Dr. Sue Carter *is an internationally recognized expert in behavioral neuroendocrinology who has studied the endocrinology of love and social bonds for more than three decades. She is Director of The Kinsey Institute and Rudy Professor of Biology at Indiana University. Dr. Carter's research program has discovered important new developmental functions for oxytocin and vasopressin, and implicated these hormones in the regulation of long-lasting neural effects of early social experiences. Recently, she has been examining the role of oxytocin and vasopressin in mental disorders such as autism, schizophrenia, anxiety, and depression. According to Google Scholar, her work has been cited in nearly 25,000 scientific articles. Dr. Carter also happens to be the wife of USABP's new Director of Research, Dr. Stephen Porges. We are most grateful for her contribution to this issue.*

Love As Embodied Medicine

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ABSTRACT

As a sentient species, humans are on the threshold of novel insights into the origins of the magnificent obsession we call "love." It is well established that healthy relationships can protect against disease and restore the body in the face of illness. Without positive relationships, especially in early life, humans fail to flourish, even if all of their basic biological needs are met. "Love lost" is one of the most powerful forms of stress and trauma. However, the mechanisms through which love protects and heals are only now becoming apparent. Love is most easily understood through the lens of our evolutionary past and in light of our contemporary physiology. At the epicenter of this story is a mammalian hormone, oxytocin, and an even more ancient molecule, known as vasopressin. These biochemical building blocks of love are not unique to humans and are shared with other highly social species. Through the study of social behavior in other mammals, we are also learning that the same physiology that lies behind the healing power of love, reduces inflammation, regulates the autonomic nervous system, the immune system, and even regulates the microbiome. Furthermore, the oxytocin-vasopressin system is regulated by experience across the lifespan, helping to explain the lasting physical consequences of both love and adversity. By examining the biology of social bonds and parenting, we are uncovering pathways that allow humans to experience and embody love.

Keywords: oxytocin, love, monogamy, nurture

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As a sentient species, humans are on the threshold of novel insights into the origins of the magnificent obsession we call "love." It is well established that healthy relationships can protect against disease, and restore the body in the face of illness. Without positive relationships, especially in early life, humans fail to flourish, even if all of their basic needs are met. "Love lost" is one of the most powerful forms of stress and trauma.

For as long as I can recall, I have been mesmerized by this set of curious puzzles. What is love? How does "love casteth out fear" and how does love heal? This gradually became my life's work as I trained myself to become a scientist. I was guided on this path by a series of events, the most relevant of which were probably the co-incidence of living in that strange vessel known as the female body, with the capacity to "fall in love," and eventually the experience of motherhood. Each of these experiences left me with more questions than answers, a few of which I share here.

Insight into the mechanisms through which love protects and restores requires awareness of mammalian evolution and neurobiology. The new science of love allows us to say that the causes and consequences of love – or its absence – are grounded in an ancient biology that operates largely below the level of human consciousness. To bring these questions into scientific focus required uncovering a kind of organic Rosetta Stone. We needed to find another creature that shared with humans the capacity for something that resembled "love."

"I hope we don't lose sight of one thing. It was all started by a mouse."
- Walt Disney

Remarkably, the origins of much of our current understanding of the science of love began in studies conducted in a small field mouse known as the prairie vole. Decades ago, my colleagues and I uncovered evidence that both in nature and in the laboratory, prairie voles were capable of forming life-long pair bonds – living together until one or both members of the pair died. Prairie voles lived together until "death parted them," and they shared with humans several other features of a human family.

In prairie voles both parents nurtured the young, with fathers carrying out all aspects of infant care except nursing. Older siblings also baby sat for younger siblings. Juvenile prairie voles moved out of the family to find mates and scrupulously avoided incest. Prairie voles exhibited the traits that humans associated with extended families, constructed around an apparently monogamous pair.

But, we soon discovered that monogamy like love can be a paradox. In the 1980s, in the early days of our studies, DNA fingerprints became possible. Like a bad outcome on a TV reality show, DNA revealed that prairie voles were having sex outside of the pair bond. Monogamy, or at least the traits associated with monogamy, were real and they were based in biology. However, monogamy was not simply about sexual exclusivity. In fact, sexual preferences were **not** the defining feature of monogamy. We did find that sexual interactions could facilitate pair bonding. But at the core of the prairie vole family were invisible social bonds and what we were observing was more accurately called "social monogamy." I came of age in a romantic era, and this part of the prairie vole story initially was a disappointment to me. But awareness that selective social behaviors were the central feature of social monogamy, and apparently more important than sexual monogamy, also opened avenues to understanding the physiological basis of social attachments.

