11. CERVICAL CANCER

SCOPE OF THE PROBLEM

Cancer of the uterine cervix (cervical cancer) accounts for about 2 percent of invasive cancers found in Connecticut women each year, and about 1 percent of cancer deaths. It is the second most common cancer among women worldwide, but is the 16th most common cancer in the U.S. (Brownson et al., 1998) and the 13th most common in Connecticut. Although it once was one of the most common causes of death among American women, it now ranks ninth among all cancer deaths (Connecticut Department of Public Health, Breast and Cervical Cancer Early Detection Program, 1999), with improvements due largely to screening, early detection, and treatment.

Stage at Diagnosis and Relative Survival Rate

In Connecticut in 1995, the last year for which data on *in situ* cervical cancers were collected, 87 percent of cervical cancers were *non-invasive,* where the 5-year relative survival rate is nearly 100 percent. Of invasive cervical cancers diagnosed in Connecticut women in 1997, 54 percent were localized, where the 5-year relative survival rate is 92 percent; 28 percent were regional, where the 5-year relative survival rate is 49 percent; and 5 percent were distant, where survival drops to 15 percent (Ries et al., 2001).

Cancer incidence and survival in the United States are reported through the SEER program (described in Appendix A). Between 1986 and 1993, the last years for which comparisons were published, the 5-year relative survival rate for cervical cancer was 69 percent nationally and 67 percent in Connecticut (Ries et al., 1997).

Incidence, Hospitalizations, and Deaths

Between 1995 and 1998, 632 new cases of invasive cervical cancer were diagnosed in Connecticut women, for an annual, age-standardized annual incidence rate of 7.5 cases per 100,000 females (Connecticut Tumor Registry, 2001),

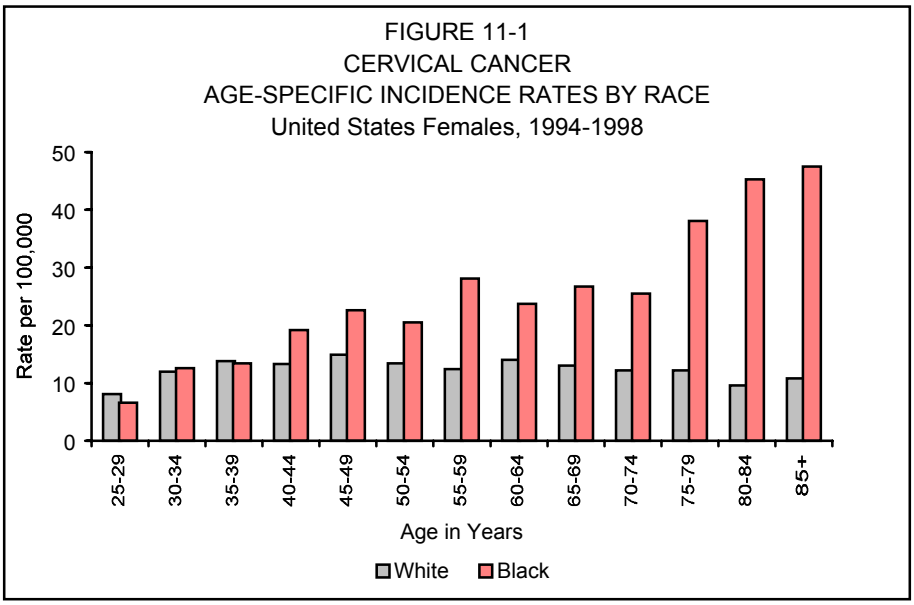
There were 188 hospitalizations of Connecticut women for cervical cancer during 1997, resulting in hospital charges of more than $2 million. The age-adjusted hospitalization rate was 10.2 hospitalizations per 100,000 females (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

Between 1996 and 1998, 127 Connecticut women died of invasive cervical cancer, for an annual, age-adjusted rate of 2.2 deaths per 100,000 females (Mueller et al., in preparation).

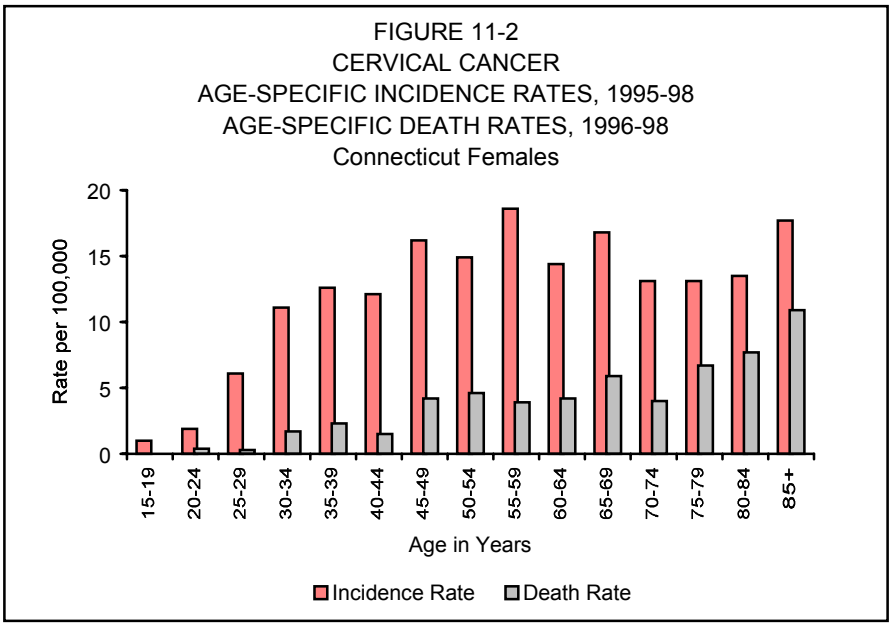
Age

Rates for *in situ* cervical cancer (not shown) peak for both blacks and whites between 20 and 30 years of age (National Cancer Institute, 2001). Incidence rates for invasive cervical cancer rise similarly in blacks and whites until 45-49 years of age, with further increase among blacks but not whites, after age 50 (Ries et al., 2001) (Fig. 11-1).

Nationally, incidence and mortality rates increase with age in both white and black women. Data for Connecticut are shown below in Figure 11-2.



Source: Ries et al., 2001.



Sources: Connecticut Tumor Registry, 2001; Mueller et al., in preparation.

Race and Ethnicity

Both incidence and death rates for cervical cancer are higher among black and Hispanic women than among white women in the Connecticut and national reporting systems. Between 1995 and 1998, the annual, age-adjusted cervical cancer incidence rates for white, black, and Hispanic females in Connecticut were 8, 15, and 18 per 100,000, respectively. Both black and Hispanic women had significantly higher rates than white women. Black and Hispanic women also had significantly higher hospital discharge rates for cervical cancer between 1993 and 1997, compared with white women (Connecticut Department of Public

Health, Division of Policy, Planning, and Analysis, 2001).

Cervical cancer death rates for black women were significantly higher than those for white women in both the 1989 through 1991, and 1996 through 1998 periods. Between 1996 and 1998 the age-adjusted death rate for black women in Connecticut was 3 times as great as that for white women (Table 11-1) (Mueller et al., in preparation). There were insufficient numbers of cervical cancer deaths among Hispanic, Asian and Pacific Islander, and Native American women to calculate reliable rates among them.

Socioeconomic Status

Low socioeconomic status is associated with a high risk of cervical cancer (Brownson et al., 1998), most likely through patterns of sexual behavior. This has also been seen when using a neighborhood measure of affluence (Krieger et al., 1999). According to the 1990 U.S. Census, Connecticut residents age 18 and over living below the poverty level, by race and ethnicity, were: white (4 percent), Asian (9 percent), black (16 percent), and Hispanic (21 percent). Figures for Native Americans in Connecticut were not reported (Miller et al., 1996).

TABLE 11-1
CERVICAL CANCER DEATHS BY RACE AND ETHNICITY
Connecticut Females, 1989-1991 and 1996-1998

	1989-91		1996-98	
Race/Ethnicity	Number of Deaths	Age Adjusted Death Rate (per 100,000)	Number of Deaths	Age Adjusted Death Rate (per 100,000)
All races	150	2.8	127	2.2
White	126	2.5	101	1.9
African American/Black	22	6.6	22	5.8‡
Asian/Pacific Islander	1	†	2	†
Native American	0	†	2	†
Hispanic/Latina	7	†	11	†

Source: Mueller et al., in preparation.
† Statistics not calculated for fewer than 15 events.
‡ Rate significantly different from that of whites ($p < .05$)
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population.

Except for the black and white races, there is considerable race and ethnicity misclassification in the reporting of cancer incidence and mortality. In SEER national data, which do not include statistical tests of race-ethnicity differences, the annual cervical cancer rates were 10.3 (incidence) and 2.7 (mortality) per 100,000 in American women from Asia and Pacific Islands, compared with 6.9 and 2.7 in white non-Hispanic Americans for 1992-98. Incidence and mortality rates were 6.4 and 2.9 in American Indian/Alaska native women (Ries et al., 2001).

In a study of six Connecticut cities between 1986 and 1995, federally-defined Medically Underserved Areas (MUAs) were associated with higher percentages of late stage cervical cancers at diagnosis (Polednak, 2000a). MUAs were defined by the ratio of primary care physicians to the population, the infant mortality rate, and the proportion of the population that is elderly and poor (Wright et al., 1996).

Geographic Region

Death rates for invasive cervical cancer in the U.S. generally are higher in the Southeast and lower in the West and Midwest (Brownson et al., 1998). Between 1994 and 1998, Connecticut

ranked 45th highest among the states and District of Columbia for annual age-adjusted cervical cancer mortality rate (Ries et al., 2001). The ranks of neighboring states were: New Jersey 23, New York 24, Rhode Island 31, Massachusetts 42, Vermont 9, New Hampshire 35, and Maine 12.

TRENDS OVER TIME

Between 1973 and 1998 cervical cancer incidence and mortality rates have both declined nationally, in both white and black, and younger and older women. The decline in mortality rates were slower since 1980 in each of the groups, compared to the 1970's. Between 1992 and 1998 the annual decrease in the cervical cancer incidence rate was 2.1 percent overall and the decline in mortality rate 2.3 percent, with larger survival improvements among blacks, Hispanics, and American Indians (Ries et al., 2001).

In 1935, cervical cancer incidence rates in Connecticut stood at about three times their present level, then declined sharply for the next fifty years (Polednak, 1994). In the past decade no significant changes have been observed (Connecticut Tumor Registry, 2001; Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

Between 1989 through 1991, and 1996 through 1998, the age-adjusted death rate for invasive cervical cancer in Connecticut women decreased from 2.8 to 2.2 per 100,000, which was not a statistically significant change (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

Between 1988 and 1995 in the SEER national program, there was a narrowing of black-white disparities in the proportion of cervical cancers detected at late stage, especially in women aged over 65 years (Polednak, 2000b).

RISK FACTORS

Human Papillomavirus

Human papillomavirus (HPV), which is transmitted through sexual contact, is believed to be the leading cause of cervical cancer. The relative risk for developing cervical cancer in women with HPV is greater than 10-fold, while the absolute risk is greater than 30 percent (Schiffman et al., 1996). The population-attributable risk of a history of sexually-transmitted diseases, including HPV, is quite imprecise. Brownson and colleagues (1998) cited an attributable risk of 5 percent, with a range of 1-50 percent. More recently (1999), Walboomers and colleagues, after reanalyzing specimens using three different polymerase chain reaction assays, estimated that HPV is present in 99.7 percent of cervical carcinomas worldwide.

Sexual Behavior

An estimated 38 percent of cases of cervical cancer are attributed to having multiple sex partners, and early age at first intercourse (less than 18 years) accounts for another 25 percent (Brownson et al., 1998). Both of these relate to the risk of and time of HPV infection. The relative risk of cervical cancer is 16 times as high in women who had first intercourse prior to age 16, compared with first intercourse after age 19, while the relative risk associated with having more than four sexual partners is 3.6 (Averette and Nguyen, 1995). The number of sexual partners of a woman's sexual partner is itself also a risk factor.

That the number of sexual partners remains an independent risk factor for cervical cancer after controlling for HPV infection may reflect false negative HPV testing or the independent role of other sexually transmitted diseases. Early age at first intercourse could be a proxy for a longer latency period of carcinogenesis, or it could suggest that the cervix is most vulnerable in adolescence (Schiffman et al., 1996). According to behavioral risk surveys conducted between 1996 and 1997, 4 percent of Connecticut women 18-64 years of age, and 25 percent of girls in grades 9 through 12, reported

having multiple sex partners. Of the students, 42 percent reported they had sex before age 18, and 3 percent said they had sex before age 13 (Adams, 2000).

In 1998, 8 percent of sexually active Connecticut women said they had more than one sex partner in the prior year. Of these, nearly three out of four (74 percent) said they don't always use condoms, and nearly one in three (32 percent) said they never use condoms. Women with multiple sex partners were almost twice as likely as those with only one sex partner to use condoms all the time (27 percent and 15 percent, respectively), however (Connecticut Department of Public Health, AIDS; Counseling and Testing Program, 2000).

HIV and Chlamydia Infections

Unprotected sex can lead to infection with HIV and *Chlamydia*. Women infected with HIV have about 3 times the risk of uninfected women for developing invasive cervical cancer. (See Chapter 21, *HIV/AIDS*).

Chlamydia is the most common sexually transmitted disease among Connecticut women (see Chapter 20, *Sexually Transmitted Diseases*). Exposure to certain types of *Chlamydia. trachomatis* bacteria may enhance the progression of HPV infection to invasive cervical cancer, and chlamydia infection may also be an independent risk factor (Anttila et al., 2001; Zenilman, 2001).

Cigarette Smoking

Cigarette smoking is a risk factor for progression of HPV infection to cervical cancer (Zenilman, 2001; Moscicki et al., 2001), and it accounts for about 32 percent of population-attributable risk for cervical cancer in the United States (Brownson et al., 1998). See the chapter on lung cancer for data concerning smoking in Connecticut.

PREVENTION AND RISK REDUCTION

The risk of developing cervical cancer can be reduced by limiting the number of sexual partners, delaying sexual intercourse until a later age, avoiding sexually transmitted diseases, by using barrier contraceptive methods (condom or diaphragms), and by not smoking (Brownson et al., 1998). Cervical cancer vaccines against HPV have been successful in several animal systems, and early phase 1 human trials indicate an enhanced immune response through vaccination, but these results have not yet been confirmed through long-term human clinical trials (Im et al., 2001).

Screening and Early Detection

Cervical cancer is slow in development, making it ideal for early detection and intervention. The Papanicolaou ("Pap") smear test is a rapid, simple, and relatively inexpensive method of detecting cervical cancer. About half of all invasive cervical cancers are diagnosed in women who never had a Pap test, whereas 99 to 100 percent of those diagnosed with *in situ* cervical cancer have had Pap tests (Holmquist, 2000). The American Cancer Society recommends annual Pap tests for all women who are or have been sexually active or who are 18 or more years of age. It is estimated that between 37 percent and 60 percent of cervical cancer deaths could be prevented by full use of the Pap test (Brownson et al., 1998).

For older women who have had a normal Pap smear, the optimum schedule for repeat testing is unknown. There is little or no benefit of routine vaginal screening for women who have had a hysterectomy for benign conditions (National Cancer Institute, 2001).

Nationally, cervical cancer screening rates are lower among certain demographic groups, including Hispanics, lesbians, women with low income, education, or literacy levels, and those living in rural areas (Brownson et al., 1998; Connecticut Tumor Registry, 1999a). During 1996 and 1997, in Connecticut, low-income women between 18 and 24 years of age, and 65 or more years of age were the least likely to have

had a Pap test. Hispanic women were less likely than black women or white, non-Hispanic women to have been tested recently or ever (Adams, 2000).

The Connecticut Breast and Cervical Cancer Early Detection Program (CBCCEDP) is described in the chapter on breast cancer. Between 1995 and 2000, 15,502 women were enrolled and 26,723 Pap test were performed. Follow-up of 518 abnormal Pap tests resulted in the diagnosis of 9 invasive and 94 *in situ* cervical cancers (Mitchell, 2001).

Table 11-2 shows the percentage of women in Connecticut and neighboring states in 2000, among those who were 18 years or older and had an intact cervix, who said they had not had a Pap smear ever or not within three years. Among the eight states listed, Connecticut ranked 3rd highest for not having had a Pap smear ever and for not having one within the past 3 years. The median prevalences of never having had a Pap smear or not within 3 years among 49 states, the District of Columbia, and Puerto Rico were 5 percent and 13 percent, respectively. Self-reports tend to exaggerate use of Pap tests, and patients recall tests as occurring more recently than they actually occurred (Holmquist, 2000).

As noted above, HPV may cause virtually all cases of cervical cancer. Thus, screening for HPV may come into widespread use in the future.

The Woman to Woman Study evaluated a peer-delivered 16-month intervention, through the cooperation of the Service Employees International Union in Boston, and designed to increase breast and cervical cancer screening. The study was intended to reach women in low-income jobs. Although the majority of women reached were in unionized state agencies and health care settings and had household incomes above $50,000, the intervention resulted in significant increase in Pap smear screening, and modest, non-significant increases in mammography and clinical breast examination rates. Having had a Pap test within the past 3 years increased from 85 percent to 90 percent in the intervention group (+4.7) and from 86 percent to 88 percent in the control group (+1.9). The authors suggested that interventions through churches or housing developments might better reach underserved populations (Allen et al., 2001).

