upon [cerebrospinal fluid](/wiki/Cerebrospinal_fluid) infusion of oxytocin, which they would not do otherwise.[[61]](#cite_note-61) 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.[[62]](#cite_note-62)\* Drug interactions: According to some studies in animals, oxytocin inhibits the development of tolerance to various addictive drugs ([opiates](/wiki/Opiate), [cocaine](/wiki/Cocaine), [alcohol](/wiki/Ethanol)), and reduces [withdrawal](/wiki/Drug_withdrawal) symptoms.[[63]](#cite_note-63) [MDMA](/wiki/MDMA) (ecstasy) may increase feelings of love, empathy, and connection to others by stimulating oxytocin activity primarily via activation of [serotonin](/wiki/Serotonin) [5-HT1A receptors](/wiki/5-HT1A_receptor), if initial studies in animals apply to humans.[[64]](#cite_note-64) The [anxiolytic](/wiki/Anxiolytic) [Buspar](/wiki/Buspar) (buspirone) may produce some of its effects via 5-HT1A receptor-induced oxytocin stimulation as well.[[65]](#cite_note-65)[[66]](#cite_note-66)\* Preparing fetal neurons for delivery: Crossing the placenta, maternal oxytocin reaches the fetal brain and induces a switch in the action of neurotransmitter [GABA](/wiki/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](/wiki/Hypoxia_(medical)).[[67]](#cite_note-67)\* Romantic attachment: In some studies, high levels of [plasma](/wiki/Blood_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. Oxytocin may aid romantically attached couples by decreasing their feelings of anxiety when they are separated.[[16]](#cite_note-16)\*Feeding: Recent evidence has suggested that oxytocin neurons in the para-ventricular hypothalamus in the brain may play a key role in suppressing appetite under normal conditions and that other hypothalamic neurons may trigger eating via inhibition of these oxytocin neurons. This population of oxytocin neurons are absent in [Prader-Willi syndrome](/wiki/Prader-Willi_syndrome), a genetic disorder that leads to uncontrollable feeding and obesity, and may play a key role in its pathophysiology.[[68]](#cite_note-68)\*Group-serving dishonesty/deception: In a carefully controlled study exploring the biological roots of immoral behavior, oxytocin was shown to promote dishonesty when the outcome favored the group to which an individual belonged instead of just the individual.[[69]](#cite_note-69)\*Intergroup bonding: Oxytocin can increase positive attitudes, such as bonding, toward individuals with similar characteristics, who then become classified as “in-group” members, whereas individuals who are dissimilar become classified as “out-group” members. Race can be used as an example of in-group and out-group tendencies because society often categorizes individuals into groups based on race (Caucasian, African American, Latino, etc.). One study that examined race and empathy found that participants receiving nasally administered oxytocin had stronger reactions to pictures of in-group members making pained faces than to pictures of out-group members with the same expression.[[70]](#cite_note-70) This shows that oxytocin may be implicated in our ability to empathize with individuals of different races and could potentially translate into willingness to help individuals in pain or stressful situations. Moreover, individuals of one race may be more inclined to help individuals of the same race than individuals of another race when they are experiencing pain. Oxytocin has also been implicated in lying when lying would prove beneficial to other in-group members. In a study where such a relationship was examined, it was found that when individuals were administered oxytocin, rates of dishonesty in the participants’ responses increased for their in-group members when a beneficial outcome for their group was expected.[[71]](#cite_note-71) Both of these examples show the tendency to act in ways that benefit people with which one feels is part of their social group, or in-group. Oxytocin is not only correlated with the preferences of individuals to associate with members of their own group, but it is also evident during conflicts between members of different groups. During conflict, individuals receiving nasally administered oxytocin demonstrate more frequent defense-motivated responses toward in-group members than out-group members. Further, oxytocin was correlated with participant desire to protect vulnerable in-group members, despite that individual’s attachment to the conflict.[[72]](#cite_note-72) Similarly, it has been demonstrated that when oxytocin is administered, individuals alter their subjective preferences in order to align with in-group ideals over out-group ideals.[[73]](#cite_note-73) These studies demonstrate that oxytocin is associated with intergroup dynamics. Further, oxytocin influences the responses of individuals in a particular group to those of another group. The in-group bias is evident in smaller groups; however, it can also be extended to groups as large as one’s entire country leading toward a tendency of strong national zeal. A study done in the Netherlands showed that oxytocin increased the in-group favoritism of their nation while decreasing acceptance of members of other ethnicities and foreigners.[[12]](#cite_note-12) People also show more affection for their country’s flag while remaining indifferent to other cultural objects when exposed to oxytocin.[[74]](#cite_note-74) It has thus been hypothesized that this hormone may be a factor in xenophobic tendencies secondary to this effect. Thus, oxytocin appears to affect individuals at an international level where the in-group becomes a specific "home" country and the out-group grows to include all other countries.

