# Sex and Gender Differences in Health and Disease

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Carolina Academic Press
Durham, North Carolina

ISBN 0-89089-471-X
LCCN

Carolina Academic Press

700 Kent Street
Durham, North Carolina 27701
Telephone (919) 489-7486
Fax (919)493-5668
www.cap-press.com

Printed in the United States of America

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# Preface

Are there differences in health and diseases between males and females? Obviously there are some physical differences, primarily in the reproductive organs, that distinguish males from females. But are the other organs anatomically and functionally the same in males and females? Do diseases manifest the same? Are medications equally efficacious? Do side effects from medications differ? Do hormones play any role in how diseases manifest in men versus women? Are some diseases (besides those of the reproductive organs) more common in one sex and if so why?

These are just a few questions that this book will attempt to address. This book is arranged by body system. Within each body system, normal anatomical and physiological differences between males and females are presented. Additionally, normal laboratory value differences between males and females are provided.

Differences in disease prevalence or manifestations are discussed by body system. Information is provided on which sex has an higher disease prevalence, the ratio of disease prevalence in males to females when it could be found, and occasionally interesting facts about different manifestations of the disease between the sexes. In certain diseases, the prevalence may be similar, but the disease may manifest differently or be more severe in one sex and this is also noted.

This book also includes a section on pharmacological and toxicological differences on how the sexes respond to medications or environmental agents. For example, the half-life and clearance of a drug may differ when administered to a male or female. Why does this difference occur? In many cases, it is unknown why, but new research is finding differences in the amounts or types of enzymes in the body which probably accounts for some of this difference.

In the final chapter, miscellaneous topics are presented that do not fit neatly into a specific body system. However, these are differences that have been frequently noted between the sexes.

This book should be of interest to physicians, geneticists, anatomists, physiologists, pharmacologists, epidemiologists, toxicologists and others interested in differences in anatomy, physiology, and disease occurrence between the sexes. It can also be used as a resource for teachers of gender studies courses. Hopefully this book will spark interest and research in finding out why differences between the sexes occur in so many diseases.

# Introduction

## Gender-Based Biology

A new field of interest, gender-based biology, identifies physiological and biological differences between women and men at the subcellular, cellular, tissue, organ, and system level and the effects of pharmaceutical agents on males and females. It is known that women in the United States live on average 7 years longer than men. The average male lifespan today is 74 years, but for females it is 81 years. Why does this difference exist? The average sex ratio at birth is 106 males for every 100 females. Over the last 20–30 years this difference has been decreasing. Is environmental pollution partly responsible? Do male and female fetuses respond differently to these pollutants which may be found in their mother's body? Certain antidepressants appear to be more effective in men versus women. Are there differences in the cytochrome enzyme systems that may explain this? Findings from gender-based biology research may help explain these differences and lead to new treatments for diseases that may vary depending upon one's sex.

## Sex versus Gender

While many scientists use these terms interchangeably, there is a difference in meaning. The normal development of humans depends on the compatibility between sex chromosomes (genetic sex), sex of the gonads, internal and external genitalia formation, somatic body characteristics, and psychic sex. The psychic sex is frequently called gender and consists of gender identity (identification of self as male or female), gender role (the aspects of behavior in which males and females differ from one another in our culture at this time) and sexual orientation (hetero-

sexual or homosexual or bisexual) and cognition (sexually dimorphic cognitive abilities). In short, the physical difference is called sex, influenced by genes and biology; the psychological difference is called gender, in which environment, cultural, and psychosocial factors have a prominent role.

## Sex and Gender Differences in Illness/Injury

Studies have shown that women experience more illnesses than men, despite the fact that they live on average several years longer than men. Why does this difference exist? Is it all biological or are there other possible explanations? Women also respond to illness differently and use more health services than men. A difference in the pattern of symptom reporting exists between men and women in many surveys. This difference may indicate that women have more symptoms; women recognize symptoms more readily because they are better informed about health problems; or women may be more likely to acknowledge and report their problems. Women's experiences of menstruation, pregnancy and childbirth, and menopause cause them to think more about their bodies, their bodily sensations, and their health in ways often different from men. This may partially explain the greater frequency of visits to medical practitioners.

Researchers, including biologists, sociologists, and anthropologists, have attempted to explain some of the reasons why differences in illness occur. Sociological explanations often focus on life style differences. For example, females may be treated as the weaker sex in some countries and their medical concerns may be downplayed or ignored. Limited financial resources may limit access to health care facilities. Women's role as the primary care giver of the children may have both positive and negative impacts on her health. If the woman stays at home to raise her family, she may have less exposure to occupational hazards such as chemicals in the workplace. On the other hand, she may have higher exposure to household indoor air pollutants. She may also have less contact with people with whom she may be able to vent her worries and frustrations.

Differences in behaviors may also play a role in differences in prevalence of disease. Males tend to be risk takers, smokers, and con-

sume alcohol more heavily than women. Men tend to be more reluctant to embrace prevention strategies. This has contributed to the spread of AIDS and other sexually transmitted diseases. Dietary differences, with women consuming less protein and calcium, may contribute to anemia and increased osteoporosis risk in females.

Occupational and recreational preferences often vary between men and women. Males are frequently involved in more outdoor activities that may increase their risk of exposure to vectors that transmit infectious agents. Males also tend to be involved in recreational activities that increase their risk of traumatic injuries such as football and bull riding.

Besides these social and lifestyle issues, that may affect one's risk of illness or injury, there are also genetic factors that may determine the risk of disease. Scientists know that autistic diseases are sex-linked and are likely to appear more in one sex (usually male). This will be discussed further below.

