# **UW** Integrative Health

Department of Family Medicine and Community Health



# Family, Friends, & Co-Workers, Part II

### **Relationships and Research: Different Ways to Connect**

Love and intimacy are the root of what makes us sick and what makes us well, what causes sadness and what brings happiness, what makes us suffer and what leads to healing.<sup>1</sup>

#### **Animal Studies**

The healing power of social connection began to receive research attention in the 1960s and 1970s. A variety of research involving numerous animal species found that if animals are exposed to a stressor, their health is less likely to deteriorate if they are in the presence of familiar cage mates, rather than alone. In fact, a stressor that would increase blood cortisol levels by 50% in an animal that is alone will not affect cortisol level when it is in familiar company.<sup>2</sup>

To learn more about benefits of relationships between animals and people, refer to the clinical tool, "<u>Animal-Assisted Therapy</u>."

#### **Human Research**

Similar effects have been found in many studies involving humans. A 2006 study evaluated functional MRI (fMRI) findings in women who were awaiting an electric shock.<sup>3</sup> Women who were alone, or those who held the hands of unknown strangers prior to being shocked, continued to have fMRI changes consistent with anxiety. Their stress hormone levels were increased. In contrast, women who held hands with their husbands, *and* who were in a marriage they rated highly in measures of mutuality (high levels of shared interests, feelings, thoughts, aspirations, and goals) felt less anxiety. Their fMRI findings showing less activity in the parts of the brain that were found to be active if they experienced the electric shocks either when they were alone or with a stranger.

These effects are not limited to the artificial environment of the laboratory. The Alameda County study, which followed over 7,000 residents of Alameda county for nine years, was one of the many studies that drove this point home.<sup>4</sup> It found that the best predictor of mortality in people over 60 was their level of social support. Having close ties to family members and friends was the *best* predictor of longevity of all the health variables studied.<sup>5</sup>

Furthermore, as was noted in a 2006 literature review of 29 studies, better social support correlates with better surgical outcomes.<sup>6</sup> A 1997 study found that people with limited positive relationships developed colds four times more frequently than others.<sup>7</sup> Just as positive support can be beneficial, negative social support can lead to worse health outcomes.<sup>8</sup> For example unhappy marriages led to 34% more coronary events, regardless of gender and social status.<sup>9</sup>

#### Significant others

In a five year follow-up study of 10,000 men with three or more risk factors for coronary artery disease, the men who answered "yes" to the question, "Does your wife show you her love?" had

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a 50% lower rate for the onset of angina than those who answered no.<sup>10</sup> The study also indicated that men who are shown love had half the incidence of ulcers.<sup>11</sup>

Other studies have shown that having confidants is the key; women experience similar benefits, and it stands to reason that people with good relationships with significant others, be they married or not, will benefit. Longevity is increased for men and women with cardiac disease who have someone with whom they can confide and share their life. A study of 1,400 men and women over a five year period who had experienced cardiac catheterization found that unmarried people who had no close confidant had triple the mortality rate.<sup>12</sup> Close personal relationships also have been found to decrease the risk of depression and mortality in the 18 month period following a myocardial infarction.<sup>13,14</sup>

As mentioned above, there are both buffering and aggravating/stressful influences of relationships on health depending on their nature. It may be that, in some cases, chronic stress is the inciting factor that decreases relationship quality. Most studies have not found a difference between married and cohabitating couples. However, it has been found that neurologic response to threat was attenuated by a spouse more than by a cohabitating partner even when matched on relationship length and quality. Being unhappily married is associated with worse health outcomes than being single, and negative partner interactions are associated with higher rates of depression, anxiety, and chronic illness. Spousal conflict is associated with poor pain tolerance and higher blood pressure and heart rate in addition to significantly worse cardiovascular outcomes, endocrine function, and immunity.<sup>15</sup> Improving relationships seems to improve mental health to a greater degree than mental health improves relationships (though that occurs as well).<sup>16</sup>

How individuals enter into relationships matters as well. Attachment insecurity (ie anxiety about or avoidance of attachment) is associated with dysregulated physiological responses to stress, risky health behaviors, susceptibility to physical illness, and poorer disease outcomes, psychological health, and well-being. These associations depend, in part, on the other partner's attachment style and behavior.<sup>17,18</sup>

There are certain situations that can add stress to an intimate-partner relationship. The transition of couples into parenthood is associated with increased conflict, less leisure time together, less satisfaction with division of household labor, and decline in sexual satisfaction and intimacy. Understanding of this stress and bringing awareness of it early into the transition can help; encouraging more equal co-parenting can be beneficial to both parents.<sup>19</sup>