### Fear and anxiety[[edit](/index.php?title=(none)&action=edit&section=2)]

Oxytocin is typically remembered for the effect it has on [prosocial behaviors](/wiki/Prosocial_behavior), such as its role in facilitating trust and attachment between individuals. Consequently, oxytocin is often referred to as the “love hormone".[[75]](#cite_note-75)[Template:Qualify evidence](/wiki/Template:Qualify_evidence) However, oxytocin has a more complex role than solely enhancing prosocial behaviors. There is consensus that oxytocin modulates [fear](/wiki/Fear) and [anxiety](/wiki/Anxiety); that is, it does not directly elicit fear or anxiety.[[76]](#cite_note-76) Two dominant theories explain the role of oxytocin in fear and anxiety. One theory states that oxytocin increases approach/avoidance to certain social stimuli and the second theory states that oxytocin increases the salience of certain social stimuli, causing the animal or human to pay closer attention to socially relevant stimuli.[[77]](#cite_note-77) Individuals who receive an intranasal dose of oxytocin identify facial expressions of disgust faster than individuals who do not receive oxytocin.[[77]](#cite_note-77)[Template:Qualify evidence](/wiki/Template:Qualify_evidence) Facial expressions of disgust are evolutionarily linked to the idea of contagion. Thus, oxytocin increases the salience of cues that imply contamination, which leads to a faster response because these cues are especially relevant for survival. In another study, after administration of oxytocin, individuals displayed an enhanced ability to recognize expressions of fear compared to the individuals who received the placebo.[[51]](#cite_note-51) Oxytocin modulates fear responses by enhancing the maintenance of social memories. Rats that are genetically modified to have a surplus of oxytocin receptors display a greater fear response to a previously conditioned stressor. Oxytocin enhances the aversive social memory, leading the rat to display a greater fear response when the aversive stimulus is encountered again.[[76]](#cite_note-76)

### Sex differences[[edit](/index.php?title=(none)&action=edit&section=3)]

It has been shown that oxytocin differentially affects males and females. Females who are administered oxytocin are overall faster in responding to socially relevant stimuli than males who received oxytocin.[[77]](#cite_note-77)[[78]](#cite_note-78) Additionally, after the administration of oxytocin, females show increased [amygdala](/wiki/Amygdala) activity in response to threatening scenes; however, males do not show increased amygdala activation. This phenomenon can be explained by looking at the role of [gonadal hormones](/wiki/Gonadal_hormones), specifically [estrogen](/wiki/Estrogen), which modulate the enhanced threat processing seen in females. Estrogen has been shown to stimulate the release of oxytocin from the [hypothalamus](/wiki/Hypothalamus) and promote receptor binding in the amygdala.[[78]](#cite_note-78) It has also been shown that testosterone directly suppresses oxytocin.[[79]](#cite_note-79) This has been hypothesized to have evolutionary significance. With oxytocin suppressed, activities such as hunting and attacking invaders would be less mentally difficult as oxytocin is strongly associated with empathy.[[80]](#cite_note-80)