TABLE 11-2
DID NOT HAVE A PAP SMEAR
Northeastern States, Females Aged 18 and Older with Intact Cervix, 2000

	Ever		Within Past 3 Years	
State	% Prevalence	95% Confidence Interval	% Prevalence	95% Confidence Interval
Connecticut	5.9	4.6, 7.2	12.0	10.2, 13.7
Maine	4.6	2.8, 6.4	11.0	8.6, 13.3
Massachusetts	5.4	4.5, 6.3	10.4	9.2, 11.6
New Hampshire	3.1	1.5, 4.7	9.9	7.7, 12.1
New Jersey	10.0	8.2, 11.7	18.1	16.0, 20.2
New York	7.6	5.9, 9.2	14.4	12.2, 16.5
Rhode Island	5.5	4.1, 6.9	11.5	9.7, 13.3
Vermont	5.8	4.2, 7.4	11.9	10.0, 13.8

Source: Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion. Behavioral Risk Factor Surveillance System Survey, 2000.

TREATMENT

In situ cervical cancers may be treated by cryotherapy (cell destruction by extreme cold), electrocoagulation (cell destruction by extreme heat), laser surgery, or traditional surgery. Invasive cervical cancers are treated surgically or with radiation, either alone or in combination. Some procedures, such as with a laser, can be performed on an outpatient basis. Surgical treatment can preserve ovarian function, prevent vaginal stenosis in young women, and avoid the bladder and bowel complications of radiotherapy. While radiotherapy shows no survival advantage, it reduces pelvic recurrences of cancer. Stage I and II cervical carcinoma is usually treated by surgery and stage III and IV by radiotherapy (Averette and Nguyen, 1995).

The National Cancer Institute provides information on types of cervical cancer, risk factors, prevention, testing, diagnosis, coping, support, and treatment, for both patients and health care providers (National Cancer Institute, 2001).

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12. OVARIAN CANCER

SCOPE OF THE PROBLEM

Ovarian cancer is the seventh most common malignancy diagnosed in Connecticut women, accounting for 3.5 percent of invasive cancers. It is the leading cause of death from gynecological malignancies, accounting for about 5 percent of cancer deaths among Connecticut women or 200 deaths each year.

Stage at Diagnosis and Relative Survival Rate

Ovarian cancer has the worst prognosis of any gynecological cancer, because it produces no symptoms until it is at an advanced stage. In the United States, cancer incidence and survival rates are reported through the SEER program (see Appendix A). Between 1992 and 1997, 26 percent of ovarian cancers were localized at diagnosis, where the five-year relative survival rate was 95 percent, 10 percent had spread regionally by the time of diagnosis, where survival was 81 percent, 59 percent were at the distant stage at diagnosis, where survival was 29 percent, and 6 percent were unstaged (Table 12-1)(Ries et al., 2001).

Ovarian cancer survival rates in Connecticut are similar to national rates. Between 1986 and 1993, the last year for which comparisons were published, the five-year relative survival rates were 46 percent nationally and in Connecticut (Ries et al., 1997). Between 1992 and 1997 the national five-year relative survival rate was 52 percent.

In Connecticut in 1997, 47 percent of ovarian cancers were diagnosed at the distant stage, 24 percent were local, 17 percent were regional, and 11 percent were unstaged (Connecticut Tumor Registry, 1999a).

Incidence, Hospitalizations, and Deaths

Between 1995 and 1998, 1,261 new cases of invasive ovarian cancer were diagnosed in Connecticut women; the annual age-adjusted incidence rate was 14.7 cases per 100,000 women (Connecticut Tumor Registry, 2001).

In 1997, there were 321 hospital admissions of Connecticut women with a principal diagnosis of ovarian cancer, resulting in hospital charges of $6.6 million. The age-adjusted hospitalization rate was 17.2 hospitalizations per 100,000 females (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

TABLE 12-1
OVARIAN CANCER STAGING AND RELATIVE SURVIVAL RATE
U.S. Females, 1992-1997 and Connecticut Females, 1997

Staging	United States, 1992-1997		Connecticut, 1997
	Percent of Total	5-Yr RSR	Percent of Total
Local	26	95.1	24
Regional	10	80.5	17
Distant	59	29.4	47
Unknown	6	27.2	11
Total	100	52.1	100

Sources: Ries et al., 2001; Connecticut Tumor Registry, 1991a. RSR=relative survival rate

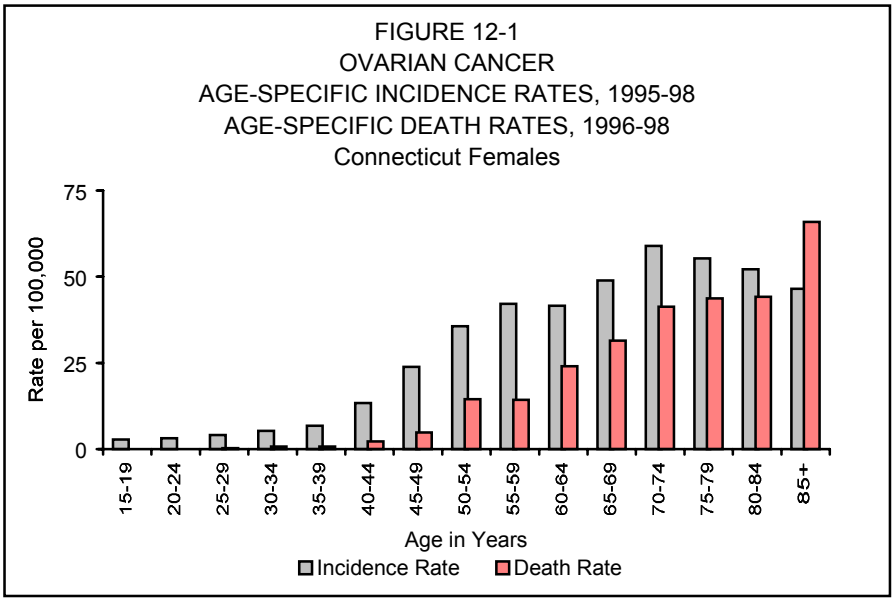
Between 1996 and 1998, 522 Connecticut women died of invasive ovarian cancer, giving an annual, age-adjusted mortality rate of 8.6 deaths per 100,000 females.

Demographic Differences

Ovarian cancer incidence and mortality rise with age (Fig. 12-1). Globally, incidence rates plateau after age 70, which is related to the exhaustion of oocytes at menopause (Weiss et al., 1996).

in the reporting of race-ethnicity other than black or white.

Between 1995 and 1998, the annual, age-adjusted ovarian cancer incidence rates for white, black, and Hispanic females in Connecticut were 17.9, 8.0, and 14.5 per 100,000, respectively; the rate in blacks was significantly lower than that in whites. Hospitalization rates between 1993 and 1997 for ovarian cancer were significantly lower in both black and Hispanic women, compared to white women (Connecticut Department of Public



Source: Connecticut Tumor Registry 2001; Mueller et al., in preparation.
Notes: U.S. Census Bureau population estimates used for rate calculations. Death rates adjusted to the 2000 U.S. standard million population. Incidence rates adjusted to 1970 U.S. standard million population.

Race and Ethnicity

The incidence rate of ovarian cancer is greatest among white and Hawaiian women, intermediate among African-American, Hispanic, and Asian-American women, and lowest among Native American women (Daly and Obrams, 1998). The mortality rate is greatest among white non-Hispanic women (Ries et al., 2001). Note that rates are affected by misclassification

Health, Division of Policy, Planning, and Analysis, 2001). Similarly, between 1996 and 1998 the age-adjusted mortality rate from ovarian cancer was significantly lower in black women compared to white women (Table 12-2) (Mueller et al., in preparation). These differences partly reflect different hormone levels and child-bearing patterns by race (see the section on risk factors, below).

TABLE 12-2
OVARIAN CANCER DEATHS BY RACE AND ETHNICITY
Connecticut Females, 1989-1991 and 1996-1998

	1989-1991		1996-1998	
Race/Ethnicity	Number of Deaths	Age Adjusted Death Rate (per 100,000)	Number of Deaths	Age Adjusted Death Rate (per 100,000)
All races	526	9.2	522	8.6
White	506	9.4	505	8.9
African American/Black	17	5.9	15	4.6‡
Asian/Pacific Islander	1	†	1	†
Native American	0	†	1	†
Hispanic/Latina	9	†	10	†

Source: Mueller et al., in preparation.
† Statistics not calculated for fewer than 15 events.
‡ Rate significantly different from that of whites (p< .05)
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population.

Socioeconomic Status

Ovarian cancer is associated with high socioeconomic status, largely through reproductive behavior.

Geographic Region

Between 1994 and 1998, Connecticut ranked 40th highest among the states and District of Columbia for average annual age-adjusted ovarian cancer mortality (Ries et al., 2001). The ranks of neighboring states were: New Jersey 7, New York 14, Rhode Island 18, Massachusetts 28, Vermont 1, New Hampshire 8, and Maine 6.

TRENDS OVER TIME

In most parts of North America and Europe, ovarian cancer incidence rates have remained nearly constant for decades (Weiss et al., 1996). In the 1980's, ovarian cancer incidence rates and mortality rates in the United States both increased slightly, while between 1991 and 1998, they each declined by about 1.1 percent annually. Both changes were statistically significant (Ries et al., 2001). Connecticut ovarian cancer incidence rates did not change significantly between 1980 and 1998. Mortality rates declined slightly by approximately 0.9 percent annually between 1989-91 and 1996-98, not a significant change.

RISK FACTORS

The principal non-modifiable risk factors for ovarian cancer are age and genetic susceptibility. Genetic predisposition is conferred in part by inherited mutations in BRCA1 and BRCA2 genes (especially BRCA1), which normally act as tumor suppressors. Carriers of these mutations account for about 8 percent of cases of ovarian cancer (Elit, 2001). The BRCA1 mutation conveys a 63 percent risk of developing ovarian cancer during a woman's lifetime, and the BRCA2 mutation a 27 percent risk (Elit, 2001). See the section G*enetic Counseling and Testing,* below.

Reproductive History and Hormone Use

Several lines of evidence point to a positive relationship between a woman's number of ovulatory cycles and the risk for development of ovarian cancer (Schildkraut et al., 1997). Ovulation is inhibited during pregnancy and by birth control pills. Accordingly, never having had a full-term pregnancy and infertility increase risk (Mosgaard et al., 1997). Risk also increases slightly with a first pregnancy before age 20 years (Cooper et al., 1999).

Oral contraceptive use reduces ovarian cancer risk by at least one-half, a benefit that grows with increasing duration of use and continues for 15 or more years after cessation of

use (Hulka, 1997; LaVecchia and Franceschi, 1999). Interestingly, other contraceptives including intrauterine device, barrier methods, tubal ligation, and vasectomy all reduced ovarian cancer risk in multigravid women, but not nulligravid women, after adjustment for other risk factors. The effects were greatest for tubal ligation and oral contraceptives. These results are compatible with a hormonal or ovulatory effect, but suggest that some contraceptives decrease ovarian cancer risk through other mechanisms (Ness et al., 2001). In another study, tubal ligation decreased ovarian cancer risk among women with the BRCA1 mutation, but not among women with the BRCA2 mutation (Narod et al., 2001).

After menopause, estrogen replacement therapy without progesterone may increase the risk of ovarian cancer mortality by more than 100 percent in women who have used ERT for 10 years or more (Rodriguez et al., 2001). This is consistent with the effects of ERT on breast and endometrial cancer risk.

Family History

Family history of breast, colon, or endometrial cancer in a first-degree relative (mother or sister) is considered a risk factor (Averette and Nguyen, 1995) and family history of ovarian cancer is present in 20 percent of ovarian cancers (Elit, 2001). Family history represents a combination of genetic inheritance and shared environment.

Diet

While evidence is inconsistent, in some studies, high consumption of cholesterol (eggs), has been associated with an increased risk of ovarian cancer. A high intake of green leafy vegetables may decrease risk (Kushi et al., 1999).

RISK REDUCTION

Because the causes of ovarian cancer are poorly understood, prevention is difficult. Risk may prove to be modifiable by changes in diet (increasing consumption of green, leafy vegetables). In 1997, less than four in ten adult Connecticut women and only three in ten high school students reported consuming five or more servings of fruits and vegetables daily, with blacks and younger adults reporting the lowest consumption (Adams, 2000). See the chapter on colorectal cancer.

Prophylactic oophorectomy (surgical removal of the ovaries) reduces risk, although not completely, and may be considered by high-risk women who have completed childbearing (Eisen et al., 2000). For women with the BRCA1 mutation, prophylactic oophorectomy would reduce both breast and ovarian cancer risk (Rebbeck, 2000). Its value in reducing mortality requires further study.

Genetic Counseling and Testing

A health care professional should determine which patients are at increased risk of breast and ovarian cancer by eliciting their personal and family histories. A family history should include at least three generations on both maternal and paternal sides. Assessment of risk is based on the number of first and second degree relatives with breast, ovarian, prostate, colon and some other cancers, their ages at diagnoses, and the occurrence of multiple or bilateral cancers. (New York State Department of Health, 1999). It is not currently recommended that widespread genetic screening of any subpopulation be initiated. For women with a history of breast and ovarian cancer in several relatives, alternatives to genetic testing include increased surveillance, participation in clinical research, and use of chemopreventive agents (e.g. tamoxifen).

Screening and Early Detection

Ovarian cancer is rarely diagnosed in its early stages, when successful treatment is possible. One step screening tests are not feasible, except perhaps in some high risk women.

A two-step screening strategy is under consideration. Elevated levels of cancer antigen 125 (CA 125) are found in women with ovarian cancer prior to clinical presentation. However, elevated levels are sometimes also found in other women. Transvaginal ultrasonography (also called endovaginal ultrasound, or EVUS), when used as a second-line test in post-menopausal women with elevated CA 125, appears to distinguish those at normal risk from those at approximately 300-fold elevated risk of ovarian cancer (Rosenthal and Jacobs, 1998; Menon et al., 1999). In a study from Yale, 252 women with a family history of ovarian cancer underwent regular pelvic examinations, screening for CA 125, and EVUS. Two ovarian cancers were detected, and 11 women developed breast cancer. The authors recommended that mammography be performed at the time of ovarian cancer screening (Taylor and Schwartz, 2001).

TREATMENT

For a larger discussion of cancer treatment, see the chapter on colorectal cancer. Ovarian cancers are treated by surgery (hysterectomy and removal of one or both ovaries), often followed by chemotherapy for women with advanced stage cancer or a family or personal history. The aggressiveness of surgery depends upon whether resection is safe (Averette and Nguyen, 1995). Patients with any stage of ovarian cancer are appropriate candidates for clinical trials (National Cancer Institute, 2001).

The National Cancer Institute provides information on types of ovarian cancer, risk factors, prevention, testing, diagnosis, coping, support, and treatment, for both patients and health care providers (National Cancer Institute, 2001).

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13. ENDOMETRIAL CANCER

SCOPE OF THE PROBLEM

Cancer of the body of the uterus (uterine corpus) is the most common cancer of the female reproductive system and is the fourth most common cancer among American women, behind breast, lung, and colorectal cancers. It accounts for more than half of gynecologic cancers and about 6 percent of all invasive cancers found in Connecticut women each year (Connecticut Tumor Registry, 2001).

Stage at Diagnosis and Relative Survival Rate

The vast majority of corpus uteri cancers in white women are endometrial, involving the lining of the uterus, as are also most corpus uteri cancers in black women (Grady and Erstner, 1996). Both endometrial and myometrial cancers, as well as a few cancers of the cervix uteri, have on occasion been reported as uterus, not otherwise specified (NOS). In the 1980's, about half of deaths reported as due to cancer of the uterus, NOS, were actually of the corpus. Over time, fewer uterine cancers are being reported as NOS (Grady and Erstner, 1996). Currently NOS represents 2% of total uterine cases (National Cancer Institute, 2001). In this chapter we group cancer of the uterine corpus and uterus, NOS together, following the practice of the SEER program. To distinguish the corpus from the uterine cervix, in this chapter we refer to the former as the endometrium, as this is a common practice, although not completely accurate.

National cancer incidence and survival rates are reported using the SEER database (see Appendix A). Between 1992 and 1997, the national five-year relative survival rate for all stages of endometrial cancers was 84 percent (Table 13-1). Seventy-three percent of endometrial cancers were diagnosed at the localized stage, where five year relative survival was 96 percent, 14 percent were diagnosed at the regionalized stage, where survival was 63 percent, 8 percent were diagnosed at the distant stage, where survival was 26 percent, and 5 percent were unstaged (Ries et al., 2001).

Endometrial cancer survival rates in Connecticut are similar to national rates. Between 1986 and 1993, the most recent years for which comparisons were published, the five year relative survival rates were 84 percent nationally and 83 percent in Connecticut (Ries et al., 1997).

TABLE 13-1
ENDOMETRIAL CANCER STAGING AND RELATIVE SURVIVAL RATE
U.S. Females, 1992-1997 and Connecticut Females, 1997

	United States, 1992-97		Connecticut, 1997	
Staging	Percent of Total	5-Yr RSR	Percent of Total	5-Yr RSR
Non-invasive	0	NA	3	
Local	73	96.1	73	
Regional	14	62.7	10	
Distant	8	25.8	5	
Unknown	5	49.1	9	
Overall	100	84.0	100	83.2*

Sources: Ries et al., 1997, 2001; Connecticut Tumor Registry, 2000.
RSR=Relative Survival Rate *1986-1993

In Connecticut in 1997, 73 percent of invasive endometrial cancers were diagnosed at the local stage, 10 percent were regional, and 5 percent were distant (Connecticut Tumor Registry, 2000). The balance of tumors were noninvasive (3 percent) or of unknown stage (9 percent).