Over the decades that followed we, and then many others, conducted experiments showing that the capacity for pair bond formation was regulated by emotional states, and these depended on physiology. Nature is conservative, and reuses neural and endocrine systems. We now know that the neurobiology of pair bonding in voles indeed had parallels with what humans call "love." We also found that prairie voles, like humans, had high levels

of a molecule known as oxytocin. Prairie voles also had heart rate patterns similar to those found in humans. The parasympathetic branch of the autonomic nervous system is regulated in part by oxytocin and both are associated with the capacity to sustain safe relationships. Prairie voles also were exquisitely sensitive to the effects of early nurture, another process that required oxytocin. The basic neurobiology of social bonding was centered around oxytocin, and shared by humans and prairie voles. Through good luck, and with help from many brilliant collaborators, we had stumbled upon a rodent model that allowed us to examine the chemistry of love.

As these stories became public, oxytocin was termed by the Media, "**the** hormone of love." It certainly would have been easier to understand the neurobiology of love if oxytocin were acting alone. Of course, that is not the case. Many molecules and neural systems work behind the scenes to support love. We were able to show that among the other factors essential for selective social attachments was a second ancient molecule, known as vasopressin.

Pair bonding required a pair of hormones. Bonding in voles, as in humans, also occurred in the context of other physiological processes, including those associated with a sense of safety or fear. These are basic and very old emotions and the story of love has its biochemical origins long before the existence of humans or even of primitive mammals.

The Evolution of "Love" Began over 600 Million Years Ago

Oxytocin and vasopressin began to appear over 600 million years ago, originating from an ancestral peptide that probably helped animals successfully move from the sea to life on dry land. Oxytocin and vasopressin are similar in structure and interact dynamically with each other's receptors. However, these molecules are difficult to study. They have sticky sulfur chemical bonds that make them hard to accurately assay. Furthermore, the actions of oxytocin and vasopressin are quickly changing, adaptive, and also strongly affected by emotional context. Under conditions of safety, oxytocin promotes social engagement. But in a context of anxiety or fear, it is possible that oxytocin functions more like vasopressin, possibly by binding to and stimulating vasopressin receptors.

Although oxytocin and vasopressin were derived from a common ancestor, their general physiological functions are strikingly different. Vasopressin is at least 100 million years older than oxytocin, and has functions that are more primitive than oxytocin. Vasopressin is strongly associated with adaptive functions that protect against dehydration, regulate blood pressure, and increase reactivity to other threats. Vasopressin is associated with the neurobiology of anxiety, fear and avoidance learning. Vasopressin and its receptors are foundational to aggression. Both males and females synthesize vasopressin. However, in areas of the brain implicated in defensiveness, vasopressin production is increased by androgens, which helps to explain sex differences in the expression of aggression.

The same novel properties that give oxytocin and vasopressin great power, also create serious challenges for understanding their functions. The oxytocin-vasopressin system is constantly changing across the life cycle. Oxytocin can directly affect the development of the brain and cardiovascular system, and programs the immune system. Receiving love in early life can influence behavior and physiology across the lifespan, in part through changes in the receptors for oxytocin and vasopressin.

As one example, my colleagues and I have demonstrated that the genes for the oxytocin receptor in voles are "epigenetically" tuned by early experience. In the presence of sensitive parenting, the genes in a baby vole that regulate the oxytocin receptor are more likely to be available for stimulation, and these changes can last for a lifetime (Perkeybile, Connelly et al., 2019).

Parenthood: The Biological Prototype for Love

The evolutionary and biochemical prototype for love and social bonds is the mother-child interaction. Processes that help to define mammals, including lactation and parental care of their young, are facilitated by oxytocin. The same physiological pathways that permit social bonds are shared with parental behavior, birth and lactation. Oxytocin is generally associated with positive social behaviors, including social engagement and bonding. Oxytocin also may induce a sense of safety, reduce reactivity to stressors, block fear, and increase trust. But even in maternal behavior, oxytocin does not work alone.

Vasopressin also is important to normal birth, parenting and care of the young. Vasopressin can increase protective behaviors and aggression, which in some cases benefits the family. Although generally directed toward intruders, the emotional states that lead to aggression may escalate and spill over into violence within the family. Vasopressin is made primarily in the brain and is a classic "stress hormone" with receptors in the cardiovascular system, kidneys, and throughout the body. States of chronic arousal or stress are especially dangerous. Medical disorders such as preeclampsia, in which pregnant women retain water, have high blood pressure, and sometimes premature labor, have been linked to excessive emotional stress and to vasopressin. Furthermore, understanding fear or stress-induced release of vasopressin or hypersensitivity of the vasopressin receptors may help to explain premature birth – among the world's most serious medical mysteries.