### Mood and depression[[edit](/index.php?title=(none)&action=edit&section=4)]

Oxytocin produces [antidepressant](/wiki/Antidepressant)-like effects in [animal models](/wiki/Animal_model) of [depression](/wiki/Depression_(mood)),[[81]](#cite_note-81) and a deficit of it may be involved in the [pathophysiology](/wiki/Pathophysiology) of depression in humans.[[82]](#cite_note-82) The antidepressant-like effects of oxytocin are not blocked by a selective antagonist of the oxytocin receptor, suggesting that these effects are not mediated by the oxytocin receptor.[[83]](#cite_note-83) In accordance, unlike oxytocin, the selective non-peptide oxytocin receptor agonist [WAY-267,464](/wiki/WAY-267,464) does not produce antidepressant-like effects, at least in the [tail suspension test](/wiki/Tail_suspension_test).[[84]](#cite_note-84) (In contrast to WAY-267,464, [carbetocin](/wiki/Carbetocin), a close [analogue](/wiki/Structural_analog) of oxytocin and peptide oxytocin receptor agonist, notably does produce antidepressant-like effects in animals.)[[84]](#cite_note-84) As such, the antidepressant-like effects of oxytocin may be mediated by modulation of a different target, perhaps the [vasopressin V1A receptor](/wiki/Arginine_vasopressin_receptor_1A) where oxytocin is known to weakly bind as an agonist.[[85]](#cite_note-85)[[86]](#cite_note-86) [Sildenafil](/wiki/Sildenafil) has been found to enhance electrically evoked oxytocin release from the [pituitary gland](/wiki/Pituitary_gland).[[81]](#cite_note-81)[Template:Qualify evidence](/wiki/Template:Qualify_evidence) In accordance, the drug shows oxytocin-dependent antidepressant-like effects in animals, and it has proposed that sildenafil may hold promise as a potential antidepressant in humans.[[81]](#cite_note-81)

## Medical uses[[edit](/index.php?title=(none)&action=edit&section=5)]

An intravenous infusion of oxytocin is used to [induce labor](/wiki/Labor_induction) and to support labor in case of slow childbirth. It is unclear whether a high dose is better than a standard dose for labor induction. It has largely replaced [ergometrine](/wiki/Ergometrine) as the principal agent to increase uterine tone in acute [postpartum hemorrhage](/wiki/Postpartum_hemorrhage). Oxytocin is also used in [veterinary medicine](/wiki/Veterinary_medicine) to facilitate birth and to stimulate milk release. The [tocolytic](/wiki/Tocolytic) agent [atosiban](/wiki/Atosiban) (Tractocile) acts as an antagonist of oxytocin receptors; this drug is registered in many countries to suppress premature labor between 24 and 33 weeks of gestation. It has fewer side effects than drugs previously used for this purpose ([ritodrine](/wiki/Ritodrine), [salbutamol](/wiki/Salbutamol), and [terbutaline](/wiki/Terbutaline)).[[87]](#cite_note-87)

### Side effects[[edit](/index.php?title=(none)&action=edit&section=6)]

Oxytocin is relatively safe when used at recommended doses, and side effects are uncommon.[[88]](#cite_note-88) The following maternal [events](/wiki/Adverse_drug_reaction) have been reported:[[88]](#cite_note-88)

* [Subarachnoid hemorrhage](/wiki/Subarachnoid_hemorrhage)
* [Increased heart rate](/wiki/Tachycardia)
* [Decreased blood pressure](/wiki/Hypotension)
* [Cardiac arrhythmia](/wiki/Cardiac_arrhythmia) and [premature ventricular contraction](/wiki/Premature_ventricular_contraction)
* Impaired [uterine](/wiki/Uterine) blood flow
* Pelvic [hematoma](/wiki/Hematoma)
* [Afibrinogenemia](/wiki/Fibrinogen#Fibrinogen_deficiency)
* [Anaphylaxis](/wiki/Anaphylaxis)
* [Nausea](/wiki/Nausea) and [vomiting](/wiki/Vomiting)
* Increase fetal blood flow

Excessive dosage or long-term administration (over a period of 24 hours or longer) have been known to result in [tetanic](/wiki/Tetanic_contraction) uterine contractions, [uterine rupture](/wiki/Uterine_rupture), postpartum hemorrhage, and [water intoxication](/wiki/Water_intoxication), sometimes fatal.