Incidence, Hospitalizations, and Deaths

True rates involving endometrial cancer depend on the number of women at risk, that is, the number of women with an intact uterus. By the 1970's, one third of American women over age 50 had received a hysterectomy and so were no longer at risk for endometrial cancer (see the section *Trends over Time*, below). However, endometrial cancer rates, including those reported in this chapter, are almost always calculated from populations that include women who have had hysterectomies, so that the rates are artificially low.

Between 1995 and 1998, 2,121 new cases of invasive endometrial cancer were found in Connecticut women, and the annual, age-adjusted incidence rate was 25 cases per 100,000 females (Connecticut Tumor Registry, 2001).

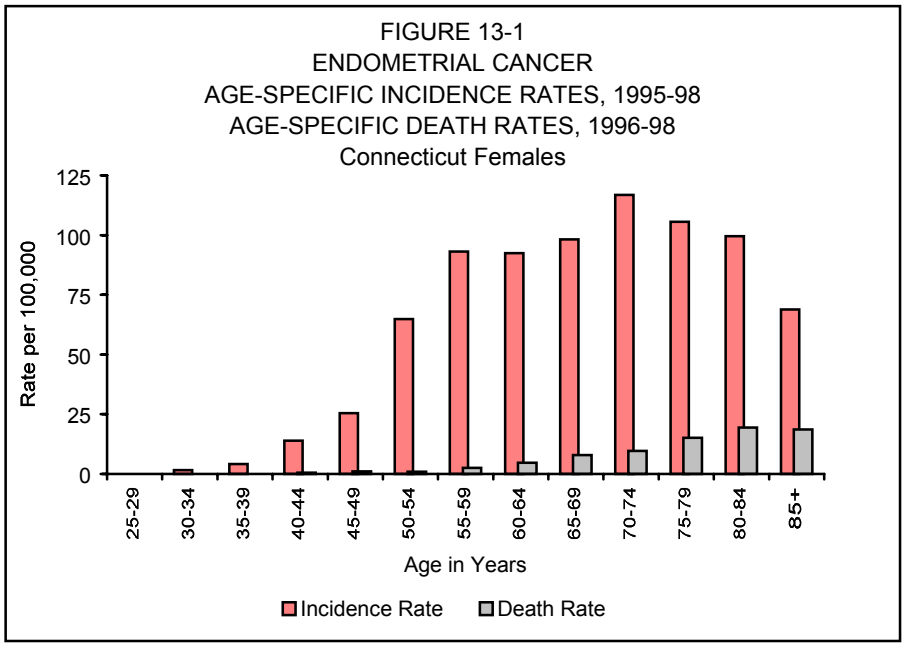
Between 1993 and 1997 the annual, age-adjusted hospitalization rate (AAHR) was 27 hospitalizations per 100,000 females. In 1997, there were 494 hospitalizations (AAHR 26 per 100,000 females), resulting in total hospital charges of $5.9 million dollars (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

Between 1996 and 1998, 135 Connecticut women died of invasive endometrial cancer, and the annual, age-adjusted rate was 2.1 deaths per 100,000 females (Mueller et al., in preparation).

Age

Endometrial cancer incidence rates increase with age, and less rapidly after the age of menopause, before falling after age. Mortality rates, however, increase slowly throughout a woman's lifetime 75 (Fig. 13-1).

FIGURE 13-1
ENDOMETRIAL CANCER
AGE-SPECIFIC INCIDENCE RATES, 1995-98
AGE-SPECIFIC DEATH RATES, 1996-98
Connecticut Females



Source: Connecticut Tumor Registry, 2001: Mueller et al., in preparation.
Notes: U.S. Census Bureau population estimates used for rate calculations. Death rates adjusted to the 2000 U.S. standard million population. Incidence rates adjusted to 1970 U.S. standard million population.

Socioeconomic Status

Endometrial cancer has been inconsistently associated with high socioeconomic status. If present, the association is probably due to estrogen replacement therapy (ERT) and more complete diagnosis in women who use ERT (Grady and Erstner, 1996).

Race and Ethnicity

In the U.S., white, non-Hispanic women have the highest annual incidence rate of endometrial cancer (23 per 100,000 between 1994 and 1998), whereas American Indian/Alaskan native (9 per 100,000), Hispanic (13), Asian/Pacific Islander (15), and black women (15) have much lower incidence rates. However, there is some misclassification of race and ethnicity in the reporting of cancer incidence and mortality. Annual mortality rates among black women (6), however, are 1.8 times greater than those of white women (3) and 2-3 times greater than those of Asian/Pacific Islanders, American Indians, and Hispanics (Ries, et al., 2001). Similarly, the relative survival rates for white women are greater than for black women at every diagnostic stage (Table 13-2). This is most evident among women aged 50 or older (American Cancer Society, 2000; Ries et al., 2001).

Better survival for white women compared to black women within each cancer stage suggests that stage may be less advanced for white women within each staging category, that they may develop more favorable histologic types of cancer, or that they have better access to the best treatment (Grady and Erstner, 1996). The latter two possibilities have been intensively studied.

Histologic types do differ by race. Cancers of the myometrium (which are primarily sarcomas) are more common among black women than white women, and these cancers are reported as uterus, NOS. In late life, mortality rates for uterus, NOS, are actually higher than for corpus both in whites and blacks (Grady and Erstner, 1996).

Some studies have suggested that the poor endometrial cancer prognoses in African American women were due to the cumulative number of poor prognostic factors, including tumor characteristics and socioeconomic status, beyond which race had no predictive value (Hicks et al., 1997). Others have found race significant even after controlling for pathologic and socioeconomic factors (Connell et al., 1999). While income generally had no effect on whether treatment was provided, African American women were treated less often by surgery, and had poorer survival than white women even for stage I adenocarcinoma treated surgically (Hicks et al., 1998). One study estimated that after adjusting for age and geographic location, the relative mortality risk in blacks was four times that in whites; 40 percent of the difference was attributed to more advanced stage, 23 percent to tumor characteristics and treatment, and 17 percent to socioeconomic, hormonal, reproductive, comorbidity, and health behavior

TABLE 13-2
ENDOMETRIAL CANCER STAGING AND RELATIVE SURVIVAL RATE BY RACE
U.S. Females, 1992-1997

	White		Black	
Staging	Percent of Total	5-Yr RSR	Percent of Total	5-Yr RSR
Local	75	96.9	52	82.9
Regional	13	65.1	22	42.7
Distant	8	27.7	18	13.1
Unstaged	4	47.6	9	48.9
Total	100	85.8	100	58.9

Source: Ries et al., 2001. RSR=relative survival rate

characteristics, but leaving 20 percent unexplained (Hill et al., 1996).

The racial disparities in stage at diagnosis seem to be due to more aggressive types of cancer appearing among black women (Barrett et al., 1995). For example, adenocarcinomas were usually diagnosed at early stage while papillary serous and clear cell cancers, which were more common in black than in white women, were diagnosed at later stages. Within each stage, patients were treated similarly regardless of cancer type or race (Matthews et al., 1997).

Recently, black and white differences have been examined at the genetic level. Among patients with stage I endometrial cancer, the mutant p53 tumor suppressor gene was found in 34 percent of blacks and 11 percent of whites, and recurrent disease, which is related to the p53 gene, was seen in more blacks than whites (Clifford et al., 1997). After collecting information about possible confounding variables, p53 alteration was found to be the most important prognostic variable, and only p53 expression and stage entered a multivariate model (Sung et al., 2000). The PTEN mutation was found more often in whites with endometrial cancer (22 percent) than in blacks (5 percent), and this mutation conferred better survival (Maxwell et al., 2000). Microsatellite instability (MSI) in DNA was associated with the absence of p53 overexpression in endometrial cancer (Maxwell et al., 2001). There is controversy over whether MSI in endometrial cancer patients is associated with white race or better survival (Basil et al., 2000; Maxwell et al., 2000, 2001).

Between 1995 and 1998 in Connecticut, the annual, age-adjusted endometrial cancer incidence rate was 29.3 per 100,000 in white women, which was significantly higher than the rate of 20.8 per 100,000 in black women or 18.7 per 100,000 in Hispanic women, a pattern also seen in hospital discharges between 1993 and 1997 (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001). Between 1996 and 1998, there were too few endometrial cancer deaths among non-white women for racial and ethnic comparisons (Table 13-3). However, between 1994 and 1998, the mortality rate in Connecticut was about 50 percent higher among blacks than whites, as was true nationally (Ries et al., 2001).

TABLE 13-3
ENDOMETRIAL CANCER DEATHS BY RACE AND ETHNICITY
Connecticut Females, 1989-1991 and 1996-1998

	1989-91		1996-98	
Race/Ethnicity	Number of Deaths	Age Adjusted Death Rate (per 100,000)	Number of Deaths	Age Adjusted Death Rate (per 100,000)
All races	133	2.2	135	2.1
White	127	2.2	126	2.1
African American/Black	6	†	9	†
Asian/Pacific Islander	0	†	0	†
Native American	0	†	0	†
Hispanic/Latina	0	†	2	†

Source: Mueller et al., in preparation.
† Statistics not calculated for fewer than 15 events.
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population.

Geographic Region

Endometrial cancer incidence rates for white, black, and Asian women in the United States are higher than for their racial counterparts in Europe and Japan (Grady and Erstner, 1996). Between 1994 and 1998, Connecticut ranked 27th highest among the states and District of Columbia for average annual age-adjusted endometrial cancer mortality. The ranks of neighboring states were: New Jersey 2, New York 4, Rhode Island 9, Massachusetts 20, Vermont 3, New Hampshire 7, and Maine 28 (Ries et al., 2001).

TRENDS OVER TIME

Since the 1950's, endometrial cancer mortality rates have apparently declined by more than 60 percent in the United States, although part of this decline is an artifact of the increased rates of hysterectomies, while including such women in the populations from which rates are calculated. One study estimated that adjustment for hysterectomy raised the age-adjusted endometrial cancer rate by 20% (National Cancer Institute, 2001). During 1996 and 1997, the proportions of Connecticut women who said they had had a hysterectomy, by age, were: 1 percent at ages 18-34 years, 9 percent at ages 35-49, 33 percent at ages 50-64, and 42 percent at ages 65 and older (Adams, 2000).

Hysterectomies are performed for a variety of reasons. In 1998 in North Carolina, cancer was the primary diagnosis for the hysterectomy in only 6 percent of cases; the leading diagnosis (34 percent) was uterine leiomyoma or fibroids (Jones-Vessey, 2000). In 1998, 645,000 hysterectomies were performed in the United States, a rate of 236 per 100,000 women (Popovic and Kozak, 2000), while 4,994 were performed as a primary hospital procedure in Connecticut, a rate of 296 per 100,000 women (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

Endometrial cancer incidence rates rose during the 1970's due to the use of high doses of unopposed estrogen by postmenopausal women, before falling to previous levels with the introduction of lower dose, combination hormone replacement therapy (Grady and Erstner, 1996). Mortality rates did not increase during the 1970's, possibly because the estrogen-induced tumors were less aggressive or were detected earlier. Among women of all ages, mortality rates between 1973 and 1998 declined more rapidly in blacks than whites. Mortality rates among blacks aged less than 50 years declined more rapidly (4.6 percent annually) than blacks aged 50 years and over (0.8 percent annually). Between 1988 and 1998, national incidence rates increased by 0.5 percent annually, while national mortality rates decreased between 1989 and 1998 by 0.6 percent annually (Ries et al., 2001); both trends were statistically significant. Between 1980 through 1984 (23.1 per 100,000), and 1995 through 1998 (24.8 per 100,000), and intermediate periods, there were no significant changes in the annual, age-adjusted incidence rate for endometrial cancer in Connecticut (Polednak, 2001). Between 1989 through 1991, and 1996 through 1998, there was no significant change in the annual mortality rate (Table 13-3).

RISK FACTORS

The most important non-modifiable risk factors for endometrial cancer are age and genetic susceptibility. For prognostic factors, see the section R*ace and Ethnicity*, above. A personal or family history of breast or ovarian cancer increases the risk for endometrial cancer, but may represent a common effect of reproductive risk factors. Polycystic ovary syndrome may be present in up to 30 percent of endometrial cancers in selected groups of pre-menopausal women (Grady and Erstner, 1996).

Estrogen is the main risk factor for the most common form of endometrial cancer. Estrogen-related factors include early onset of menstruation, late menopause, a history of failure to ovulate, never having children, use of tamoxifen, and estrogen replacement therapy

(ERT). The relative risk of endometrial cancer from ever using ERT is 2.3, with risk increasing according to estrogen dose and duration of usage (Grady and Erstner, 1996). When estrogen is taken in lower doses with progesterone (hormone replacement therapy, HRT), however, the risk is actually lower than in women not taking hormones (Grady and Erstner, 1996). Smoking may reduce the risk of endometrial cancer incidence through an androgenic effect. However, smoking may not reduce endometrial cancer mortality risk, if it prevents only clinically unimportant tumors (Grady and Erstner, 1996).

The most important modifiable risk factor for endometrial cancer is obesity, which increases risk by 3 to 10 times (Merck & Co., 2000). Body weight, weight gain, and accumulation of central body fat all are positively associated with endometrial cancer (Ballard-Barbash and Swanson, 1996). The body converts adipose tissue to estrogens (see the chapter on breast cancer). Diabetes and gallbladder disease are associated with endometrial cancer (Grady and Erstner, 1996), probably through their link with obesity.

Table 13-4 shows the prevalence of being overweight or obese among females in Connecticut and neighboring states. (Technically defined, *obesity* is a greater body mass index than *overweight*; BMI is calculated from weight and height; for the formula, see Appendix A.) Of the eight states listed, Connecticut was the 4th highest for overweight or obesity. For not restricting calories or exercise to lose weight among overweight or obese women, Connecticut ranked 7th. The median prevalences for being overweight or obese, and among these, for not attempting to lose weight by eating fewer calories or exercising, were 49 percent and 51 percent, respectively, in 50 states, the District of Columbia, and Puerto Rico. In 1997, the Youth Risk Behavior Surveillance Survey found that one-third of female high school students in Connecticut were overweight, then defined as a BMI of 27.3 or above (Kann et al., 1998).

Table 13-5 shows the prevalence of being overweight or obese in Connecticut by race-ethnicity. Obesity was most common in black women and least common in white women.

TABLE 13-4
OVERWEIGHT OR OBESE
Northeastern States, Females, 2000

	Overweight or Obese*		Not Eating Fewer Calories or Exercising to Lose Weight*	
State	% Prevalence	95% Confidence Interval	% Prevalence	95% Confidence Interval
Connecticut	45.1	42.7, 47.4	47.1	43.4, 50.8
Maine	48.6	45.3, 51.9	53.1	48.1, 58.0
Massachusetts	41.9	40.1, 43.6	49.5	46.7, 52.3
New Hampshire	42.8	39.4, 46.2	51.0	45.6, 56.3
New Jersey	47.0	44.5, 49.4	52.8	49.0, 56.6
New York	49.2	46.5, 51.8	53.9	49.8, 58.0
Rhode Island	44.6	42.1, 47.1	51.1	46.9, 55.2
Vermont	44.3	41.8, 46.7	45.7	41.9, 49.5

Source: Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion. Behavioral Risk Factor Surveillance System Survey, 2000.
*Body mass index greater than or equal to 25.0

TABLE 13-5
OVERWEIGHT OR OBESE BY RACE AND ETHNICITY
Connecticut Females, 2000

	Overweight*		Obese**	
Race-Ethnicity	% Prevalence	95% Confidence Interval	% Prevalence	95% Confidence Interval
White, Non-Hispanic	28.1	26.7, 29.6	14.7	13.9, 15.4
Black, Non-Hispanic	33.8	27.9, 39.6	30.1	24.8, 35.3
Hispanic, All Races	30.0	25.7, 34.2	24.0	20.6, 27.4

Sources: Connecticut Department of Public Health, Bureau of Community Health, unpublished data, 2001 (prevalence); Division of Policy, Planning and Analysis, 2001 (95% confidence intervals).

*Body mass index between 25.0 and 29.9 **Body mass index greater than or equal to 30.0

PREVENTION AND RISK REDUCTION

Sequential estrogen and progestin oral contraceptives increased the risk of endometrial cancer, and were removed from the market in the 1970's. Long-term use of combination oral contraceptives substantially reduces the risk of endometrial cancer (Grimes and Economy, 1995; Grady and Erstner, 1996). Weight control may prevent endometrial cancer, also through hormonal mechanisms (Hulka and Brinton, 1995; Ballard-Barbash and Swanson, 1996).

Tamoxifen's benefits in reducing breast cancer risk outweigh its risks of increased endometrial cancer in women with a history of breast cancer, but in women at low to moderate breast cancer risk, the risks incurred by tamoxifen use may exceed its benefits (Grady and Erstner, 1996).

Screening and Early Detection

There is no recommended screening procedure for endometrial cancer, although cytological screening is under investigation (Yoshida et al., 2001). Screening may detect clinically unimportant tumors, as the experience in the 1970's with ERT showed (Grady and Erstner, 1996).

More than 90 percent of women with endometrial cancer have abnormal bleeding, and about one-third of women with postmenopausal bleeding have endometrial cancer (Merck & Co., Inc., 2000). Endometrial biopsy, performed in a physician's office, is the definitive method of diagnosis and is recommended at menopause and periodically thereafter for high-risk women or when irregular pre- or post-menopausal bleeding occurs (American Cancer Society, 2000).

TREATMENT

Endometrial cancers are usually treated with surgery (hysterectomy plus salpingo-oophorectomy), radiation for those with any risk factors, medroxyprogesterone, and chemotherapy when systemic disease is present (American Cancer Society, 2000).

The National Cancer Institute provides information on types of endometrial cancer, risk factors, prevention, testing, diagnosis, coping, support, and treatment, for both patients and health care providers (National Cancer Institute, 2001).