Technological and medical advances may have an impact on the outcome of disease treatment between the sexes. For years, females were excluded from drug trials, partly due to the fear of adverse fetal outcomes if the female would happen to become pregnant while on an investigational drug. It was often assumed (occasionally incorrectly) that females would respond to the drug the same as males. However, females today are now more likely to be included in drug trials and the results of these trials may show that females react similarly or differently to a drug. Likewise, some surgical treatments may be more technically difficult on females due to smaller organ or blood vessel size. This may cause more surgical complications and lead to increased morbidity or mortality rates in females. As surgical techniques improve, one may note the complication rate differences between the sexes to lessen.

## Genetic Disorders

Genetic disorders fall into one of these categories: Chromosomal disorders; Mendelian or simple inherited disorders; and multifactorial disorders. Chromosomal disorders involve abnormal arrangement, deletion, or addition of chromosomal material. Mendelian disorders are due to mutation in a gene. Mendelian disorders display patterns of inheritance that involve the autosomes or sex chromosomes (X and Y), and

are classified as dominant or recessive modes of inheritance. Most common disorders such as hypertension and heart disease are multifactorial in etiology. As the name implies, multifactorial disorders are caused by interaction of multiple genes and multiple exogenous factors.

As this book is concerned with sex differences, X-linked chromosome disorders are of concern. There are at least 350 X-linked genetic disorders known, the majority of which are recessive. X-linked recessive disorders affect males, whereas female carriers are usually spared. This is due in part to random inactivation of one of the two X-chromosomes in all female somatic cells. Thus, in female carriers of an X-linked mutation, on average 50% of the cells have the normal allele on the active X-chromosome. These functionally normal cells are usually sufficient to avoid or markedly lessen the clinical effects of an X-linked disorder in females.

How does X-linked recessive inheritance work? Usually the female sex chromosomes of an unaffected carrier mother have one faulty gene and one normal gene. The father has normal genes on the X and Y chromosomes. The resulting risk of developing the disorder in the male and female offspring are as follows: For males, there is a 50% risk of the disorder and 50% chance of being normal. For females, there is a 50% risk of being a carrier like the mother and a 50% chance of being normal.

| Parent | Carrier mother | | Normal father | |
|---|---|---|---|---|
| | Xx | | Xy | |
| Offspring | Xx | xy | XX | Xy |
| | Carrier female | Disorder male | Normal female | Normal male |

If the male is affected and marries a normal female, then all of the female children are carriers, but the male children are normal.

| Parent | Normal female | | Disorder male | |
|---|---|---|---|---|
| | XX | | xy | |
| Offspring | Xx | Xx | Xy | Xy |
| | Carrier female | Carrier female | Normal male | Normal male |

In X-linked recessive disorders, female children are only affected if an affected male fathers a child of a female carrier.

| Parent | Carrier female | Disorder male |
|---|---|---|
| | Xx | xy |

| | | | | |
|---|---|---|---|---|
| Offspring | Xx<br>Carrier<br>female | xx<br>Disorder<br>female | Xy<br>Normal<br>male | xy<br>Disorder<br>male |

Dominant X-linked disorders are rare. Affected mothers transmit to one half her sons and one half her daughters. Affected fathers transmit to all daughters and no sons. The disorder tends to be less severe in heterozygous affected females than the hemizygous affected males. In some X-linked dominant disorders, there is lethality in the hemizygous male fetus. Characteristics of these dominant X-linked disorders include: The disorder occurs only in females heterozygous for the mutation; affected mothers transmit to one half of her daughters; and increased frequency of abortions occur in affected women, the abortions being of affected male fetuses.

## Non-Genetic Disorders

Many differences in illnesses between males and females may be explained by non-genetic mechanisms. Exposure to various risks often differs between males and females. Males are often more likely to be risk takers, and accidental injuries and deaths are usually more prevalent in males as well as homicides.

The nature of one's work and hobbies also may put one sex or the other at increased risk. For example, hunters, primarily males, are more likely to be exposed to disease carrying insects and thus are more likely to have a higher prevalence of certain insect-transmitted diseases. Females are more likely to perform secretarial work such as typing. This may increase the females' chances of developing carpal tunnel syndrome.

Economic status may also play a role especially in third world countries where females may have jobs that pay substantially less. As a result, the type of food that can be purchased may be of lower quality and the female may be more likely to suffer from nutritional deficiencies. Housing conditions may be poorer and the female may be more likely to be exposed to weather-related problems such as heat or cold stress.

Lifestyle behaviors also may be different between males and females and partially explain some of the difference seen. Males tend to smoke, drink, and use more illicit substances than females. Males are also more likely to have medical disorders related to the abuse of these products.

However, females are increasingly using these products and are rapidly catching up with men in some disease categories such as lung cancer from tobacco use.

## Multifactorial Influences

Many diseases are determined by multiple genes and their subsequent interaction with environmental factors. We know that hypertension may be due to the interaction of several different genes. Salt intake may exacerbate blood pressure changes in certain individuals with hypertension. The effects of environmental agents on various genes and the resultant adverse effect, if any, are becoming better known through advances in molecular research. Scientists are aware of many chemical agents that may form DNA adducts in the human body. The concern is that certain cancers may result due to these interactions. Certain exogenous agents may act as promoters instead of initiators of carcinogenesis. Other agents may act as teratogens causing birth defects. Research has also shown that exposure to various forms of radiation may induce illness in humans. Certain individuals with genetic defects (xeroderma pigmentosum) do not tolerate ultraviolet rays from the sun and are very susceptible to developing skin cancers from sun exposure. A growing field of inquiry is the effect endocrine disruptors may have on fetal and postnatal development in humans. As we learn more about the interactions of genes, gene proteins, and environmental agents, we may begin to get a better understanding of why differences in the prevalence of certain diseases occur between the sexes.