During pregnancy, increased uterine motility has led to [decreased heart rate](/wiki/Bradycardia), cardiac [arrhythmia](/wiki/Arrhythmia), seizures, [brain damage](/wiki/Brain_damage), death in the fetus/neonate:[[88]](#cite_note-88)

### Administration[[edit](/index.php?title=(none)&action=edit&section=7)]

Oxytocin is destroyed in the [gastrointestinal tract](/wiki/Gastrointestinal_tract), so it is not active [orally](/wiki/Oral_administration) and must be administered by [injection](/wiki/Injection_(medicine)) or as [nasal spray](/wiki/Nasal_spray). The compound has a [half-life](/wiki/Half-life) of typically about three minutes in the blood when given [intravenously](/wiki/Intravenous_therapy). Peripherally administered (e.g., intravenous) peptides like oxytocin cross the [blood-brain-barrier](/wiki/Blood-brain-barrier) very poorly, although very small amounts (< 1%) do appear to enter the [central nervous system](/wiki/Central_nervous_system) in humans when given via this route.[[89]](#cite_note-89) In contrast to peripheral administration, when administered [intranasally](/wiki/Intranasal_administration) via a nasal spray, oxytocin reliably crosses the [blood–brain barrier](/wiki/Blood–brain_barrier) and exhibits [psychoactive](/wiki/Psychoactive) effects in humans.[[90]](#cite_note-90)[[91]](#cite_note-91) In addition, also unlike the case of peripheral administration, intranasal oxytocin has a central duration of at least 2.25 hours and as long as 4 hours.[[92]](#cite_note-92)[[93]](#cite_note-93) In likely relation to this fact, endogenous oxytocin concentrations in the brain have been found to be as much as 1000-fold higher than peripheral levels.[[89]](#cite_note-89)

## Structure[[edit](/index.php?title=(none)&action=edit&section=8)]

[thumb|Oxytocin (ball-and-stick) bound to its carrier protein neurophysin (ribbons)](/wiki/File:Oxytocin-neurophysin.png) Oxytocin is a [peptide](/wiki/Peptide) of nine [amino acids](/wiki/Amino_acid) (a [nonapeptide](/wiki/Nonapeptide)). Its systematic name is cysteine-tyrosine-isoleucine-glutamine-asparagine-cysteine-proline-leucine-glycine-amide ([cys](/wiki/Cysteine) – [tyr](/wiki/Tyrosine) – [ile](/wiki/Isoleucine) – [gln](/wiki/Glutamine) – [asn](/wiki/Asparagine) – [cys](/wiki/Cysteine) – [pro](/wiki/Proline) – [leu](/wiki/Leucine) – [gly](/wiki/Glycine) – NH2, or CYIQNCPLG-NH2). Oxytocin has a [molecular mass](/wiki/Molecular_mass) of 1007 [daltons](/wiki/Dalton_(unit)). One [international unit](/wiki/International_unit) (IU) of oxytocin is the equivalent of about 2 [micrograms](/wiki/Microgram) of pure peptide. While the structure of oxytocin is highly conserved in placental mammals, a novel structure of oxytocin was recently reported in [marmosets](/wiki/Marmoset), [tamarins](/wiki/Tamarin), and other new world [primates](/wiki/Primates). Genomic sequencing of the gene for oxytocin revealed a single [in-frame mutation](/wiki/In-frame_mutation#in-frame) ([thymine](/wiki/Thymine) for [cytosine](/wiki/Cytosine)) which results in a single amino acid substitution at the 8-position ([proline](/wiki/Proline) for [leucine](/wiki/Leucine)).[[94]](#cite_note-94) The biologically active form of oxytocin, commonly measured by [RIA](/wiki/Radioimmunoassay) and/or [HPLC](/wiki/High-performance_liquid_chromatography) techniques, is also known as the octapeptide "oxytocin disulfide" (oxidized form), but oxytocin also exists as a reduced dithiol nonapeptide called oxytoceine.[[95]](#cite_note-95) It has been theorized that open chain oxytoceine (the reduced form of oxytocin) may also act as a [free radical](/wiki/Free_radical) scavenger (by donating an electron to a free radical); oxytoceine may then be oxidized back to oxytocin via the [dehydroascorbate](/wiki/Dehydroascorbate) <---> [ascorbate](/wiki/Ascorbate) redox couple.[[96]](#cite_note-96) The structure of oxytocin is very similar to that of [vasopressin](/wiki/Vasopressin) (cys – tyr – [phe](/wiki/Phenylalanine) – gln – asn – cys – pro – [arg](/wiki/Arginine) – gly – NH2), also a nonapeptide with a sulfur bridge, whose sequence differs from oxytocin by two amino acids. A table showing the sequences of members of the vasopressin/oxytocin superfamily and the species expressing them is present in the [vasopressin](/wiki/Vasopressin) article. Oxytocin and vasopressin were isolated and synthesized by [Vincent du Vigneaud](/wiki/Vincent_du_Vigneaud) in 1953, work for which he received the [Nobel Prize in Chemistry](/wiki/Nobel_Prize_in_Chemistry) in 1955.