Due to its primitive characteristics, vasopressin can be a double-edged sword. Generally, oxytocin tempers fear and increases both trust and social behavior. But in individuals who have a history of neglect, trauma, or extreme stress, oxytocin's actions may paradoxically trigger the vasopressin system, enhancing fear and protective responses. The unique properties of the oxytocin and vasopressin systems allow these two molecules to be highly adaptive and to dynamically support individual survival, as well as emotions that are associated with love. However, stimulating the vasopressin receptors may induce the dark side of love, including jealousy, territoriality, and aggression.

The Healing Power of Love

"Only love can break a heart. Only love can mend it again."
- From the 1962 popular song by Gene Pitney

Good relationships are powerful medicine with health benefits that are recognized throughout most cultures. Epidemiological studies searching for secrets for longevity showed that individuals, especially men living in psychological isolation, were more likely to die after a heart attack than those with companions. After the death of a partner, especially in the elderly, the second member of the pair may become vulnerable to disease. Correlational studies such as these do **not** prove that oxytocin is the magic that explains social support. However, oxytocin does facilitate social engagement, and under some

conditions, can increase a psychological sense of safety. The cardioprotective effects of the autonomic nervous system, and especially the parasympathetic nervous system, are regulated by oxytocin. This integrated system allows a dynamic balance between growth and restoration, while enabling the body to respond quickly and adaptively to acute stress.

Experimental studies support the importance of oxytocin in the cardiovascular systems. Mice that are genetically deficient in oxytocin develop abnormal hearts. Oxytocin is part of the mechanism guiding normal heart development. In tissue culture (and thus even in the absence of a central nervous system) oxytocin acts on undifferentiated stem cells, transforming these cells into clusters of miniature hearts beating in synchrony. Furthermore, in laboratory models of atherosclerotic plaques, oxytocin reduces inflammation. Through processes such as these, oxytocin might be able to prevent or even reverse the effects of heart disease, with some of the benefits occurring locally at the site of damage.

Many other beneficial practices are associated with oxytocin. For example, exercise is one of the most reliable ways to both protect against disease and to release oxytocin. Oxytocin in turn helps to restore heart rate and blood pressure to normal, with potential benefits to the cardiovascular system. Heart disease is only one of many disorders that may benefit from the healing power of both exercise and oxytocin. It has been shown in animal models that exercise is beneficial in slowing the growth of breast cancer. Remarkably, animal studies suggest that this effect of exercise also is mediated by oxytocin.

Oxytocin is a central component of the immune system. The thymus is a source of oxytocin and expressed an abundance of oxytocin receptors. Early experiences "educate" the immune system through functions that require the presence of oxytocin. In a group of volunteers deliberately exposed to a treatment that causes inflammation, a concurrent exposure to oxytocin blocked symptoms such as fever. The capacity of oxytocin to reduce inflammation also is likely to be a factor in the beneficial effects of this molecule. But before we become excited about oxytocin as a "wonder drug," the full picture that is emerging from this literature needs to be considered.

Biochemical Magic Beneath the Power of Love?

Oxytocin was essential to human evolution and the development of the massive human cortex. Even in modern humans, oxytocin continues to facilitate the birth, growth, and nurture of immature babies. Oxytocin helps, directly and indirectly, to promote healing and restoration. For example, oxytocin has anti-inflammatory properties. Oxytocin also regulates the immune system and the generally protective vagal branch of the autonomic nervous system. Vagal pathways, regulated by oxytocin, are necessary for social communication and engagement through actions on the muscles of the face and head. Oxytocin is secreted in the presence of extreme stressors, and may protect against "shut-down" responses to trauma. Furthermore, the autonomic nervous system regulates all of our internal organs, as well as the distribution of blood and nutrients throughout the body. Through effects on the autonomic nervous system, oxytocin regulates oxygen to the brain, thus supporting human cognition, culture, and eventually civilization. The autonomic nervous system is one portal through which the peptide systems and love may be accessed and influenced. Thus, oxytocin's actions on the autonomic nervous system are critical components of the healing power of love.

Does Oxytocin Have a Dark Side?