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14. CHRONIC OBSTRUCTIVE PULMONARY DISEASE

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a term for several lung diseases all characterized by progressive airflow limitation that is not reversible (Barnes, 2000). COPD is one of the most common diseases of adults in industrialized countries, with an estimated 16 million Americans considered to be symptomatic. More than half of these people are probably undiagnosed. Many more Americans have asymptomatic forms of the disease (Petty and Master, 2000). COPD exacts enormous human and economic costs, affecting people during their peak work years. After several years with the disease, most COPD patients are disabled by chronic shortness of breath, coughing, and wheezing, and are no longer able to work productively (Goldring et al., 1998). At a time when the mortality rates for other major conditions are decreasing, COPD death rates are rising among women in the U.S. and Connecticut. Reasons for the increase probably include reduced mortality from other causes as well as an increase in cigarette smoking (Barnes, 2000). Part of this increase may be artificial due to changes in reporting practices (Centers for Disease Control and Prevention, 2001a).

Subgroups of COPD

Chronic obstructive pulmonary disease includes the diseases of emphysema and chronic bronchitis. Asthma, a clinically distinct condition, is also commonly included in COPD surveillance. These three diseases may be present singly or together in any individual person.

Chronic bronchitis, emphysema, and chronic airway obstruction are oftentimes grouped as COPD because, from a clinical standpoint, they may be difficult to distinguish from one another. *Chronic bronchitis* is diagnosed when a patient has a persistent cough caused by excessive airway mucus secretion over a long period of time. Persons with chronic bronchitis may also experience difficulty in breathing due to narrowing of the airways. *Emphysema* is a condition defined as the permanent destruction of the alveoli, the small elastic air sacs of the lung. This loss of elasticity can also cause narrowing or collapse of the bronchioles, or small air passages, which then limits airflow from the lungs. *Chronic airway obstruction* is a term used to identify other obstructed airway conditions that are not classified in any other subcategories (Goldring et al., 1998).

TABLE 14-1
MAIN SUBCATEGORIES OF COPD AND ALLIED CONDITIONS

Disease (ICD-9 code)	Definition
Chronic Bronchitis (490-491)	Excessive mucus production associated with narrowing of the bronchial airways and cough
Emphysema (492)	Alveolar destruction and associated airspace enlargement
Asthma (493)	Airway obstruction with airway inflammation and increased airways responsiveness to a variety of stimuli
Chronic Airway Obstruction (496)	Generalized airway obstruction not classifiable as chronic bronchitis or chronic obstructive bronchitis

Adapted from Goldring et al., 1998.

Asthma is an inflammatory response of the airways to a variety of stimuli that results in a usually temporary airway obstruction. Inadequate treatment of asthma may lead to chronic airway obstruction and asthma patients are considered to have COPD only when their airflow obstruction cannot be reversed by medication (Goldring et al., 1998).Because of its importance as a chronic condition affecting increasing numbers of women, asthma is discussed in depth in Chapter 15 of this report. Table 14-1 summarizes the main subgroups referred to as "COPD and Allied Conditions" in mortality and morbidity surveillance.

SCOPE OF THE PROBLEM

In the 1996 to 1998 period, COPD and allied conditions was the fourth leading cause of death among Connecticut women of all ages. Most COPD deaths were categorized as chronic airway obstruction (1,536 deaths), followed by emphysema (277 deaths), asthma (114 deaths), and bronchitis (50 deaths) (Figure 14-1).

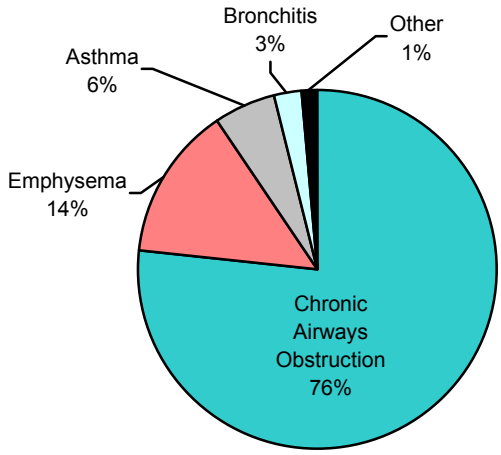
Death in COPD patients, however, often results from some other medical condition or complication. For this reason, and because its contribution to other major causes of death is not always considered, the importance of COPD as a cause of death is probably underestimated. COPD was the primary cause of death for 2,005 Connecticut women from 1996 to 1998. During the same period, COPD was a contributing cause in the deaths of 4,336 women, more than double the number for COPD alone (Mueller et al., in preparation).

Chronic obstructive pulmonary disease is a leading cause of hospital admissions among Connecticut women, with about 5,000 per year during the 1993 to 1997 period. In 1997, there were 5,110 hospitalizations, resulting in total hospital charges of $51.6 million dollars (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001). All COPD hospitalizations are considered "avoidable," that is, hospitalizations that could be avoided with appropriate and timely primary care (Pappas et al., 1997).

Age

Deaths due to chronic obstructive pulmonary disease increase dramatically with age. Women 65 years of age and older, who represent less than 17 percent of Connecticut's

FIGURE 14-1
COPD AND ALLIED CONDITIONS DEATHS
Connecticut Females, 1996-1998



Source: Mueller et al., in preparation.

female population, accounted for 90 percent of COPD deaths in the 1996 to 1998 period.

Race and Ethnicity

Age-adjusted death rates for COPD among Connecticut women rose significantly by an average of 3.6 percent per year from 1989 and 1998 and increased significantly between the periods 1989 to 1991 and 1996 and 1998. This change is accounted for by an increase in the death rate among white females (Table 14-2). The annual increase was the greatest noted for any of the selected causes discussed in this report (Mueller et al., in preparation).

compared with 28 percent of black, and 39 percent of Hispanic female COPD deaths.

These findings are consistent with available national data that show blacks have lower COPD, but higher asthma mortality compared with whites (Gillum, 1990). COPD mortality was higher in white compared with black women in 1992, although time trends indicate a similar sharp increase in COPD mortality for both white and black women from 1980 to 1992 (Centers for Disease Control and Prevention, 2001b). Similar national comparisons of COPD mortality in Hispanic, Asian and Pacific Islander, and Native American women are not available. Continued

TABLE 14-2
COPD AND ALLIED CONDITIONS DEATHS
BY RACE & ETHNICITY
Connecticut Females, 1989-1991 and 1996-1998

	1989-1991		1996-1998	
Race/Ethnicity	Number of Deaths	Age Adjusted Death Rate (per 100,000)	Number of Deaths	Age Adjusted Death Rate (per 100,000)
All races	1,412	23.0	2,005	29.9*
White	1,369	23.3	1,955	30.7*
African American/Black	43	15.3‡	50	15.1‡
Asian/Pacific Islander	0	†	0	†
Native American	0	†	0	†
Hispanic/Latina	19	14.7‡	31	16.2‡

Source: Mueller et al., in preparation.
* Change in rates from 1989-91 to 1996-98 period is statistically significant (p< .05).
† Statistics not calculated for fewer than 15 events.
‡ Rate significantly different from that of whites (p< .05).
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population.

COPD death rates were significantly higher in white women compared with black and Hispanic women in both the 1989 to 1991 and 1996 to 1998 periods. There were, however, differences in the racial and ethnic populations by subcategories of COPD deaths. For example, in the 1996 to 1998 period, 77 percent of white female COPD deaths were due chronic airway obstruction compared with 58 percent of black and 45 percent of Hispanic female COPD deaths; 14 percent of white compared with 10 percent of black and Hispanic female COPD deaths were due to emphysema. Only 5 percent of white female COPD deaths were due to asthma, investigation of racial and ethnic differences in COPD mortality may enhance understanding of its etiology and prevention.

Black and Hispanic women had significantly more hospitalizations due to COPD and allied conditions compared with white women during the 1993 to 1997 period (Table 14.3). Asian and Pacific Islander women had significantly fewer hospitalizations due to COPD compared with white women. There were too few COPD hospitalizations among Native American women to calculate reliable rates. Racial and ethnic subgroups differed in their types of COPD hospitalizations. For example, about 89 percent of all COPD hospitalizations

among Latinas and about 83 percent of those among black women were due to asthma compared with about 40 percent of COPD hospitalizations among white women. Forty-two percent of COPD hospitalizations among white women were due to chronic bronchitis compared with 8 percent of such hospitalizations among Latinas and 12 percent among black women during this period. These data suggest there are barriers to adequate or timely primary care for COPD among Connecticut women and that such barriers are greater for blacks and Latinas compared with white women.

Increases in COPD mortality nationwide are closely linked to the widespread adoption of smoking behaviors among American women beginning in the post-World War II era (U.S. Department of Health and Human Services, 1990). In Connecticut, cigarette smoking rates among women have been relatively stable since 1990 (Centers for Disease Control and Prevention, 2001c). In 1999, about 21 percent of adult females ages 18 and older were current smokers (Adams, 2001). Most adult smokers initiate the habit during adolescence, so high rates of adolescent usage are a serious public health concern. About one in three (32 percent) female students, grades 9-12 in Connecticut reported current cigarette smoking in 1999 and about 14 percent said they smoked on at least 20 of the last 30 days (Kann et al., 2000).

TABLE 14-3
COPD AND ALLIED CONDITIONS HOSPITALIZATIONS
BY RACE & ETHNICITY
Connecticut Females, 1993-1997

Race/Ethnicity	Number	Age Adjusted Rate (per 100,000)
All races	25,463	279.4
White	18,486	225.9
African American/Black	3,278	489.1‡
Asian/Pacific Islander	57	40.8‡
Native American	13	†
Hispanic/Latina	3,413	664.7‡

Source: Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001.
† Statistics not calculated for fewer than 25 events.
‡ Rate significantly different from that of whites (p<.05).
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population.

RISK FACTORS

Cigarette Smoking

Cigarette smoking is the key risk factor for the development of COPD. Smokers have ten times the relative risk of non-smokers for COPD occurrence (Goldring et al., 1998). Although not all smokers develop COPD, its prevalence does increase with age. Among current smokers 40 years and older, COPD prevalence is estimated to increase from 17 percent to 43 percent with increasing age (Stang et al., 2000). An estimated 90 percent of all COPD deaths among women are attributable to smoking (Centers for Disease Control and Prevention, 2001b).

Environmental Pollutants and Other Factors

Outdoor air pollution at high levels (especially ozone, sulfur dioxide, and particulates), exposure to chemical fumes or dust in occupational settings, exposure to second-hand tobacco smoke, and use of solid fuels for heating and cooking in poorly ventilated spaces all can contribute to COPD. Low birth weight appears to increase the risk of COPD, and a deficiency of a protein called alpha-1-antitrypsin may be associated with emphysema (Barnes,

2000). The effects of multiple risk factors for COPD seem to be additive, so it is important to identify persons with more than one risk.

PREVENTION AND TREATMENT

Because cigarette smoking is the key causative factor in the development of chronic obstructive pulmonary disease, smoking cessation for those who smoke and avoiding second-hand smoke for non-smokers are key preventive measures. Minimizing exposure to occupational and environmental air pollutants, another important preventive measure, is best achieved through environmental and workplace safety regulations. Government agencies are charged with regulating worker exposure levels to harmful occupational pollutants. Regulation of outdoor air pollution in the U.S. began with the Air Pollution Control Act (1955) and Clean Air Act (1963) and its amendments (1970, 1977, and 1990). States and municipalities have passed clean indoor acts to prohibit indoor pollutants such as cigarette smoke and pesticides. Many municipalities issue air pollution alerts when air pollution levels exceed standards, so that persons with COPD know to limit unnecessary activities (Goldring et al., 1998).

COPD has been widely underdiagnosed in primary care settings (Voelkel, 2000), particularly among women (Chapman, et al., 2001). Signs and symptoms alone are not adequate for the diagnosis of COPD. Early detection can be performed by spirometry, lung airflow measurement, in a primary care setting. The National Lung Health Education Program recommends widespread use of spirometry by primary care providers for at-risk patients, that is, current smokers 45 years or older (Ferguson et al., 2000). If people are identified in the early and asymptomatic stages of COPD, interventions like smoking cessation can prevent further disease progression (Petty and Master, 2000; Ferguson et al.; 2000). Smoking cessation can slow the progression of the disease, but no treatment can reverse the damage that has already occurred. Common medical interventions include inhaled corticosteroid and bronchodilator drugs, antibiotics, and home oxygen therapy. Pulmonary rehabilitation—a structured program of education, exercise, breathing retraining, and psychosocial support—can improve the exercise capacity and quality of life of COPD patients (Barnes, 2000).

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15. ASTHMA

INTRODUCTION

Asthma is a chronic inflammatory disorder of the airways that become hypersensitive and undergo changes when stimulated by an allergen or other environmental trigger. There are gender differences in asthma development and treatment. Girls are at substantially lower risk than boys of developing asthma during childhood, but after puberty the risk in women increases until it is higher than that in men (deMarco et al., 2000). There is evidence that female high-risk asthma patients are admitted for hospitalization twice as often as male patients and tend to have longer admissions (Trawick et al., 2001). Research suggests that the size of a person's airway, in addition to hormonal factors, could explain the different patterns of asthma incidence in males and females (de Marco et al., 2000).

SCOPE OF THE PROBLEM

Approximately 1 in 16 persons (17 million) in the U.S. and 1 in 12 persons (266,000) in Connecticut reported having asthma in 1998 and 1999 (U.S. Department of Health and Human Services, 2000; Connecticut Department of Public Health, Bureau of Community Health, 2001). In Connecticut, adult women reported current asthma (9 percent) at a significantly higher prevalence rate than adult men (5 percent) (Connecticut Department of Public Health, Bureau of Community Health, 2001).

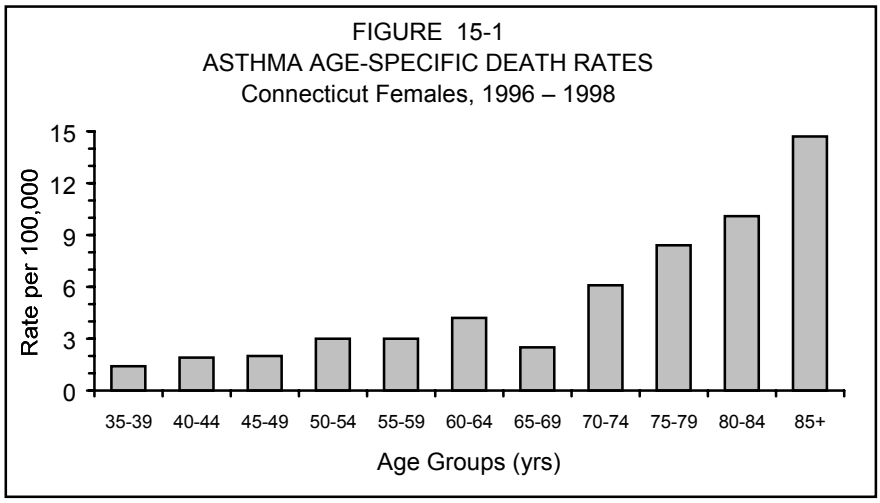
Asthma is not a leading cause of death, and mortality rates have remained stable over the past decade. However, more Connecticut females died from asthma than males (114 and 52 deaths, respectively) and the age-adjusted mortality rates from 1996 to 1998 were significantly higher for females than males (2 and 1 deaths per 100,000, respectively) (Mueller et al., in preparation).

Asthma prevalence can be measured according to the number of asthma and asthma-related conditions. Asthma may be secondary and related to a primary diagnosis of pneumonia, COPD, or other respiratory conditions. The age-adjusted hospitalization rate for asthma, as a primary diagnosis, decreased from 166 per 100,000 females in 1993 to 149 per 100,000 in 1997. Conversely, there was a significant increase in the hospitalization rate for all asthma-related diagnoses from 454 per 100,000 females in 1993 to 556 per 100,000 in 1997.

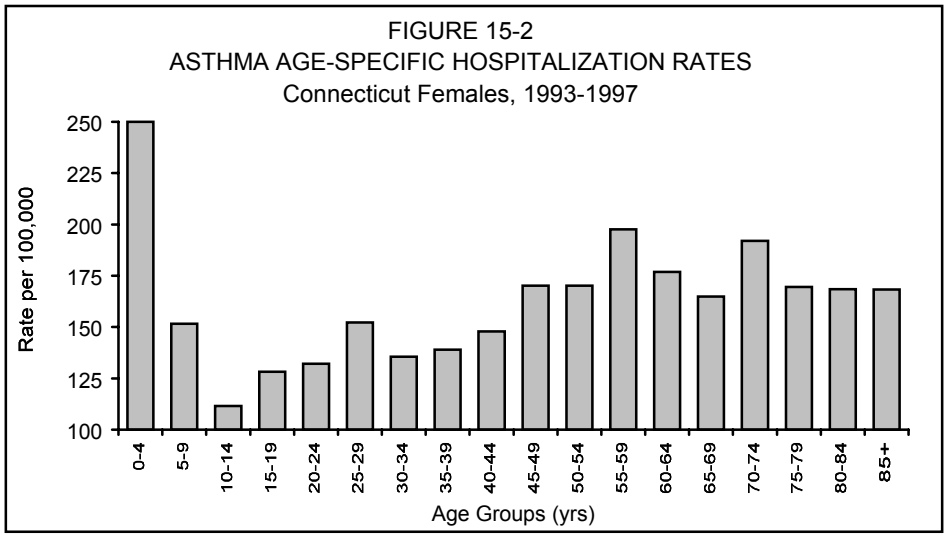
Age

Asthma mortality is low throughout the first seven decades of life, rising steadily thereafter. The highest asthma mortality rate occurs in females aged 85 years and older (Fig. 15-1).