Oxytocin and vasopressin are the only known hormones released by the human [posterior pituitary gland](/wiki/Posterior_pituitary_gland) to act at a distance. However, oxytocin neurons make other peptides, including [corticotropin-releasing hormone](/wiki/Corticotropin-releasing_hormone) and [dynorphin](/wiki/Dynorphin), for example, that act locally. The [magnocellular neurosecretory cells](/wiki/Magnocellular_neurosecretory_cell) that make oxytocin are adjacent to magnocellular neurosecretory cells that make vasopressin. These are large neuroendocrine neurons which are excitable and can generate action potentials.

## Synthesis, storage, release, and metabolism[[edit](/index.php?title=(none)&action=edit&section=9)]

[Template:#invoke:Infobox gene](/wiki/Template:#invoke:Infobox_gene)

The oxytocin [peptide](/wiki/Peptide) is synthesized as an inactive precursor protein from the *OXT* [gene](/wiki/Gene).[[97]](#cite_note-97)[[98]](#cite_note-98)[[99]](#cite_note-99) This precursor protein also includes the oxytocin carrier protein [neurophysin I](/wiki/Neurophysin_I).[[100]](#cite_note-100) The inactive precursor protein is progressively hydrolyzed into smaller fragments (one of which is neurophysin I) via a series of enzymes. The last hydrolysis that releases the active oxytocin nonapeptide is catalyzed by [peptidylglycine alpha-amidating monooxygenase](/wiki/Peptidylglycine_alpha-amidating_monooxygenase) (PAM).[[101]](#cite_note-101) The activity of the PAM enzyme system is dependent upon [vitamin C](/wiki/Vitamin_C) (ascorbate), which is a necessary vitamin cofactor. By chance, sodium ascorbate by itself was found to stimulate the production of oxytocin from ovarian tissue over a range of concentrations in a dose-dependent manner.[[102]](#cite_note-102) Many of the same tissues (e.g. ovaries, testes, eyes, adrenals, placenta, thymus, pancreas) where PAM (and oxytocin by default) is found are also known to store higher concentrations of vitamin C.[[103]](#cite_note-103) Oxytocin is known to be metabolized by the [oxytocinase](/wiki/Oxytocinase), [leucyl/cystinyl aminopeptidase](/wiki/Leucyl/cystinyl_aminopeptidase).[[104]](#cite_note-104)[[105]](#cite_note-105) Other oxytocinases are also known to exist.[[104]](#cite_note-104)[[106]](#cite_note-106) [Amastatin](/wiki/Amastatin), [bestatin](/wiki/Bestatin) (ubenimex), [leupeptin](/wiki/Leupeptin), and [puromycin](/wiki/Puromycin) have been found to inhibit the enzymatic degradation of oxytocin, though they also inhibit the degradation of various other peptides, such as vasopressin, [met-enkephalin](/wiki/Met-enkephalin), and [dynorphin A](/wiki/Dynorphin_A).[[106]](#cite_note-106)[[107]](#cite_note-107)[[108]](#cite_note-108)[[109]](#cite_note-109)