Certain characteristics in a committed partnership are more likely to foster true connectedness. A meta-analysis of 21 studies totaling 2,739 participants showed higher relationship satisfaction when empathetic accuracy (extent to which people accurately perceive their peers' thoughts, feelings, and other inner mental states) was higher between couples, especially when it was higher for negative emotions.<sup>20</sup> Linkage (synchronization of people's moment-to-moment physiological states) may confer benefits, but also may put couples at risk if they become entrenched in patterns of conflict or stress.<sup>21</sup>



#### Parental and adolescent relationships

The closeness of relationships with parents has a significant impact on health. For example, a study conducted at Johns Hopkins that looked at relationships with parents and disease in later life found that, when other variables were taken into account, cancer rates were higher for people who were less close to their parents.<sup>22</sup>

A 35-year follow-up of the Harvard Mastery of Stress Study followed health outcomes for 126 men.<sup>23</sup> These included coronary artery disease, cancer, hypertension, ulcers, and substance abuse. The study looked at each man's relationship with his father and mother and whether it was "very close," "warm and friendly," "tolerant or strained," or "cold." When the relationship with one or both of the parents was "tolerant or strained," a man was two times more likely to have significant health issues than one who had "warm and close" parental relationships. Men who had a "tolerant or strained" relationship with their fathers had an 82% likelihood of a significant health issue, and those with such a relationship with their mother had a 91% risk. The risk rose to 100% if both parental connections were lacking. Researchers concluded that healthy behaviors, coping styles, and spiritual values or practices developed in childhood due to warm and close relationships with parents led to improved health later in life.<sup>23</sup>

It has been known that divorce and domestic violence have a negative impact on a child's psychopathology. More recent data also indicates that the quality of parental interpersonal interactions around conflict impacts the child's emotional, behavioral, social, academic outcomes, and their own future interpersonal relationships.<sup>24</sup> In addition, challenges in managing conflict and hostility during adolescent years is associated with chronically elevated interleukin-6, a marker of immune system dysfunction, in their late 20s.<sup>25</sup>

#### Social networks, support systems, and community relationships

It is helpful for clinicians to recognize each individual as being influenced by his or her community as well. What resources are available (or not), be they social, political, cultural, or spiritual, also has an effect on health outcomes. Perhaps nowhere has the healing power of community been illustrated as clearly as in studies of Roseto, Pennsylvania.<sup>26</sup> Researchers noted that the town's residents had a lower incidence of heart disease, despite being as likely to have multiple risk factors, such as poor diet and tobacco use. They described what made the community unique:

There was a remarkable cohesiveness and sense of unconditional support within the community. Family ties were very strong, and what impressed us most was the attitude toward the elderly. In Roseto, the older residents weren't put on the shelf, they were promoted to the "supreme court." No one was ever abandoned.<sup>26</sup>

Sadly, over the course of 50 years, as the community moved away from these patterns, the incidence of heart disease gradually rose to match that of the surrounding communities.

The concept of "social capital" comes into play here. Social capital involves all the benefits that are expected to come when a person participates cooperatively with others, either in individual relationships or within groups.<sup>27</sup> By offering support to others, one increases the chances of receiving support in the future. A 2012 review of multilevel studies of social capital and health found that social capital did have positive effects on health outcomes but noted that there is a

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need for more research.<sup>28</sup> A 2014 review of 17 studies found a positive correlation between social capital and chronic disease *prevention.*<sup>29</sup> It seems that even the health risks associated with poorer socioeconomic status are attenuated by stronger social connections. <sup>30</sup>. A 2008 study of 944 pairs of twins found that higher ratings for individual-level social capital variables— social trust, volunteer activity, community participation, and sense of belonging—correlated with better mental and physical health.<sup>31</sup> Ideally, health care programs can work in conjunction with community groups to optimize the provision of health in a community, doing what they can to augment the effects of community efforts.