Asthma mortality is highest for elder females, but the highest rate of asthma hospitalization occurs among children. Asthma, as a primary diagnosis, was the eighth leading cause of hospitalization for all females in Connecticut but third for females under 15 years of age (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001). This was due to the large number of hospitalizations of children under age 5. The age-specific hospitalization rate for females 0-4 years of age was higher than for any other age group from 1993 to 1997 (250 hospitalizations per 100,000 females) (Fig. 15-2).



Source: Mueller et al., in preparation.
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population.



Source: Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001.
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population.

Race and Ethnicity

There were significant differences in asthma hospitalization rates by race and ethnicity for Connecticut females. During the 5-year period from 1993 to 1997, the age-adjusted hospitalization rate for black, non-Hispanic females, and all Hispanic females was significantly higher than the rate for white, non-Hispanic females. (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001) (Table 15-1).

TABLE 15-1
ASTHMA HOSPITALIZATIONS BY RACE AND ETHNICITY
Connecticut Females, 1993-1997

Race/Ethnicity	Number of Discharges	Age Adjusted Hospitalization Rate (per 100,000)
All races	13,403	158.6
White, non-Hispanic	7,452	104.4
Black, non-Hispanic	2,708	380.4‡
Asian & PI, non-Hispanic	48	30.5‡
Native American, non-Hispanic	11	†
Hispanic/Latina	3,043	546.4‡

Source: Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001.
‡ Rate significantly different from that of whites (p< .05)
† Statistics not calculated for fewer than 25 events.
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population.

Racial and ethnic differences in asthma mortality cannot be reliably measured due to insufficient numbers of asthma deaths among black and Hispanic females between the two periods from 1989 to 1991 and 1996 to 1998 (Table 15-2). There were no asthma deaths among Asian and Pacific Islanders and Native Americans during these time periods.

TABLE 15-2
ASTHMA DEATHS BY RACE AND ETHNICITY
Connecticut Females, 1989-1991 and 1996-1998

	1989-1991		1996-1998	
Race/Ethnicity	Number of Deaths	Age Adjusted Death Rate (per 100,000)	Number of Deaths	Age Adjusted Death Rate (per 100,000)
All races	85	1.5	114	1.9
White	73	1.3	100	1.8
African American/Black	12	†	14	†
Hispanic/Latina	7	†	12	†

Source: Mueller et al, in preparation.
† Statistics not calculated for fewer than 15 events.
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population.

RISK FACTORS

Risk factors for the development of asthma are poorly understood, but likely include a family history of the disease, allergies, and environmental exposures. Environmental tobacco smoke is the leading modifiable agent for both the development of asthma in childhood and exacerbation of existing asthma.

Triggers that worsen asthma symptoms in susceptible persons include dust mites, pet dander, cockroach antigens, perfumes, and fungi (Institute of Medicine, 2000). Ambient air pollutants (e.g., ozone, sulfur dioxide, nitrogen dioxide, acid aerosols, and particulate matter), airborne allergens, and cold weather also exacerbate the condition. Medications like aspirin and some types of food, such as eggs in young children, can be asthma triggers due to allergic reactions. Stress, exercise, and emotional or psychological problems can stimulate asthma attacks or exacerbate the asthma condition.

Asthma in women is affected by hormonal changes related to menstrual cycles and pregnancy. In a recent study, one-third of emergency department visits for asthma among women occurred during the preovulatory phase of the menstrual cycle (days 5-11) (Zimmerman et al., 2000). Endometriosis also has been associated with allergic and immunological factors and may worsen asthma symptoms in women (Frieri, 1997).

Recent studies identify overweight and obesity as risk factors for asthma, particularly in females. Girls who become overweight or obese between the ages of 6 and 11 years have a sevenfold increased risk of developing new asthma symptoms at age 11 or 13 (Castro-Rodriguez et al., 2001).

ECONOMIC BURDEN

People with asthma can lead normal, productive lives with effective symptom management. However, inadequate control is costly, can have physical consequences, and can lower a person's quality of life. Annual direct health care costs for asthma total nearly $10 billion in the U.S. and $75 million in Connecticut (Connecticut Department of Public Health, 2001).

The indirect, nonmedical costs associated with asthma account for approximately 50 percent of total illness costs (U.S. Department of Health and Human Services, 2000). Indirect costs include days missed from work or school, caregiver expenditures, travel and waiting time, early retirement due to disability, and premature mortality. According to a national survey, asthma resulted in nearly half of children missing school, and more than one-quarter of adults missing work (Glaxo Wellcome, 1998).

PREVENTION AND MANAGEMENT

Asthma prevention has not been studied sufficiently, however, reducing early infections and early exposure to allergens or tobacco smoke are considered important interventions (U.S. Department of Health and Human Services, 2000). Asthma management reduces the likelihood of hospitalization, but requires a comprehensive approach that includes the use of asthma medication, reduction of specific environmental factors that trigger attacks, and patient education and self-management (Brownson et al., 1998). The leading medications for controlling asthma are corticosteroids, leukotriene-antagonists, and cromolyn. Short-acting bronchodilators are used to open airways quickly during an attack, whereas long-acting bronchodilators are considered an effective preventive treatment.

Public health interventions in Connecticut include environmental controls established through clean air legislation that reduce air pollution. Restriction of cigarette smoking in public places in Connecticut also reduces exposure to environmental tobacco smoke. Local housing codes do not directly address asthma risk factors, but they do regulate ventilation and moisture control, which are contributing factors to asthma.

Healthy People 2010 objective 24-8 recommends that states establish a surveillance system for tracking asthma mortality and morbidity, the impact of occupational and environmental factors on asthma, access to medical care, and asthma management (U.S. Department of Health and Human Services, 2000). No such comprehensive surveillance system currently exists.

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16. DIABETES

INTRODUCTION

Diabetes mellitus is a metabolic disorder in which the body is unable to produce or use insulin, a hormone it needs to convert food into energy. Diabetes affects approximately 70,000 Connecticut women aged 18 and over (Centers for Disease Control and Prevention, 1998), with another 35,000 women estimated to have, but not to have been diagnosed with the disease (U.S. Department of Health and Human Services, 1998). Between 1990 and 1998, the prevalence of diagnosed diabetes in the U.S. increased by 33 percent. Diabetes prevalence rates increased 70 percent for women aged 30 to 39 (Centers for Disease Control and Prevention, 2001).

Because symptoms develop gradually and severe symptoms may not occur for several years, diabetes is often undiagnosed or not recognized until a later stage. The disease primarily affects the circulatory system and increases the risk for a variety of disabling conditions including stroke, heart disease, arteriosclerosis (hardening of the arteries), kidney failure, blindness, and lower extremity amputations. Diabetes is the leading cause of non-traumatic amputations, blindness among working-aged adults, and end-stage renal disease. These disabling conditions contribute to a severe decrease in a person's quality of life (U.S. Department of Health and Human Services, 2000).

The economic burden of diabetes is enormous. It is a major cause of disability, morbidity, and mortality. Diabetes' direct medical costs and the indirect costs of lost productivity and premature mortality were estimated at $1.2 billion in 1997 in Connecticut, or approximately $12,000 per year for every person with diabetes (Connecticut Department of Public Health, Diabetes Control Program, 2000).

TYPES OF DIABETES

There are three types of diabetics. Approximately 5 to 10 percent of all people with diabetes have "type 1" diabetes, a condition that typically begins in childhood or adolescence and requires lifelong insulin treatment. The vast majority of people with diabetes (90 to 95 percent) have "type 2" diabetes, a condition that typically develops in adults over 30 who have a family history of diabetes, are overweight, or are physically inactive. Type 2 diabetes can be controlled through a combination of proper diet, weight loss, and exercise, although oral medications or insulin are often necessary. A third type, "gestational" diabetes, develops during pregnancy and can have harmful effects on both the mother and child because of elevated glucose levels. It is estimated that up to 4 percent of all women develop gestational diabetes during pregnancy. In most cases, blood glucose levels return to normal following the pregnancy. Women with gestational diabetes, however, have up to a 45 percent increased risk of recurrence with the next pregnancy and up to a 63 percent increased risk of developing type 2 diabetes in later life (Centers for Disease Control and Prevention, 2001).

SCOPE OF THE PROBLEM

Mortality due to diabetes and diabetes-related causes among Connecticut resident females is shown in Table 16-1. Because more people with diabetes die from complications of the disease rather than the disease itself, diabetes death rates alone understate the extent to which diabetes contributes to mortality. Between 1996 to 1998, more than 1,000 Connecticut women died as a direct result of diabetes. Almost four times that many women died from diabetes-related causes (Table 16-1).

Between 1993 and 1997, there were more than 1,800 hospitalizations of Connecticut females each year for diabetes as a primary diagnosis. People with diabetes, however, are often hospitalized for the complications of diabetes rather than for the disease itself, so these numbers understate the extent of total hospitalizations for diabetes. During the 1993 to 1997 period, there were 11 times as many hospitalizations for diabetes as a secondary diagnosis (105,620) as there were for diabetes as a primary diagnosis (9,462) among Connecticut females (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

Race and Ethnicity

Black women suffer a disproportionate number of deaths from diabetes. While diabetes was the seventh leading cause of death for all Connecticut women, it was the fourth leading cause among black women for the period 1996 to 1998. During this time, the diabetes death rate of black women was more than twice that of white and Hispanic women (Table 16-1). Similarly, the diabetes-related death rate was highest for black women, more than twice that for white, and almost twice the rate for Hispanic women during this period (Table 16-1). There were too few diabetes and diabetes-related deaths among Asian and Pacific Islander and Native American women in Connecticut during these time periods to calculate reliable rates.

The diabetes death rate for Connecticut females increased significantly between the periods 1989 to 1991 and 1996 to 1998 (Table 16-1). Between 1989 and 1998, diabetes death rates increased by 2.5 percent per year. This change is accounted for by the increase in the death rate among white and black women. There

TABLE 16-1
DIABETES AND DIABETES-RELATED DEATHS
BY RACE AND ETHNICITY
Connecticut Females, 1989-1991 and 1996-1998

	1989-1991		1996-1998	
Race/Ethnicity	Number of Deaths	Age Adjusted Death Rate (per 100,000)	Number of Deaths	Age Adjusted Death Rate (per 100,000)
DIABETES DEATHS				
All races	822	13.5	1,058	16.2*
White	735	12.6	941	15.1*
African American/Black	83	30.7‡	115	36.3‡
Asian/Pacific Islander	1	†	1	†
Native American	0	†	1	†
Hispanic/Latina	25	20.6	33	17.8
DIABETES-RELATED DEATHS				
All races	3,784	61.5	3,949	59.1
White	3,453	58.4	3,516	55.1
African American/Black	314	117.7‡	416	134.2‡
Asian/Pacific Islander	4	†	11	†
Native American	5	†	6	†
Hispanic/Latina	80	60.1	133	73.3‡

Source: Mueller et al., in preparation.
* Change in rates from 1989-91 to 1996-98 period is statistically significant (p<.05).
† Statistics not calculated for fewer than 15 events.
‡ Rate significantly different from that of whites (p< .05)
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population.

were no significant changes in diabetes death rates among Hispanic women during these time periods. Death rates due to diabetes-related causes (Table 16-1) remained unchanged between the 1989 to 1991 and 1996 to 1998 periods.

Hospitalization rates for diabetes for the period from 1993 to 1997 in Connecticut were highest among African American and black women, followed by Hispanic, and white women (Table 16-2). African American and black women had more than four times and Latinas almost twice the rate of hospitalizations for diabetes listed as a primary diagnosis compared with white women. There were too few hospitalizations of Asian and Pacific Islander and Native American women during this period to calculate reliable rates.

diabetes among black and non-Hispanic white women (Robbins et al., 2001). Low-income women are less likely to have adequate diet and physical activity, and appropriate medical care, factors known to affect the development and course of the disease. The relative importance of these and genetic factors in explaining the higher prevalence of type 2 diabetes in minority women is not well understood (Carter et al., 1996).

The risk of developing type 2 diabetes increases with age and usually develops after age 40, occurring when the body's cells become resistant to insulin. The exact cause of type 2 diabetes is unclear, although several factors have been linked to the risk of developing the disease (Table 16-3). Women at risk for developing type 2 diabetes include those who are overweight, have high blood pressure, and/or a sedentary

TABLE 16-2
DIABETES* HOSPITALIZATIONS BY RACE AND ETHNICITY
Connecticut Females, 1993-1997

Race/Ethnicity	Number	Age Adjusted Rate (per 100,000)
All races	9,462	103.7
White	6,723	83.8
African American/Black	1,967	337.3‡
Asian/Pacific Islander	14	†
Native American	4	†
Hispanic/Latina	646	156.6‡

Source: Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001.
* Diabetes as a primary diagnosis.
† Statistics not calculated for fewer than 25 events.
‡ Rate significantly different from that of whites (p< .05).
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population.

RISK FACTORS

Not everyone in the population is equally at risk for developing diabetes. While the prevalence of type 1 diabetes tends to be higher among white than among minority Americans, the prevalence of type 2 diabetes tends to be higher among black, Hispanic, and Native Americans than among whites (Brownson et al., 1998). Low socioeconomic status is strongly associated with higher prevalence of type 2

lifestyle, and who have a history of gestational diabetes. Findings from the Behavioral Risk Factor Surveillance Survey (1990-1996) indicate that among Connecticut women not diagnosed with diabetes: 25 percent are overweight, 52 percent have insufficient physical activity, and 20 percent have high blood pressure (Frost, 2000).

About 80 percent of the people with type 2 diabetes are obese at the time of diagnosis. Evidence suggests that the number of years of obesity, a high fat diet, and a lack of physical activity are risk factors for development of the

disease. Research findings also suggest that cigarette smoking may be another risk factor for development of the disease. For people who have already developed the disease, factors such as smoking and hypertension interact to increase the likelihood of complications like stroke and heart disease (Brownson et al., 1998).

clinical trial of prevention of type 2 diabetes conducted in Finland confirm this link. Researchers found that lifestyle changes reduced the risk of progression to type 2 diabetes in the intervention group by 58 percent over a four-year period, concluding that type 2 diabetes can be prevented by lifestyle changes in high-risk subjects (Tuomilehto, et al., 2001). Another major study, the diabetes prevention program, is currently underway in the U.S. and will be completed by 2002 (Diabetes Prevention Program Research Group, 1999). Findings from these key prospective studies should provide valuable information for the implementation of programs aimed at the prevention of type 2 diabetes.

TABLE 16-3
RISK FACTORS FOR TYPE 2 DIABETES

- Family history of diabetes among parents or siblings
- History of obesity (≥ 20 percent over desired weight)
- History of hypertension (blood pressure ≥ 140/90 mmHg)
- History of physical inactivity
- Previous test indicating Impaired Fasting Glucose or Impaired Glucose Tolerance
- History of gestational diabetes mellitus or delivery of babies over 9 pounds
- Age of 40 years or older

Source: Brownson et al., 1998.

PREVENTION AND TREATMENT

Clinical recommendations for the treatment of diabetes emphasize preventing the complications of the disease. Studies have documented that diabetes can be controlled by maintaining blood glucose at normal levels through diet, exercise, and oral medications or insulin injections (Padgett et al., 1988; Clement, 1995). Such self-management measures can reduce some long-term complications of the disease such as retinopathy and neuropathy (eye and nerve damage). Blood glucose monitoring is an essential part of self-management because it can indicate progress or impending problems related to the disease. Management of diabetes is a life-long process that requires knowledge and active involvement of the woman with diabetes in following diet and related lifestyle practices, and regular assessments by her health care team.

The evidence supporting the feasibility of primary prevention of diabetes (that is, preventing the disease before it develops) is accumulating. Type 2 diabetes has long been associated with overweight, physical inactivity, and dietary habits. Findings from a recent

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17. OSTEOPOROSIS

INTRODUCTION

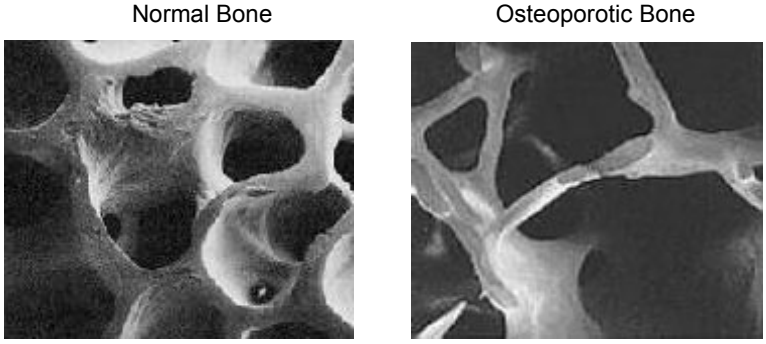
Osteoporosis is a serious, degenerative bone condition affecting the health of approximately 23 million American women. More than 8 million women have the disease, while over 14 million have osteopenia or "low bone mass" placing them at increased risk of developing osteoporosis (National Osteoporosis Foundation, 2001a).

The development of maximum bone strength and density begins in early childhood, and the skeletal bones reach their peak density by about age 30. Throughout life, bone is constantly being removed and replaced with new bone in a process called remodeling. However, as the body ages, too much bone may be removed or not enough new bone replaced or both. This leads to bone deterioration, low bone mass, osteoporosis, and an increased risk of bone fracture. The lack of optimal bone development in childhood is a important consideration

Declining hormone levels in women at the time of menopause, inadequate calcium intake during child- and young adulthood, and a lack of weight-bearing exercise all affect the bone remodeling process negatively. The loss of estrogen through natural menopause or surgical removal of the ovaries accelerates this process, causing rapid mineral depletion and thinning of the bones. Bone loss associated with aging averages about 0.5 percent a year, and increases to about 1 to 2 percent a year at menopause. The average women will lose 20 percent of her bone mass between the ages of 40 and 70.