### Neural sources[[edit](/index.php?title=(none)&action=edit&section=10)]

In the [hypothalamus](/wiki/Hypothalamus), oxytocin is made in [magnocellular neurosecretory cells](/wiki/Magnocellular_neurosecretory_cell) of the [supraoptic](/wiki/Supraoptic_nucleus) and [paraventricular](/wiki/Paraventricular_nucleus) nuclei, and is stored in [Herring bodies](/wiki/Herring_bodies) at the axon terminals in the posterior pituitary. It is then released into the blood from the [posterior lobe](/wiki/Posterior_pituitary) ([neurohypophysis](/wiki/Neurohypophysis)) of the [pituitary gland](/wiki/Pituitary_gland). These [axons](/wiki/Axons) (likely, but [dendrites](/wiki/Dendrites) have not been ruled out) have collaterals that innervate oxytocin receptors in the [nucleus accumbens](/wiki/Nucleus_accumbens).[[9]](#cite_note-9) The peripheral hormonal and behavioral brain effects of oxytocin are thought to be coordinated through its common release through these collaterals.[[9]](#cite_note-9) Oxytocin is also made by some neurons in the paraventricular nucleus that project to other parts of the brain and to the spinal cord.[[110]](#cite_note-110) Depending on the species, oxytocin receptor-expressing cells are located in other areas, including the [amygdala](/wiki/Amygdala) and [bed nucleus](/wiki/Bed_nucleus_of_the_stria_terminalis) of the [stria terminalis](/wiki/Stria_terminalis).

In the [pituitary gland](/wiki/Pituitary_gland), oxytocin is packaged in large, dense-core vesicles, where it is bound to [neurophysin I](/wiki/Neurophysin_I) as shown in the inset of the figure; neurophysin is a large [peptide](/wiki/Peptide) fragment of the larger precursor [protein](/wiki/Protein) molecule from which oxytocin is derived by [enzymatic](/wiki/Enzyme) cleavage.

Secretion of oxytocin from the neurosecretory nerve endings is regulated by the electrical activity of the oxytocin cells in the hypothalamus. These cells generate [action potentials](/wiki/Action_potential) that propagate down [axons](/wiki/Axon) to the nerve endings in the pituitary; the endings contain large numbers of oxytocin-containing vesicles, which are released by [exocytosis](/wiki/Exocytosis) when the nerve terminals are depolarised.

### Non-neural sources[[edit](/index.php?title=(none)&action=edit&section=11)]

Outside the brain, oxytocin-containing cells have been identified in several diverse tissues, including in females in the [corpus luteum](/wiki/Corpus_luteum) [[111]](#cite_note-111)[[112]](#cite_note-112) and the placenta,[[113]](#cite_note-113) in males in the testicles' [interstitial cells of Leydig](/wiki/Leydig_cell),[[114]](#cite_note-114) the retina,[[115]](#cite_note-115) the adrenal medulla,[[116]](#cite_note-116) the thymus[[117]](#cite_note-117) and the pancreas.[[118]](#cite_note-118) The finding of significant amounts of this classically "neurohypophysial" hormone outside the central nervous system raises many questions regarding its possible importance in these different tissues.

#### Male[[edit](/index.php?title=(none)&action=edit&section=12)]

The [Leydig cells](/wiki/Leydig_cells) in some species have been shown to possess the biosynthetic machinery to manufacture testicular oxytocin *de novo*, to be specific, in rats (which can synthesize vitamin C endogenously), and in guinea pigs, which, like humans, require an exogenous source of vitamin C (ascorbate) in their diets.[[119]](#cite_note-119)

#### Female[[edit](/index.php?title=(none)&action=edit&section=13)]

Oxytocin is synthesized by [corpora lutea](/wiki/Corpora_lutea) of several species, including ruminants and primates. Along with estrogen, it is involved in inducing the endometrial synthesis of [prostaglandin F2α](/wiki/Prostaglandin_F2alpha) to cause regression of the corpus luteum.

### Miscellaneous[[edit](/index.php?title=(none)&action=edit&section=14)]

[Estrogen](/wiki/Estrogen) has been found to increase the [secretion](/wiki/Secretion) of oxytocin and to increase the [expression](/wiki/Gene_expression) of its [receptor](/wiki/Receptor_(biochemistry)), the [oxytocin receptor](/wiki/Oxytocin_receptor), in the [brain](/wiki/Brain).[[120]](#cite_note-120) In women, a single dose of [estradiol](/wiki/Estradiol) has been found to be sufficient to increase circulating oxytocin concentrations.[[83]](#cite_note-83)

## Evolution[[edit](/index.php?title=(none)&action=edit&section=15)]

Virtually all [vertebrates](/wiki/Vertebrate) have an oxytocin-like [nonapeptide](/wiki/Nonapeptide) hormone that supports reproductive functions and a vasopressin-like nonapeptide hormone involved in water regulation. The two genes are usually located close to each other (less than 15,000 bases apart) on the same [chromosome](/wiki/Chromosome), and are transcribed in opposite directions (however, in [fugu](/wiki/Fugu),[[121]](#cite_note-121) the homologs are further apart and transcribed in the same direction).

