Sex and Gender Issues in Pain

I. Understand the differences in the terms “sex” and “gender” (Pardue et al. 2001).
   A. Be aware of the biological (e.g. physical, anatomical, developmental) and chromosomal differences between males and females (human and nonhuman), which are typically referred to as “sex.”
   B. Be aware that “gender” refers to one’s self-identity as being female or male, based on social and environmental as well as biological factors.

II. Understand the nature of sex differences in the epidemiology of pain in relation to age and reproductive history.
   A. Know that in population-based surveys, women typically report more frequent and/or severe pain than men (Unruh 1996).
   B. Know that women are at greater risk for several chronic painful disorders, including temporomandibular disorders, fibromyalgia, migraine headache, interstitial cystitis, joint pain, irritable bowel syndrome, complex regional pain syndrome, and trigeminal neuralgia (Unruh 1996; Jones and Nyberg 1997; LeResche 1999; Buckwalter and Lappin 2000; Dao and LeResche 2000). Be aware that these differences vary with age and are associated with endogenous or exogenous sex hormone changes, for example, in the case of migraine headaches (Silberstein 2001). Women are at greater risk for autoimmune disorders that have a pain component, such as rheumatoid arthritis, lupus, and scleroderma (Buckwalter and Lappin 2000).
   C. Know that men are at greater risk for some pain disorders, including cluster headache and pancreatitis (Dodick et al. 2000; Lin et al. 2000).
   D. Recognize that several pain conditions are unique to reproductive organs—either to women, including dysmenorrhea, vulvodynia, and labor pain, or to men, such as testicular pain and pain associated with prostatitis (Wesselmann and Reich 1996).
   E. Know that some studies suggest greater procedural and postoperative pain among females than males (Froehlich et al. 1997; Averbuch and Katzper 2000; Taenzer et al. 2000), while other studies have reported no sex differences (Lander et al. 1990; Gear et al. 1996).

III. Understand sex differences in nociceptive responses and pain perception in both animal (acute and chronic) and human (acute) experimental pain models.
   A. Know that nonhuman animal models reveal sex differences in nociceptive responses, but the results vary across pain assays. For example, females are more sensitive to electrical stimuli and to chemical provocations such as formalin (Aloisi et al. 1994, 1995; Mogil et al. 2000). Be aware that findings from studies of heat stimuli are less consistent, with more studies than not reporting no sex differences (Mogil et al. 2000).
   B. Know that hormonal responses to nociceptive stimuli differ according to sex (Aloisi 1997).
   C. Know that among humans, women report lower pain thresholds and tolerances than men, and that ratings of supratherreshold stimuli are often higher among women than men across a wide range of painful stimuli (Fillingim and Maixner 1995; Riley et al. 1998).
IV. Understand differences in analgesic responses both within the same sex (e.g., during childbearing) and between sexes.

A. Know that endogenous analgesic responses can differ both quantitatively and qualitatively by sex (Bodnar et al. 1988; Mogil et al. 1993) and that there are female-specific endogenous analgesic systems, including pregnancy-induced analgesia (Gintzler and Liu 2000) and analgesia produced by vaginocervical stimulation (Komisaruk and Whipple 2000).

B. Be aware that nonhuman animal research, primarily in rodents, suggests greater opioid analgesia in males than females (Fillingim and Ness 2000; Kest et al. 2000). Limited research on non-opioid analgesics suggests that sex differences may also be present for these agents (Walker and Carmody 1998; Chiari et al. 1999).

C. Know that among humans, research suggests that sex differences can be measured between mu- and kappa-opioid agonists. For example, following oral surgery, females experienced either more robust or more prolonged analgesia than males using kappa- (or weak mu-) opioid analgesics (Miaskowski et al. 2000). Be aware that limited experimental research suggests that women show greater analgesic responses to potent mu-opioid agonists (Sarton et al. 2000; Zacny 2002).

D. Know that for nonsteroidal anti-inflammatory drugs, the variability in response may be gender-related such that females demonstrate less effect than males (Walker and Carmody 1998), although findings of no sex difference have also emerged (Averbuch and Katzper 2000).

V. Understand biological and psychosocial contributions to sex differences in pain responses (Fillingim 2000).

A. Know that developmental factors influence the structural and functional sex differences in nervous system development (McEwen 2001). Be aware that brain function and activation during pain can differ between males and females (Paulson et al. 1998).

B. Know that sex hormone receptors can influence nociceptive activity through genomic and nongenomic or membrane effects (Aloisi 2000).

C. Know that sex differences in immune responses can contribute to sex differences in pain sensitivity (Da Silva 1999; Gregory et al. 2000).

D. Be aware of the normal biological differences between the sexes, e.g., weight and body mass composition, as they apply to pharmacokinetic differences as well as cyclical hormonal variations with age (Berkley and Holdcroft 1999).

E. Know that hormonal fluctuations associated with the estrous or menstrual cycle have been associated with pain and analgesia (Riley et al. 1999; Fillingim and Ness 2000). Exogenous hormones have also been related to clinical pain (LeResche et al. 1997; Wise et al. 2000; Musgrave et al. 2001) and to experimental pain sensitivity (Fillingim and Edwards 2001).

F. Know that genetic factors appear to determine some sex differences in pain and analgesia (Mogil 2000).

G. Know that multiple psychosocial variables may contribute to sex differences in clinical and experimental pain responses, including (but not limited to) anxiety (Edwards et al. 2000), abuse history (Spertus et al. 1999), coping (Affleck et al. 1999; Keefe et al. 2000), gender roles (Robinson et al. 2001), and family history (Fillingim et al. 2000).

VI. Understand that the patient’s sex may influence treatment seeking, delivery of treatment, and treatment effectiveness.

A. Know that women seek more pain-related health care than men (Unruh 1996; Barsky et al. 2001), and that women in the general population are more likely than men to use prescription narcotics (Eggen 1993; Simoni-Wastila 2000).
B. Know that women are more likely than men to suffer an adverse effect after analgesia (Ciccone and Holdcroft 1999).

C. Know that women and men presenting with pain complaints (e.g., ischemic cardiac pain or back pain) may be offered different diagnostic tests and/or treatments (Safran et al. 1997; Roger et al. 2000; Weisse et al. 2001).

D. Be aware that some research suggests that rehabilitation and multidisciplinary pain treatment produces more robust clinical improvement in women than men (Jensen et al. 2001), while other findings indicate similar treatment gains for women and men (Mannion et al. 2001).

E. Be aware that the determinants of treatment effectiveness may differ for women and men (Burns et al. 1998).

VII. Understand the factors that may influence the outcome of pain experiments or therapies for men and women.

A. Know that health care delivery occurs in a sociocultural context and that the characteristics of providers and patients and the setting in which health care is provided may influence women and men in different ways.

B. Know that the attitude of the person matters and that within-sex variation in pain is greater than between-sex variation in pain.

C. Know that time (e.g., daily circadian rhythms) and environmental factors (e.g., music, lighting) may influence women and men differently.

REFERENCES