While almost everyone experiences some bone loss with age, osteoporosis is not a normal part of aging and should not be ignored (National Osteoporosis Foundation, 1997). Another cause of osteoporosis, called secondary osteoporosis, may develop following long-time use of oral steroid drug therapy for other diseases and conditions. Figure 17-1 presents micrograph examples of normal and weakened osteoporotic bone.

FIGURE 17-1
OSTEOPOROTIC BONE MICROGRAPHS



Reproduced from *J Bone Miner Res* 1986; 1:16-21 with permission of the American Society For Bone and Mineral Research.

SCOPE OF THE PROBLEM

Osteoporosis is accurately named the "silent disease" because it weakens and thins bones without early warning signs or symptoms. The first sign of the disease is often a sudden fracture of the hip or spine. In advanced osteoporosis, the bones are so fragile that they fracture with only slight exertion, such as picking up a grocery bag, a child, or merely bending over. In the first five to seven years after menopause, bone density

may decline by as much as 20 percent (National Institutes of Health, 2000a). One in two women over 50 will have an osteoporosis-related fracture during her lifetime (National Institutes of Health, 2000a) and almost all fractures in older adults are due in part to low bone density (National Osteoporosis Foundation, 2001a).

Nationally, osteoporosis is responsible for 1.5 million fractures per year or one fracture every 20 seconds (National Osteoporosis Foundation, 2001b). The consequences of osteoporotic fractures can be severe, and cause major lifestyle changes and a diminished quality of life, especially for older women. The collapse of weakened bone structures in the spine or hip may result in physical deformity, lifelong pain, the loss of independence, and the need for long-term care.

Prevalence

Eighty percent of people with osteoporosis are women. Females experience hip fractures at a rate two to three times higher than males. One in five persons dies within a year of sustaining an osteoporotic hip fracture (National Institutes of Health, 2001). A woman's lifetime risk for an osteoporosis-related hip fracture is equal to her risk of breast, uterine, and ovarian cancer combined (National Osteoporosis Foundation, 2001a).

The consequences of an osteoporosis-related hip fracture can be severe. Twenty-four percent or one in every five persons who sustains an osteoporotic hip fracture dies within the first year (National Osteoporosis Foundation, 1999). Fifty percent will be unable to walk alone, while another 25 percent will require long-term nursing care (National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2000).

In 1996, the estimated osteoporosis prevalence rate for Connecticut females age 50 and over was 213 per 1,000 females compared to the U.S. prevalence rate of 209 per 1,000. For females age 50 and over with osteoporosis and low bone mass, the estimated prevalence rate was 617 per 1,000 females in 1996, compared with the U.S. rate of 611 per 1,000 (National Osteoporosis Foundation, 1997). By 2015, the number of Connecticut females with both osteoporosis and low bone mass is expected to increase by 36 percent, from 316,613 to 429,000 (National Osteoporosis Foundation, 1997).

Hospitalization

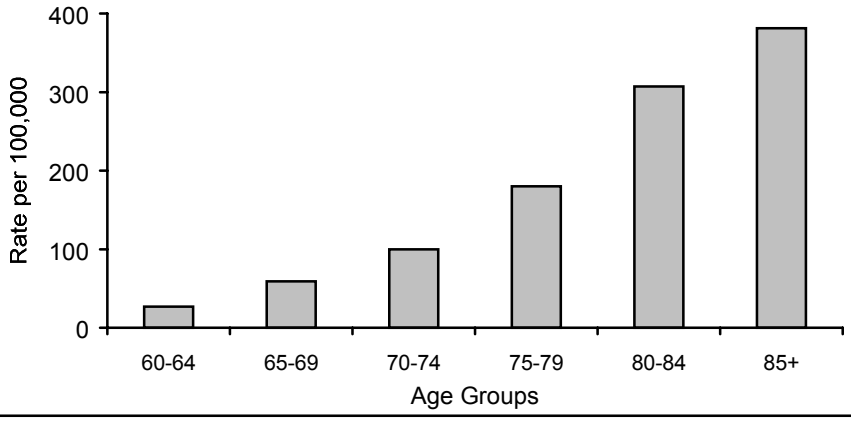
Between 1993 and 1997, there were 2,827 females discharged from Connecticut acute care hospitals with a primary diagnosis of osteoporosis and 17,046 female discharges that were osteoporosis-related. The age-adjusted hospitalization rates for black, non-Hispanic females (8 per 100,000) and all Hispanic females (7.5 per 100,000) were significantly lower than the rate for white, non-Hispanic females (27 per 100,000) (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis).

As shown in Figure 17-2, the osteoporosis hospitalization rate nearly doubles between each five-year age group beginning at age 60. Females aged 85 and over were hospitalized for osteoporosis at about three times the rate of females aged 70 to 74.

Total Connecticut hospitalization charges for osteoporosis between 1993 and 1997 were a little over $38 million (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001). When all osteoporosis-related discharges are considered, the total five-year hospitalization charges reached $234,174,766.

Nationwide, more than 1.5 million fractures occur annually as a result of osteoporosis including 300,000 hip fractures and 700,000 vertebral fractures. Costs associated with osteoporotic fractures in the United States is estimated at $13.8 billion a year or $38 million each day (National Institutes of Health, 2000a).

FIGURE 17-2
OSTEOPOROSIS AGE-SPECIFIC HOSPITALIZATION RATES
Connecticut Females, 1993-1997



Source: Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001.
Notes: Osteoporosis as a primary diagnosis.
U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population. Based on OA primary diagnoses only.

RISK FACTORS

A woman's risk for osteoporosis increases with the number of her risk factors. Table 17-1 presents the modifiable and non-modifiable risk factors for osteoporosis.

Persons of all ages can develop the disease, but females are at greater risk and the risk grows with age. Women with a family history of the disease, as well as those who have a small body frame or experience early menopause are at greatest risk of developing the disease.

PREVENTION

Osteoporosis is highly preventable and treatable, but as of now there is no cure. Prevention efforts are targeted toward two processes in a woman's life: the development of a greater peak bone mass early in life and slowing the rate of bone loss after menopause.

TABLE 17-1
OSTEOPOROSIS RISK FACTORS

NON-MODIFIABLE	MODIFIABLE
♦ Female	♦ Current cigarette smoking
♦ Advanced age	♦ Low calcium intake (lifelong)
♦ Family history of osteoporosis	♦ Low vitamin d intake
♦ Small body frame	♦ Low body weight (under 127 pounds)
♦ Caucasian or Asian race	♦ Anorexia
♦ Estrogen deficiency	♦ Lack of weight-bearing exercise
♦ Early menopause (before 45) -from surgical removal of both ovaries -abnormal absence of menstrual periods (>1 yr)	♦ Long-time use of certain medications (steroids, anti-convulsants, excessive thyroid hormone, etc.)

The critical window of opportunity for building peak bone mass is childhood and young adulthood, the primary bone-building years. From birth through approximately age 30, the skeletal bones increase in size and density. Bones need sufficient calcium, 400 and 800 IU of Vitamin D, and regular weight-bearing exercise on a daily basis to reach peak bone mass. If calcium consumption is too low to meet the body's metabolic needs, calcium will be taken from the bones. Women also need extra calcium when they are pregnant or breastfeeding.

Physical activity is important for building bone strength, agility, and balance, and should include weight-bearing exercise, such as walking, stair climbing, running, cross-country skiing, gardening, dancing, and weight lifting. The NOF also cautions women to limit their intake of caffeine beverages and soft drinks, as caffeine may interfere with calcium absorption (National Osteoporosis Foundation, 1999). Smoking and excessive alcohol consumption negatively affect bone health, but both are modifiable risk factors.

SCREENING AND TREATMENT

Bone mineral density screening exams are relatively quick, painless, and noninvasive tests that can detect, predict, and monitor a person's risk for an osteoporosis fracture. These exams are covered by most insurance plans, including Medicare, which began covering the costs of bone density screening in July, 1998.

Although there is no cure for osteoporosis, there are a growing number of Federal Drug Administration (FDA) approved pharmaceuticals for preventing and treating the disease. Hormone replacement therapy (HRT), alendronate, risedronate, and raloxifene, are approved for the prevention and treatment of osteoporosis. Salmon calcitonin is approved only for the treatment of osteoporosis.

HRT is known to increase the risk of breast cancer and thrombosis in some patients (see Chapter 9 *Breast Cancer* and Chapter 6 *Coronary Heart Disease*). Women who are unable or unwilling to receive HRT therapy may be helped by one of the other FDA-approved prevention or treatment pharmaceutical therapies.

Natural estrogens, especially those that are plant-derived, are popular osteoporosis prevention alternatives for many women, but their effectiveness is still under investigation (National Institutes of Health, 2000b).

Vertebral fractures are more common than hip fractures, but not as disabling. Two new, minimally invasive procedures called kyphoplasty have been developed to treat these types of fractures. In both techniques, bone cement is injected into the fractured vertebra to stabilize the spinal column and relieve pain. Additional studies are needed to determine the long-term effect of the procedure on adjacent vertebrae (National Institutes of Health, 2000b).

Osteoporotic hip fractures may require surgical intervention including total hip replacement. Up to one-fourth of these patients requires an extensive recovery period at home or in a nursing home. Hip fractures are discussed further in Chapter 25 of this report.

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18. OSTEOARTHRITIS

INTRODUCTION

Osteoarthritis (OA) is a chronic, degenerative joint disease and the most commonly occurring form of the more than 100 known types of arthritis and rheumatic diseases and conditions. An estimated 21 million adults (12 percent of Americans aged 25-74) have OA, and approximately 16 million (76 percent) are women (Arthritis Foundation et al., 1999).

While OA can occur in any body joint, it most frequently affects weight-bearing joints: the hips, knees, feet, and hands. OA affects the entire joint structure including the ligaments, muscles, bone, and soft tissue. The disease usually develops slowly and progresses in response to the breakdown of articular cartilage that cushions the ends of joint bones. Without cartilage, the bones directly rub against each other causing pain and inflammation. Cartilage inflammation stimulates the growth of bone spurs in the affected joint and small pieces of bone or cartilage can break off and float in the joint fluid, causing additional pain, inflammation, and damage.

Early in the development of the disease, OA pain is usually associated with movement or weight bearing, and disappears at rest. However, as the disease progress, joint pain often becomes continuous. In addition to pain, persons with OA may experience morning stiffness, tenderness, swelling, and limited joint function with or without inflammation. Symptoms range from mild to very severe and profoundly affect the quality of everyday life and emotional well being of those with OA, their families, and caregivers. When severe, OA prevents people from exercising, going to school, or earning a living. It isolates its victims and robs them of their independence.

SCOPE OF THE PROBLEM

Prevalence

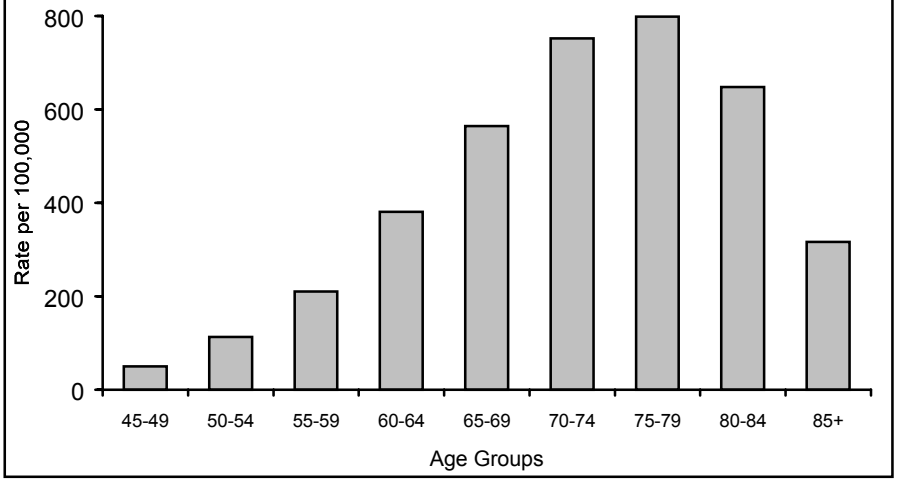
OA most frequently affects persons over 45, and its prevalence increases with age at least through age 74 (Brownson et al., 1998). One in two persons aged 65 or older shows x-ray evidence of OA in at least one joint, though they may be asymptomatic (Felson et al, 2000). OA is debilitating and the second most common reason after chronic heart disease leading to Social Security Disability payments because of long-term absence from work (La Plante, 1988). OA is expected to increase significantly by the year 2030 primarily because of the aging of the population.

Forty-two percent of adult females who responded to the 2000 Connecticut Behavioral Risk Factor Surveillance Survey (BRFSS) indicated that they had aching, stiffness, pain, or swelling in or around a joint during the last 12 months. Of these, 56 percent reported that the symptoms were present on most days for at least a month. Twenty-eight percent of adult women respondents indicated that a doctor had told them they had arthritis and one-third (36%) had been told they had OA. A surprising 42 percent of women responded that they did not know what kind of arthritis they had (Centers for Disease Control, 2000).

Hospitalization

Between 1993 and 1997, a total of 12,026 Connecticut females or a rate of 143 discharges per 100,000 were hospitalized with a primary diagnosis of OA. Eighty-one percent of these discharges were for females aged 74 and under. The frequency of female age-specific OA hospitalizations increased sharply between ages 45 and 79 during this same period (Fig. 18-1).

FIGURE 18-1
OSTEOARTHRITIS AGE-SPECIFIC HOSPITALIZATION RATES
Connecticut Females, 1993-1997



Source: Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001.
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population. Based on OA primary diagnoses only.

When all osteoarthritis-related females discharges are considered for the same time period, the total number more than triples to 36,428 or a rate of 342 per 100,000 (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

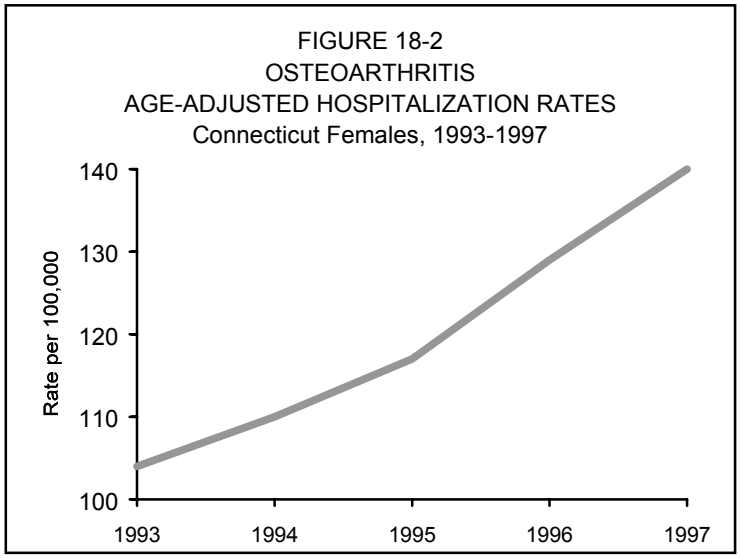
As shown below in Table 18-1, OA hospitalization rates in Connecticut between 1993 and 1997 were highest for black, non-Hispanic women (124 per 100,000) and white, non-Hispanic women (122 per 100,000). These rates were three times higher than the rate of OA hospitalizations for Hispanic women (45 per 100,000) (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

TABLE 18-1
OSTEOARTHRITIS* HOSPITALIZATIONS BY RACE AND ETHNICITY
Connecticut Females, 1993-1997

Race/Ethnicity	Number of Hospitalizations	Age Adjusted Hospitalization Rate (per 100,000)
All races	12,026	120.5
White	11,070	121.6
African American/Black	626	123.9
Asian/Pacific Islander	9	†
Native American	7	†
Hispanic/Latina	143	45.3‡

Source: Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001
Notes:
* Osteoarthritis as a primary diagnosis
† Statistics not calculated for fewer than 25 events.
‡ Rate significantly different from that of whites ($p < .05$)

Osteoarthritis age-adjusted hospitalization rate for females has significantly increased (7.8% annually) from 103.9 per 100,000 women in 1993 to 140.3 in 1997 (Fig. 18-2).



Source: Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001.
Notes: U.S. Census Bureau population estimates used for rate calculations. Rates adjusted to the 2000 U.S. standard million population. Based on OA primary diagnoses only.

OA is second only to chronic heart disease as a leading cause of work disability (National Institutes of Health, 1998). The loss of wages and cost of treatments reduce the quality of life for OA patients, their families, and others who care for them. In Connecticut, inpatient hospitalization charges for females with a primary diagnosis of OA averaged $18,773, and totaled $244 million over the five-year period from 1993 to 1997. The total 5-year charges for Connecticut OA-related hospitalizations was $528 million with an average charge of $14,506 per discharge (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

RISK FACTORS

OA's non-modifiable and modifiable risk factors are shown below (Table 18-2). Inherited genetic factors predispose certain population groups to a higher risk for OA disease and are the underlying cause for at least 50% of hand and hip OA cases. For example, females with bony node syndrome of the finger joints known as Herberden nodes are known to be at greater risk of developing OA of the hands (Brownson et al., 1998). Persons with congenital or developmental bone and joint diseases; prior inflammatory joint problems such as gout or rheumatoid arthritis; and those with metabolic diseases such as hyper- and hypo-parathyroidism and chrondacalcinosis are also at increased risk.