The Experience Corps, initially started in Baltimore, Maryland, is an excellent example of a program that improved health at many levels within a community—individuals, schools, and the community as a whole.<sup>32</sup> The program brings elderly volunteers into public elementary schools with the goal of creating an impact on the educational outcomes of children, while simultaneously improving the health and well-being of the volunteers.<sup>33</sup> Children, parents, teachers, and residents within the community were all involved. Research indicates that health promotion programs that focus on bringing benefit to a community as a whole have better health outcomes than programs targeting only individual health behaviors.<sup>34</sup>

Another novel program aimed at enriching social connection and improving health is the Community Men's Sheds (CMS), developed in 1978 in Australia. There is an intentional effort to provide men with biopsychosocial support; this increases self-esteem and empowerment, offers respite from families, enhances the sense of belonging in the community, and offers them the opportunity to exchange ideas related to personal, family, community, and public health issues. Most CMS have a woodworking area, trade tools, and equipment next to a "tea room;" some even provide support for men with mental health or physical disabilities or support youth and the unemployed.<sup>35</sup> Evidence indicates these facilities create a space in which interaction and support can help overcome many social, health, and well-being concerns.<sup>36</sup>

As we learn more about the importance of connection and health, organizations have begun to use volunteers to support vulnerable community members. A review of 14 trials including 2,411 participants indicated that volunteer befriending programs seem to improve symptoms of depression, anxiety, mental illness, cancer, physical illness, and dementia—although not always to a level of statistical significance. However, they did seem to have a statistically significant improvement on patient-reported outcomes.<sup>37</sup>

# Relationships and Research: Effects on Specific Illnesses

#### COPD

A 2015 review of 31 studies indicated that mental health and self-efficacy were consistently better in those COPD patients with good social support.<sup>38</sup>

#### **Heart Disease**

 Family support in heart failure patients influences self-care behaviors and chronic disease self-management. It positively influences decision-making processes related to management of symptoms and inquiries about treatment options.

- Better-quality relationships between heart failure patients and their informal family caregivers results in reduced mortality, increased health status, less distress, and lower caregiver burden.<sup>39</sup>
- The health-related quality of life of patients with left ventricular assist devices is significantly improved with higher social support.<sup>40</sup>

#### **Diabetes Mellitus**

- A review of 35 studies found that connection, especially to family, was important to people with type 2 diabetes. Participants used a variety of technologies to connect with their health care team and other people with the same disease. This type of connection seems to improve objective measures of disease control (hemoglobin A1c, cholesterol) and risk factors (body weight, physical activity, healthy eating).<sup>40</sup>
- A study of 700 veterans in the Pacific Northwest found that diabetes-specific social support was associated with better adherence to diabetic diet and regular physical activity.<sup>41</sup>
- Diabetics also seem to have better disease control in the setting of trusting relationships with clinicians and health teams.<sup>42</sup>

#### **Mental Health**

- People seek out grief groups for support and sharing. Groups seem to improve wellbeing, but there is disagreement as to whether it decreases symptoms of grief. Therapeutic factors related to sharing and support, interpersonal learning, and meaningmaking all have some potential to affect grief outcomes and well-being for those with and without symptoms of complicated grief (CG). Some processes may also affect outcomes indirectly by influencing group member behaviors such as treatment engagement, which can be low among individuals with CG.<sup>43</sup>
- Social support from research personnel, healthcare professionals, family members, and peers plays an important role in initiating and maintaining physical activity in individuals with schizophrenia.<sup>44</sup> This is very important given the metabolic risks of many of the antipsychotic medications.
- The risk of PTSD, anxiety, and depression after exposure to natural disasters or conflictaffected settings is decreased by greater social capital.<sup>45</sup>
- More satisfactory social support positively impacts outcomes of depression, schizophrenia, bipolar disorders, and anxiety disorders.<sup>46</sup>
- Social support is extremely important for the successful recovery from severe mental illness and substance misuse.<sup>47,48</sup>

#### Cancer

- A meta-analysis of 15 studies showed that more insecure attachment style is associated with poorer outcomes in terms of psychological adjustment to the cancer diagnosis and ability to perceive and access social support. Caregivers with insecure attachment style have more depression, higher stress levels, decreased motivation for care-taking, and increased difficulty with caregiving.<sup>49</sup>
- Lower levels of social support increase inflammation, pain, and depressive symptoms in breast cancer survivors.<sup>50</sup>

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## **Mechanisms of Action: Physiological Effects of Relationships**

#### **Mirror Neurons**

It is clear that relationships affect health. How are these effects mediated? One potential answer is that mirror neurons play a role. Mirror neurons are a class of neurons discovered just over 20 years ago by an Italian research team.<sup>51</sup> The team noted that when a macaque watched another macaque perform an action, its brain would activate on imaging studies the same way that it would when the macaque performed the action itself.