A number of studies link social support and other methods for reducing stress to reductions in cancer. Studies of certain breast cancer cell lines suggest that oxytocin can inhibit tumor growth. However, under other conditions (at present not well identified), oxytocin appears to increase cellular proliferation and may stimulate the growth of cancers. The strongest evidence for the capacity of oxytocin to increase the growth of malignant and nonmalignant tissue comes from studies of cells from the prostate. The conditions under which oxytocin is protective, or alternatively promotes the proliferation of cancers, may depend on the type of subcellular processes that are stimulated.

The pathways for negative effects of oxytocin, especially on processes that might cause tumor growth, are not well identified. Furthermore, it is likely, that large doses of oxytocin, and chronic exposure to oxytocin, have different consequences from effects seen when this molecule is produced internally. Studies of individual and sex differences in endogenous oxytocin and the oxytocin receptor are missing from our current understanding of both the benefits and dangers associated with this molecule. Furthermore, as discussed above, the complex interactions between oxytocin and vasopressin and their receptors could be another important source of variation in the response to oxytocin treatments, which at present remains largely unexplored. Because, the relationship between oxytocin and the growth of cancer cells is not well understood, this has to be a concern in the use of oxytocin as a "drug."

Adding to the complexity of this emerging story is the capacity of reproductive steroids, including estrogen, progesterone and testosterone to regulate sensitivity to the actions of oxytocin and vasopressin. Dynamic changes in these steroid hormones, especially around the time of birth, prepare the maternal brain for oxytocin and facilitate attachment to the baby. Actions of steroid hormones also lie behind sex differences in anatomy and behavior, including positive forms of infant care and defense of the young. Steroid-peptide interactions are at present not well understood, but probably differ between males and females. In some cases the responses to oxytocin and vasopressin are in opposite directions in men and women.

Love Lost or Found

Love is one of nature's most rewarding experiences. But what happens when love is absent or lost. Behaviorally, the effects are well documented. The absence of love or a loving relationship, especially in early life, is associated in later life with patterns of self-defense and a sense of threat. If not repaired, this loss can inhibit the later capacity for love. With knowledge of the mechanisms beneath either the presence or absence of love, there is an opportunity to inform both optimal parenting and responsible interventions. Because of the evolved and conserved nature of love, awareness of mechanisms through which negative or positive experiences across the lifespan affect this system will help us understand, predict, and possibly heal the consequences of neglect or trauma.

Love is intrinsically beautiful, but also complex and mysterious. Although love can be difficult to define, the list of love's functions is long. Love influences all aspects of human existence. Love is powerful medicine. The mechanisms through which love protects and heals are only now being discovered. Throughout life, oxytocin influences sociality, and social experiences influence oxytocin. Knowledge of the neurobiology of love helps to explain the exceptional reproductive success of humans and also our resilience in the face

of fear and aggression. The emotional and physical health and longevity of our species, and perhaps our planet, depends on our capacity to understand and apply our knowledge of the biology of love, especially in this time of trauma.

Dr. Sue Carter *is an internationally recognized expert in behavioral neuroendocrinology. She is Director of The Kinsey Institute and Rudy Professor of Biology at Indiana University. Dr. Carter studies social bonding, male and female parental behavior, the social control of stress reactivity, and the social control of reproduction. Her research program has discovered important new developmental functions for oxytocin and vasopressin, and implicated these hormones in the regulation of long-lasting neural effects of early social experiences. She also has a long-standing concern regarding the consequences of medical manipulations for human development and parent-child interactions, including the use of pitocin to induce labor and the consequences of breast-feeding for the mother and child. Recently, she has been examining the role of oxytocin and vasopressin in mental disorders such as autism, schizophrenia, anxiety, and depression.*

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REFERENCES

Carter, C.S. (2014). Oxytocin pathways and the evolution of human behavior. *Annual Review of Psychology*, Vol.65:17-39. https://www.ncbi.nlm.nih.gov/pubmed/24050183

Carter, C.S. (2017). The oxytocin-vasopressin pathway in the context of love and fear. *Frontiers in Endocrinology*. https://www.ncbi.nlm.nih.gov/pubmed/?term=Carter+love+and+fear

Carter, C.S. (2018). The monogamy paradox: What do love and sex have to do with it? *Frontiers in Ecology and Evolution*. https://www.frontiersin.org/articles/10.3389/fevo.2018.00202/full

Carter, C.S. (2019). Early nurture epigenetically tunes the oxytocin receptor. https://www.sciencedirect.com/science/article/pii/S0306453018306103?via%3Dihub