Advancing age and being female are two key non-modifiable risk factors leading to OA. Before age 50, men have a higher prevalence of OA in most joints, but after age 50, the trend reverses and more women are affected by OA of the foot, hand, and knee (National Institute of Health, 2000). On average, females have a higher number of OA afflicted joints than men (Brownson et al., 1998). Researchers expect OA to increase significantly by 2030, fueled by increasing longevity, especially of women, and the aging of the baby boomer generation.

TABLE 18-2
OSTEOARTHRITIS RISK FACTORS

Non-Modifiable	Modifiable
♦ genetic disposition	♦ joint trauma
♦ female (over 50)	♦ repetitive joint use
♦ age	♦ obesity
♦ metabolic disorders and prior inflammatory diseases	

A history of joint trauma is the strongest modifiable risk factor associated with the development of unilateral hip or knee OA (Brownson et al., 1998). Injuries in young adulthood or middle age are associated with a fivefold greater risk of developing knee OA. Younger people, especially those with a history of performing heavy, repetitive, or continuous physical work, or those with injuries including sports injuries are at increased risk of developing OA in later life (Felson, 2000).

Obesity is recognized as a significant, but modifiable risk factor for OA of the knee. Data from the 1992 Framingham Study showed that being overweight in young adulthood was a strong predictor of future development of OA in the knee. The study also showed that women who had lost an average of 11 pounds prior to the study decreased their risk of developing symptomatic knee OA by 50 percent (Felson et al., 1992).

PREVENTION

Primary prevention strategies for OA are limited, but effective. Reducing repetitive joint movement on the job, such as kneeling, squatting and heavy lifting helps protect joints and greatly reduces the risk for future OA development. At the same time, properly performed exercise and physical activity keeps joints limber and helps alleviate pain. Research suggests that obesity contributes to OA by placing increased mechanical stress on weight-bearing joint cartilage, especially of the knee. With each one pound increase in weight, the overall force across the knee in a single-leg stance increases by 2 to 3 pounds (Felson, 2000) emphasizing the need for reduction of body fat for persons with OA.

Nutrition plays an important part in OA prevention. Studies have shown there is an association between high intakes of vitamin C, less knee pain, and lower x-ray rates of OA (National Institute of Health, 2001). Sufficient levels of Vitamin D are also important and help protect against new and expanding OA disease. Supplements with Vitamin D may be needed during the winter months when there is less sunlight.

TREATMENT

There is no known cure for OA, but the disease is treatable with a number of different nonpharmacologic and pharmacologic options. Non-pharmacologic treatments include heat and cold therapies, braces, canes, and other adaptive devices. Range-of-motion, strengthening, and endurance exercises can help relieve pain and restore joint function. Equally important is rest and joint care to prevent overexcersing an affected joint.

The most common pharmaceutical therapies for OA are aspirin, acetaminophen, topical pain-relieving creams, rubs or sprays applied directly to the skin, and non-steroidal anti-inflammatory drugs (NSAIDs) such as ibupofern. Long term use of aspirin or NSAIDs, particularly by the elderly, is associated with stomach irritation, ulcers, bleeding and perforation. Overuse of NSAIDs can affect kidney function.

Acetaminophen is one of the safest analgesics for OA, but its use has been associated with adverse events in patients with existing liver disease. The Federal Drug Administration has approved two new NSAID drugs known as COX II (Cyclooxygenase) inhibitors for the treatment

of OA. While they cause less gastric irritation than NSIAD (COX I) medications, they can impair renal function and cause sodium and water retention. Intra-articular corticosteroid injections or opioid pain medication may be used when joint symptoms are severe or do not respond to other treatments.

Nontraditional approaches for treating OA include acupuncture, glucosamine, and chondroitin sulfate therapies. Studies on the efficacy of acupuncture for OA have been inconclusive to-date; however, a multi-site clinical trial funded by the National Institute of Health (NIH) is underway and expected to provide additional information in June, 2001. Glucosamine and chondroitin therapies have gained popularity in recent years and have shown positive results primarily in manufacturer-funded studies. An NIH funded, double-blind, placebo-controlled study of patients taking glucosamine alone, chondroitin sulfate alone, glucosamine and chondroitin sulfate together, or a placebo is underway and will be completed in 2004 (Felson, 2000).

Improvement in joint function is often achieved through a combination of rest and physical and occupational therapy. Range of motion, flexibility, muscle conditioning, and aerobic cardiovascular exercise are also important for maintaining or regaining joint function.

Tertiary treatment, in the form of surgery is considered if nonsurgical treatments are unsuccessful or unsatisfactory. There are four categories of surgical treatments currently in use: osteotomy, arthroscopy, arthrodesis and arthroplasy or total joint replacement. In early OA, osteotomy, (cutting and repositioning the affected bones) is sometimes used to alleviate symptoms and slow the progression of the disease. Arthroscopic debridement and lavage of the joint is also used to alleviate symptoms. In this procedure the surgeon visualizes the joint through small incisions and cleans debris out of the joint space. Joint fusion or arthrodesis is often used in the small joints of the spine, hand, foot and wrist, but is not appropriate for the major joints of the lower and upper extremities. Total joint replacement or arthroplasty is considered the most effective of all medical interventions for OA, and is a cost-effective way to relieve pain and restore joint function in more severe OA cases. Usually, surgery is postponed as long as possible because the implants only remain functional for about 20 years (Felson, 2000).

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19. AUTOIMMUNE DISEASES

INTRODUCTION

The function of a healthy immune system is to produce antibodies that protect the body against "non-self" invaders such as viruses, bacteria, fungi, parasites, or malfunctioning (e.g., cancerous) cells. Autoimmune diseases (ADs) occur when the immune system fails to recognize the body's own normal tissues, cells, or proteins as "self," and begins to manufacture autoantibodies to attack them.

SCOPE OF THE PROBLEM

Clinical studies, data, and preventive strategies are limited or non-existent for many ADs (Quill, 1998). However, a recent University of Connecticut study demonstrated that the total 1995 U.S. death count for all ADs combined exceeded that for chronic liver disease and cirrhosis, the 10th leading cause of death, among women under age 65. In that study, multiple sclerosis and rheumatic fever were the two leading autoimmune diseases based on the underlying cause of death among women below age 65, but type 1 diabetes deaths were included only for women younger than 35 years. Systemic lupus erythematosus was the underlying cause of death for more women than any other autoimmune disease between ages 25 and 44, and type 1 diabetes, though only counted for ages 25 to 34, was second (Walsh and Rau, 2000). Collectively, ADs are the fourth major cause of disability among American women (National Women's Health Information Center, 2000).

Prevalence

Nationwide prevalence of autoimmune disorders has been estimated as ranging from at least 10 million (National Institutes of Environmental Health Sciences, 1999) to as many as 50 million people (American Autoimmune Related Diseases Association, 2000b). This discrepancy reflects the current lack of consensus surrounding which diseases meet the definition of autoimmunity. Also, correct diagnosis is not easy and may take place several years after medical care is first sought, and prevalence estimates may include undiagnosed cases. Several of the autoimmune diseases share some of the same symptoms.

AD disproportionately affects women. Seventy-five percent of all cases first appear in women between 15 and 44 years of age. Examples of ADs by body system are listed in Table 19-1.

Hospitalization

In Connecticut, hospitalizations are used to estimate the prevalence of the most severe cases of AD. For the five years between 1993 and 1997, over 2,300 women were hospitalized for a select number of ADs. Table 19-2 shows hospitalizations with an autoimmune disease among any of the first ten diagnoses listed on the hospital discharge abstract.

TABLE 19 - 1
EXAMPLES OF AUTOIMMUNE DISEASES BY BODY SYSTEM

Neuromuscular Diseases	Connective Tissue
♦ Multiple Sclerosis	♦ Rheumatoid Arthritis
♦ Myasthenia Gravis	♦ Systemic Lupus Erythematosus
♦ Fibromyalgia	♦ Sicca/Sjogren Syndrome
Blood and Blood Vessels	Endocrine
♦ Pernicious Anemia	♦ Graves' /Hyperthyroidism
♦ Hemolytic Anemia	♦ Hashimoto's Thyroiditis
♦ Temporal Arteritis	♦ Juvenile Diabetes Type I
Gastrointestinal System	Skin Diseases
♦ Autoimmune Hepatitis	♦ Psoriasis
♦ Crohn's Disease	♦ Vitiligo
♦ Ulcerative Colitis	

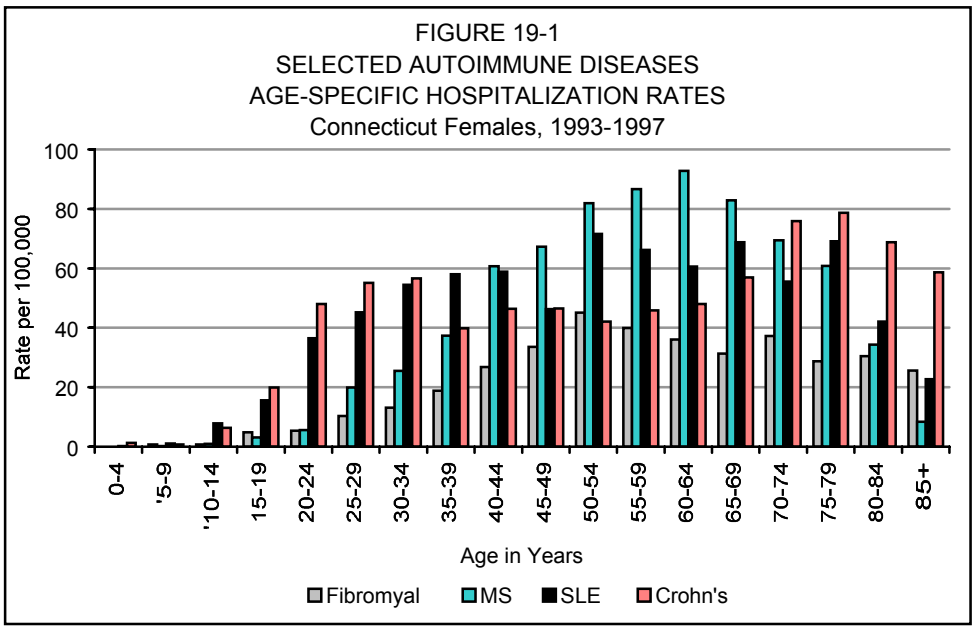
Source: American Autoimmune Related Diseases Association, 2000a.

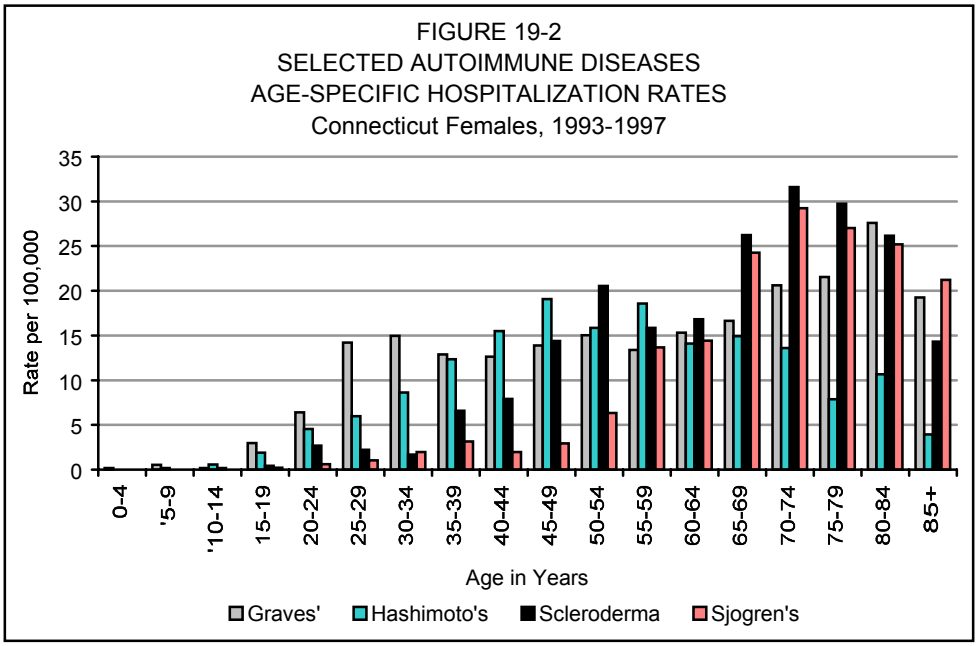
TABLE 19-2
AUTOIMMUNE DISEASES
HOSPITALIZATIONS AND CHARGES
Connecticut Females, 1993-1997

Autoimmune Condition	Hospital Discharges	Age-Adjusted Rate	Mean Charge, $	Total Charges, $
Rheumatoid Arthritis	9,334	92.6	13,438	125,434,357
Lupus Erythematosis	3,575	41.0	14,059	50,262,256
Crohn's Disease	3,434	38.5	13,238	45,458,701
Multiple Sclerosis	3,212	37.0	13,059	41,945,337
Ulcerative Colitis	1,692	18.3	15,099	25,548,318
Fibromyalgia	1,632	18.7	10,256	16,738,346
Graves' Disease	955	10.5	10,239	9,778,654
Scleroderma	805	8.8	16,353	13,163,964
Hashimoto's Thyroiditis	775	9.0	8,638	6,694,448
Sjogren's Syndrome	564	5.8	12,953	7,305,344
Not Otherwise Stated	88	1.0	18,144	1,596,673

Source: Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001.
Note: Diagnoses are not mutually exclusive and discharges rather than people were counted. Rates are per 100,000 women per year, adjusted to the 2000 US population standard.

Figures 19-1 and 19-2 show the hospitalization rates in Connecticut women for selected autoimmune diseases, according to age. Note that the vertical scales differ between the figures. Declining rates for multiple sclerosis after age 64 may reflect early mortality. Rates for rheumatoid arthritis, which are not shown, increased with each age group.





RISK FACTORS

As indicated in Table 19-3, ADs have been linked to genes, infections, and the environment (Smith and Germolec, 1999). ADs frequently occur in one form or another within a family. The Human Leukocyte Antigen (HLA) regions on chromosomes are associated with several autoimmune diseases. Prenatal exposure to certain immunotoxicants may play a role in compromising autoimmunity in adult life (Holladay, 1999). A hormonal component is also suspected, because some types of AD worsen during pregnancy (lupus) while others improve (Hashimoto's thyroiditis, Graves'disease, rheumatoid arthritis) only to worsen when the baby is delivered. It should be noted that in a comparison of all relevant studies, silicone breast implants were not associated with connect tissue diseases, including rheumatoid arthritis, systemic lupus erythematosus, scleroderma, and Sjogren's syndrome (Janowsky et al., 2000).

TABLE 19-3
GENDER RATIO AND RISK FACTORS FOR SELECTED AUTOIMMUNE DISEASES

Disease	Female to Male Ratios	Heritable Pattern	Environmental and Other Risk Factors
Rheumatoid Arthritis	4:1	Strong genetic	Infectious arthritis, gout, repeated injuries, obesity, age, occupational exposure to silica dust.
Systemic Lupus Erythematosus	9:1	Strong genetic, black race	Ultraviolet light, hormonal factors, industrial chemicals; stress may cause a relapse.
Multiple Sclerosis	2:1	Strong genetic	Exposure to a virus or bacteria, smoking.
Crohn's Disease	>1:1	Genetic, Jewish	Lack of earlier exposure to infections.
Ulcerative Colitis	<1:1	Genetic	Same as Crohn's disease.
Fibromyalgia	6:1	?	Injury, trauma, stress, or a virus.
Graves' Disease	7:1	Strong familial	Physical or emotional stress. Environmental factors may trigger.
Scleroderma	3:1	Black race	Occupational exposure to silica dust or vinyl chloride. Childbearing years.
Hashimoto's Thyroiditis	50:1	Strong familial	Iodine intake, lithium, age; subacute form may be caused by a virus.
Sjogren's Syndrome (Sicca)	9:1	Strong familial	Mid-adult years.
Type 1 Diabetes	1:1	Strong genetic	Viruses may trigger.

Sources: Cooper et al., 1999; Autoimmune Related Disease Association, 2000a; National Institute of Environmental Health Sciences, 2000; Dayan and Daniels, 1996; Reveille and Arnett, 1992; Steenland et al., 2001; Karlinger et al., 2000.

PREVENTION AND TREATMENT

At present, there is no known way to prevent autoimmune diseases. However, with proper medication and careful monitoring, many people are able to live fairly normal lives. There are four general immunologic approaches to autoimmune disease treatment: altering thresholds of immune activation, modulating antigen-specific responses, reconstituting the immune system with autologous (one's own) or allogeneic (genetically different) stem cells, and sparing of target organs (Davidson and Diamond, 2001). Non-surgical treatment for the rheumatic ADs (e.g., rheumatoid arthritis, lupus, and scleroderma) includes healthy diet, prompt treatment of infections, immunosuppressants, corticosteroids, and anti-inflammatory medications. Current treatment protocols for the more severe outcomes of ADs include organ transplants and surgery to repair or replace damaged joints.

It is predicted that genetic research will enable earlier and more precise diagnosis of ADs and highly individualized drug treatment (Koopman, 2001; Kimberly, 2001).

SELECTED AUTOIMMUNE DISEASES

The following auto-immune diseases, discussed below, either affect large numbers of people, or are associated with high mortality rates.

- Rheumatoid Arthritis
- Systemic Lupus Erythematosus
- Multiple Sclerosis
- Irritable Bowel Disease
- Type 1 Diabetes
- Psoriasis
- Fibromyalgia and Chronic Fatigue Syndrome

Rheumatoid Arthritis (RA)

Rheumatoid arthritis causes pain, swelling, warmth, redness, and stiffness in the joints due to immune attack upon the joint capsule. An antibody called rheumatoid factor is often detected in laboratory tests. About a quarter of patients develop rheumatoid nodules, bumps under the skin, near joints. The same joints on both sides of the body are usually affected, and the proximal (closer to the hand) rather than the distal finger joints. Symptoms are worse upon arising from rest, and vary from day to day. Change in weather can precipitate a painful episode, called a flare. As RA progresses, the cartilage and bone destruction are readily visible on x-rays.