Subsequent studies have demonstrated that humans also have mirror neurons<sup>52</sup>, and it has been observed that these neurons respond not only to observed movements of others, but also emotional states and tactile experiences of others who are being observed.<sup>53</sup> If a person observes another person experiencing disgust because of a bad smell, the observer's brain will activate as though he or she is also feeling disgust.<sup>54</sup> The same thing occurs if a person sees another person experiencing soft touch; the touch center of the observer's brain becomes active in the area corresponding with the part of the body observed being touched in another person.<sup>55</sup> This has been referred to as "tactile empathy." It would seem it is built into our brains to be able to establish rapport with our fellow humans. In fact, it is possible to tell two people are in rapport because their posture, vocal pacing, and movements become synchronized.<sup>56</sup>

The details of how motor neurons are related to empathy are still being elucidated. When a person witnesses facial cues and body postures associated with emotion in another person, the people with the highest empathy scores also have proportionately higher activity in areas of the brain containing mirror neurons. Mirror neurons seem to activate a system of understanding another's experience that happens without cognitive or reflective effort. Some propose that these neurons allow a sort of inner imitation of another's experience or a resonance of the minds of the observer and the observed.<sup>57</sup>

#### Inflammation

There is a growing body of research showing a direct link between the quality of a person's relationships and levels of inflammation in the body.<sup>58</sup> A US study followed the relationship quality of 647 adults over 10 years and measured markers of inflammation (C-reactive protein, interleukin-6, fibrinogen, E-selectin, and intracellular adhesion molecule-1). The investigators found that support from family, friends, and spouses was associated with lower inflammation levels. They noted that relationship stress with these individuals increased inflammation and that the stress was a stronger influence on inflammation than the positive impact of supportive relationships.<sup>59</sup> These findings were further supported in a meta-analysis of 41 studies including 73,037 participants which showed that social support was inversely correlated with levels of inflammatory biomarkers.<sup>60</sup> People with cold, unsupportive, and conflict-ridden relationships have more chronic inflammation.<sup>61</sup> It has even been found that past troubled relationships, not only current ones, can have a lasting impact on levels of inflammation.<sup>61</sup>

How does the impact of relationships result in this inflammation? Exposure to stress causes the release of hormones from the hypothalamus, leading to increased release of cortisol. This in turn results in transcription of genes that suppress immune function and increase inflammation. However, exposure to *chronic* stress, say in a dysfunctional relationship or chronic loneliness, causes the body to resist the hyperactivation by cortisol, leading to changes in baseline levels of

cortisol and glucocorticoid receptor resistance. This decrease in the anti-inflammatory effects of cortisol results in increased chronic inflammation, which is associated with increased disease frequency, severity, mortality, and poorer subjective health ratings.

Negative experiences with relationships (negative expectations, hostility, anger, negative marital interactions) tend to intensify the stress response and have been associated with outcomes such as worse immune function, delayed wound healing, more arterial calcifications, higher blood pressure, and worse asthma, as well as higher incidence of strokes, heart attacks, and ulcers. In contrast, positive relationship experiences are associated with less cortisol reactivity in stressful situations, even in the setting of low socioeconomic status. They are also linked to, healthier diurnal cortisol slopes, lower blood pressure, and decreased risk of re-hospitalization and death from cardiovascular disease.<sup>62</sup>

#### Oxytocin

Several researchers have theorized that oxytocin is the critical link between connecting with others and health. Oxytocin levels increase in a mother when she gazes at her child, in a father when he touches his child to initiate play, and in someone who hears the comforting voice of his/her mother in conversation after a significant life stressor. Exogenously provided oxytocin increases social engagement of fathers with their toddlers, which in turn increases the toddlers' endogenous oxytocin levels. This reciprocal effect was also seen between a dog owner and dog when the dog was given oxytocin. Intranasal oxytocin level to rate their partners as more attractive.<sup>63</sup> These studies clearly show that oxytocin lives up to its nickname of "the love hormone."

Oxytocin impacts the hypothalamus-pituitary-adrenal (HPA) axis by inhibiting cortisol release; this effect is enhanced by social support from close relationships. Oxytocin also acts in the brain stem to regulate vagal output. Exogenous oxytocin increases respiratory sinus arrhythmia (a marker of favorable vagal tone) and may decrease blood pressure. Exogenous oxytocin can reduce the inflammatory cytokines of a bacterial infection—possibly via modulation of vagal output. Blocking oxytocin receptors in rats prevents the positive effects of social housing. Oxytocin in animal models protects against myocardial infarction, hypertension, and obesity. Women who suffered childhood abuse have less oxytocin in their cerebral spinal fluid as adults and men with a history of early life stress have lower serum oxytocin levels. Children of mothers who frequently withdrew love, have less altruistic behavior after receiving oxytocin as adults—perhaps because of a reduced investment in social bonds.<sup>63</sup>

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