The two genes are believed to result from a [gene duplication](/wiki/Gene_duplication) event; the ancestral gene is estimated to be about 500 million years old and is found in [cyclostomata](/wiki/Cyclostomata) (modern members of the [Agnatha](/wiki/Agnatha)).[[45]](#cite_note-45)

## History[[edit](/index.php?title=(none)&action=edit&section=16)]

The word *oxytocin* was coined from the term oxytocic. [Greek](/wiki/Greek_language) ὀξύς, *oxys*, and τόκος, *tokos*, meaning "quick birth")

Its uterine-contracting properties were discovered by British pharmacologist Sir [Henry Hallett Dale](/wiki/Henry_Hallett_Dale) in 1906.[[122]](#cite_note-122) And its milk ejection property was described by Ott and Scott in 1910[[123]](#cite_note-123) and by Schafer and Mackenzie in 1911.<ref name=Schafer\_Mackenzie\_1911>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>

Oxytocin became the first polypeptide hormone to be sequenced[[124]](#cite_note-124) or synthesized.[[125]](#cite_note-125)<ref name=Ressler\_1954>[Template:Cite journal](/wiki/Template:Cite_journal)</ref>[[126]](#cite_note-126) Du Vigneaud was awarded the Nobel Prize in 1955 for his work.[[127]](#cite_note-127)

## Research[[edit](/index.php?title=(none)&action=edit&section=17)]

Oxytocin nasal sprays have been used to stimulate breastfeeding, but the efficacy of this approach is doubtful.[[128]](#cite_note-128) The trust-inducing property of oxytocin might help those with [social anxiety](/wiki/Social_anxiety) and [depression](/wiki/Depression_(mood)),[[41]](#cite_note-41) but with the potential for abuse with [confidence tricks](/wiki/Confidence_trick)[[129]](#cite_note-129)[[130]](#cite_note-130) and military applications.[[131]](#cite_note-131) The use of oxytocin in [relationship counseling](/wiki/Relationship_counseling#Novel_practices) is being investigated, as research has shown the hormone could both enhance trust and improve people's ability to interpret the emotions of others correctly.[[132]](#cite_note-132) A [nasal spray](/wiki/Nasal_spray) formulation of oxytocin branded Syntocinon is under development by [Retrophin](/wiki/Martin_Shkreli#Retrophin) for the treatment of [lactation deficiency](/wiki/Lactation_deficiency) and as a novel treatment for [autism](/wiki/Autism) and [schizophrenia](/wiki/Schizophrenia).[[133]](#cite_note-133) [Template:As of](/wiki/Template:As_of), it has reached [phase III](/wiki/Phase_III), [phase II](/wiki/Phases_of_clinical_research#Phase_II), and phase II [clinical trials](/wiki/Clinical_trial) for these indications, respectively.[[134]](#cite_note-134) In October 2014, Retrophin divested Syntocinon to [Turing Pharmaceuticals](/wiki/Martin_Shkreli#Turing_Pharmaceuticals).[[135]](#cite_note-135)

## Society and culture[[edit](/index.php?title=(none)&action=edit&section=18)]

### Brand names[[edit](/index.php?title=(none)&action=edit&section=19)]

Synthetic oxytocin is sold as proprietary [medication](/wiki/Medication) under the trade names Pitocin and Syntocinon, and as [generic](/wiki/Generic_drug) oxytocin.

## References[[edit](/index.php?title=(none)&action=edit&section=20)]

[Template:Reflist](/wiki/Template:Reflist)

## Further reading[[edit](/index.php?title=(none)&action=edit&section=21)]

[Template:Refbegin](/wiki/Template:Refbegin)

* [Template:Cite book](/wiki/Template:Cite_book)
* [Template:Cite journal](/wiki/Template:Cite_journal)
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