More than two million Americans have RA. Recently the number of cases appears to have decreased slightly. The peak incidence occurs between ages 35 and 45, while the prevalence of RA increases with age. After ten years with the disease, about half of patients are unable to work. Mortality rates are increased two-fold in persons with RA (Koopman, 2001).

As with many diseases, RA results from a combination of genetic and environmental factors. Hormones, bacteria, and viruses may be involved.

Drug treatment of RA is intended to reduce pain and inflammation and improve function. Non-steroidal drugs such as aspirin have long been used. Methotrexate is now considered the first-line drug (Davidson and Diamond, 2001). Gold, antimalarial drugs, penicillamine, and sulfasalazine are sometimes prescribed to alter the course of rheumatoid arthritis. They require monitoring and have side effects. Corticosteroids and immunosuppressants, when used, require close monitoring. Alcohol may interfere with medications. Overuse of injected steroids may accelerate joint destruction.

Biologics are based upon substances naturally occurring in the body, and are used against specific aspects of the inflammatory process. A tumor necrosis factor inhibiting biologic was more effective than the standard RA treatment in a recent trial, but the cost of $10,000-$12,000 per patient per year is the chief barrier to entry into general use (Klippel, 2000). Omega-3 fatty acids, which are found in some fish or plant seed oils, may reduce inflammation in RA. However, some people may not tolerate the large quantities of oil needed to reach a benefit (National Institute of Health, 2000).

Rest and exercise are both needed at different times. Moist heat to an arthritic joint before exercise and a cold pack afterwards may facilitate exercise. Swimming is an activity that does not put much weight onto joints. Emotional stress is not thought to bring on rheumatoid arthritis or flares, but relaxation techniques are helpful. Surgery, including tendon reconstruction and joint replacement, may be necessary to relieve pain, correct deformity, and improve function.

Systemic Lupus Erythematosus (SLE)

Lupus erythematosus is found in three major forms. The systemic form is the most common, and is described in more detail below. The discoid form primarily affects the skin in sun-exposed areas, with red, scaly, circular rashes and possible scarring. Lupus may be induced by some prescription medications including procainamide (for heart problems), hydrazine (for hypertension), and dilantin (for seizures). There is no gender difference in the incidence of drug-induced lupus, and this form usually goes away when the causative drug is stopped.

SLE is a multi-organ autoimmune disease characterized by hyperactivity of immune B cells with overproduction of antibodies, and the deposition of immune complexes in organs, resulting in inflammation and damage. Periods of disease "flares" are followed by periods of remission. There is substantial mortality from coronary heart disease and kidney disease. Between ages 35 and 44, coronary artery disease may be 50 times as common among women with SLE than women without it (Karrar et al., 2001). Prior to the advent of dialysis, severe kidney damage from lupus was fatal.

It is possible that SLE represents several diseases with common final pathways (McQuire and Lambert, 1997). Several genes may increase susceptibility to SLE. When one twin has SLE the other twin has a 30 percent chance of also getting it, which shows that both genetic and environmental factors are involved. SLE is diagnosed by the sequential or simultaneous appearance of at least four features from a list of eleven. Prominent features include butterfly rash across the nose and cheeks, photosensitivity, fever, fatigue, oral ulceration, painful swelling in two or more joints, chest pain on breathing, heart, kidney, neurologic, bleeding, and immunologic disorders, and especially antibodies against DNA or other parts of the person's own cells. Symptoms may change over time in a person.

It is estimated that 240,000 Americans are living with lupus. The highest incidence rates for SLE are between ages 20 and 40. SLE is ten times more common among women than men during the female reproductive years, and about twice as common in women as men, after the age of menopause. Worldwide, the highest rates of disease have been reported in Afro-Caribbean, Chinese, Asian, and South American Indian women (Snaith and Isenberg, 1996). In the United States, the incidence rate in black women is three to four times that of white women (Hochberg, 1993), and the rates in Hispanics (Kimberly, 2001) and Native Americans (Peschken and Esdaile, 2000) are also higher than white Americans. Both incidence and length of survival continue to increase (Ruiz-Irastorza et al., 2001).

SLE disease activity, SLE disease damage, and poverty were independently associated with mortality in a multiethnic cohort (Alarcon et al., 2001).

Ultraviolet light in the 295-305 nanometer range is toxic to SLE patients, and sunlight can trigger a flare. Lupus patients metabolize estrogen and testosterone abnormally, and it is thought that pregnancy, menses, and contraceptives containing estrogen may alter the course of SLE (Ahmed and Tal, 1993). The role of retroviruses and bacterial infection in SLE are being studied.

Treatment consists largely of nonsteroidal anti-inflammatory drugs (for fever and arthritis), corticosteroids (injection, oral, or cream), immunosuppressants (including anti-malarial drugs), prompt attention to infections, avoidance of direct sunlight, and reduction of stress. These drug treatments have side effects. Hormone and other treatments are under investigation. Patients can improve their quality of life by learning to

recognize warning signs of SLE flares and how to manage their disease with help from doctors, friends, family, and support organizations (National Institutes of Health, 2001).

Multiple Sclerosis (MS)

Multiple sclerosis is the most common chronic neurologic disease of adults between ages 20 and 50. Immune T cells react with both a peptide from the autoantigen myelin basic protein and peptides from the Epstein-Barr virus, influenza type A, and human papillomavirus (Davidson and Diamond, 2001). Plaques or lesions of the myelin sheath surrounding the neuron characterize MS. Symptoms include disturbances of vision, balance, sensation, bowel and bladder function, tremor, and weakness. The diagnosis may be established using magnetic resonance imaging of the brain and cerebrospinal fluid analysis in addition to clinical signs Common disabilities include difficulty bathing, dressing, and climbing stairs, sexual dysfunction, and inability to drive, but many MS patients continue to work full time (McDonnell and Hawkins, 2001). Depression and suicide are not uncommon. 20 percent of cases are chronic and progressive, the rest are intermittent and relapsing.

Worldwide, the prevalence of MS increases with distance from the equator, in most ethnic groups (Brownson et al., 1998). In the United States there are between 250,000 and 350,000 patients (Noseworthy et al., 2000). If a person has MS, the risk of MS in an identical twin is 31 percent and in a non-identical twin, 5 percent. The absolute risk of MS in a first-degree relative is less than 5 percent, and 85 percent of MS patients do not have an affected relative (Jr and Sriram, 2001); however, this is 20-40 times the risk in the general population.

There is no consensus about the early causes of MS. Although infectious causes of MS have been suggested, and *Chlamydia pneumonia* in cerebrospinal fluid has been associated with MS, this organism has also been found in other neurological diseases (Gieffers et al., 2001). In the Nurses' Health Study, cigarette smoking was associated with a 60 percent increase in risk (Hernan et al., 2001).

Corticosteroids are often used to treat MS. Interferon has a proven benefit in established MS and also appears effective as initial therapy (Jacobs et al., 2000).

Irritable Bowel Disease (IBD)

Irritable bowel disease or syndrome is also known as chronic ileitis, regional enteritis, or granulomatous colitis. IBD is a chronic, relapsing and remitting inflammatory disease of the digestive tract. Diarrhea or constipation may be present with abdominal pain. Ulcerative colitis affects the superficial cell layer of the colon and Crohn's disease affects several cell layers, but they are otherwise quite similar. Both begin relatively early in life and while not fatal, are associated with increased gastrointestinal cancer incidence and with two-fold increased mortality rate. Depression or emotional stress are common antecedents (Berkow and Talbot, 1977).

Worldwide the prevalence of IBD has been increasing (Karlinger et al., 2000). It is estimated that 830,000 Americans have IBD, and 45,000 new cases occur each year, with no gender predilection (Blumberg and Strober, 2001).

IBD is a disease of urban areas, and also has a genetic element that leads to abnormal T helper cell function. The immune system normally tolerates certain intestinal bacteria which live in symbiosis with humans and aid the digestive process. In IBD the immune system appears to target these bacteria. One theory is that in urban environments people may not encounter the microbial antigens necessary to proper immune system maturation, due to improved hygiene, vaccination, antimicrobial medication, and the decline in consumption of naturally fermented and dried foods (Isolauri, 2001).

Diagnosis involves, among other things, ruling out food allergies and infection by bacteria other than normal intestinal flora. Treatment may involve steroids (which have side effects), or even removal of part of the colon. In order to

withdraw steroids, or in patients who become refractory to steroid treatment, immunomodulators, tumor necrosis factor-alpha antibody, or budesonide have been used (Lichtenstein, 2001). Stress and diet should be monitored to prevent relapses. Antibody-based treatments have been initiated, based upon animal studies. Future research will involve genetic and molecular studies, possibly for identification of therapies based upon harmful and protective bacteria strains for genetic subsets of patients (Blumberg and Strober, 2001). More simply, "probiotic" diets that have been developed to treat acute diarrhea have the potential to reinforce normal gut function (Isolauri, 2001).

Type 1 Diabetes

Type 1 diabetes is also known as insulin dependent diabetes or juvenile onset diabetes. It is the most common chronic disease of childhood. The coxsackie virus P2-C protein peptide resembles a peptide from the autoantigen glutamic acid decarboxylase (Davidson and Diamond, 2001). The cause of type 1 diabetes is autoimmune attack on the islet cells of the pancreas, which produce the insulin by which blood glucose is regulated. Symptoms include abrupt onset of unexplained thirst, weight loss with excessive urination, protein in the urine, and an absolute need for insulin to sustain life. Diagnosis is confirmed with a blood glucose test.

The prevalence of type 1 diabetes varies tremendously worldwide. In the United States 300,000 to 500,000 people are estimated to have type 1 diabetes, with 30,000 new cases annually. Seven percent of diabetes diagnosed between ages 30 and 74 years is adult onset type 1 diabetes. The incidence rate is higher among whites than blacks, and does not differ by gender (Laporte et al., 1995).

There is seasonal variation in type 1 diabetes incidence, which has been attributed to patterns of infection, nutrition, or hormones as triggers in genetically susceptible persons (Seikikawa and LaPorte, 1998). An international study is testing the hypothesis that geographic differences in diabetes risk reflect variation in the frequencies of susceptibility genes (Dorman, 1997).

Diabetes affects especially the eyes, kidney, and neurologic system through microvascular disease, and the heart through accelerated atherosclerosis. Acute complications such as diabetic coma are the leading causes of death in early years (<10 years diabetes duration), renal disease during the middle years, and cardiovascular disease in persons with more than 30 years of diabetes duration. The mortality rate is higher among blacks than whites (Portuese and Orchard, 1995). Acute complications accounted for the differences, suggesting that some of the excess mortality may be preventable (Tull and Barinas, 1996; Lipton et al., 1999). Depression is common due to the progressive course of disabilities, and there is considerable stress upon the family of the affected child.

Persons with type 1 diabetes utilize more medical resources than those without diabetes. In the 1989 National Health Interview Survey, 17.4 percent of persons with type 1 diabetes and aged 18-44 reported that they had been hospitalized in the previous year. The risk of hospitalization was associated with the presence of diabetic complications (Aubert et al., 1995). Adolescent girls have somewhat more hospitalizations than boys (Cohn et al., 1997). In an insurance program, inpatient rates for the type 1 diabetic population were 8.3 times higher for established complications (e.g. myocardial infarction, heart failure, and coronary bypass surgery) than the nondiabetes population. Rates of use of physician services were about ten times higher for each of endocrinologists, ophthalmologists, and nephrologists (Laditka et al., 2001).

In Connecticut between 1993 and 1997, there were 2,574 hospital discharges with any diagnosis of type 1 diabetes among females aged less than 30 years. During these ages the annual hospitalization rate was 81 per 100,000. 1,263 of the 2,574 discharges were with a first diagnosis of type 1 diabetes, and the average charge among these patients was $6,612 (Connecticut

Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

Mortality rates from type 1 diabetes have declined markedly among person diagnosed in 1975-79 compared to 1965-69. This trend is consistent with the introduction of testing for glycosylated hemoglobin (which indicates average glucose levels over several weeks time), home glucose monitoring, and improved blood pressure therapy in the 1980's (Nishimura et al., 2001). The use of specialist care is associated with better glucose control and fewer complications, compared to care by a generalist. Receiving specialist care is associated with income, education, health insurance, and female gender (Zgibor et al., 2000).

The management of diabetes involves control of blood sugar levels through monitoring and insulin administration, frequent medical attention, control of risk factors for heart disease (smoking, hypertension, lipid levels) and early treatment of complications. Pregnancy was formerly discouraged in women with type 1 diabetes but it can now be considered, if the diabetes is well managed. Tight glucose control delays the incidence and progression of microvascular disease (Diabetes Control and Complications Trial Research Group, 1993). The danger of trying to maintain glucose levels close to normal is that of going too low and bringing on hypoglycemic shock, coma, and death. One advance in control is the insulin pump, which delivers insulin without injection. If advanced atherosclerotic disease can be detected before clinical symptoms appear, vigorous risk factor management may avert a catastrophic cardiac event. Promising screening modalities include ankle blood pressure, subtle electrocardiographic changes, and measures of insulin resistance (Olson et al., in press).

Attempts to avoid the need for insulin administration have included pancreas or islet cell transplants, combined with immunosuppressant drugs. Newer gene therapy approaches are being investigated. These attempt to block the immunologic attack on islet cells before diabetes appears (Giannoukakis et al., 1999), and may be thought of as a vaccine.

Psoriasis

Psoriasis is a chronic, recurrent skin disease, of which several varieties are recognized. Severity varies from a few lesions to widespread scaling. In exfoliative psoriatic dermatitis, the entire skin is red and covered with scales. Pustular psoriasis is characterized by sterile pustules on the palms and soles, or may be generalized. Psoriatic arthritis resembles rheumatoid arthritis and may be crippling. When patients were asked to evaluate their quality of life, the impact of psoriasis on physical and mental functioning was comparable to that of cancer, arthritis, hypertension, heart disease, diabetes, and depression (Rapp et al., 1999).

Estimates of *psoriasis vulgaris* prevalence range from 0.3 to 2.5 percent, while incidence was 60.4 per 100,000 in one study (Plunkett and Marks, 1998). Excluding persons with RA, SLE, and several other arthritic conditions, the sex and age-adjusted incidence of psoriatic arthritis was 6.6 per 100,000 and the prevalence 0.1 percent, with an average age of 40.7 years at diagnosis in Olmstead County, Minnesota. There was little gender difference, and survival was not different from the general population, in contrast to referral-based studies (Shbeeb et al., 2000).

Psoriasis vulgaris is associated with T cell-mediated attack on skin components. Streptococcal throat infection can trigger guttate psoriasis, which is assumed to be a cross-reaction due to the resemblance of streptococcal proteins to skin proteins (Prinz, 2001). Atopic allergic diseases and contact sensitization were common among psoriasis patients in a study from Italy (Pigatto, 2000).

The initial treatment of psoriasis is often topical, with phototherapy for more advanced cases, and oral pharmaceuticals for the most serious cases. Tumor necrosis factor-α blockade with or without methotrexate is used in refractory psoriasis (Davidson and Diamond, 2001).

Lubricating creams are applied alone or with corticosteroids (Berkow and Talbot, 1977); some local treatments combine a corticosteroid and a noncorticosteroid (Feldman, 2000).

Although antistreptococcal drugs have been recommended, there is no evidence of benefit from them (Owen et al., 2000).

Phototherapy with ultraviolet radiation has been used with psoralen (PUVA) as a sensitizer, or without it (UVB). PUVA treatment, although very effective, was recently associated with increased risk of melanoma, and life-long follow-up is recommended for patients receiving PUVA (Wolf, 1997).

Few randomized trials have compared treatments for acute guttate psoriasis; however, an intravenous n-3 fatty acid rich emulsion was superior to placebo (Chalmers et al., 2000).

The combination of systemic treatments is controversial, and safety must be balanced against effectiveness (Van de Kerkof, 2001a). Various combinations of treatments involving calcipotrial, cyclosporin, PUVA, UVB, dithranol, acitretin, and coal tar may be useful, while other combinations are contraindicated. Rotation of therapies is a way to avoid toxicity (Van De Kerkhof, 2001b). Men are more likely than women to receive intensive therapies, at least in part because of potential teratogenesis from treatment during pregnancy (Hotard et al., 2000).

Monoclonal antibodies are being developed to target abnormal new blood vessels, which are characteristic of diseases such as RA and psoriasis (Halin and Neri, 2001).

Fibromyalgia and Chronic Fatigue Syndrome

Fibromyalgia (also called fibromyalgia syndrome, or FMS) and chronic fatigue syndrome are both mysterious conditions. They tend to be (and ought to be) diagnoses assigned only after attempts to establish better-known diagnoses fail. Little is known about their prevalence, causes, and treatment. They are generally considered autoimmune diseases although this link has not been established either. It is not unlikely that further research will identify subsets of individuals who are more alike in their disease characteristics, thus facilitating investigations into causes and cures.

Many people who meet the definition of an unexplained clinical condition (fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, multiple chemical sensitivity, temporomandibular disorder, tension headache, interstitial cystitis, postconcussion syndrome) also meet the definition for another unexplained condition, so that the diagnosis depends somewhat on which specialist first sees the patient (Aaron and Buchwald, 2001; Natelson, 2001). The diagnosis of fibromyalgia requires widespread pain persisting for 3 months or more in 10 or more specified muscles, tendons, or ligaments. Rheumatoid arthritis or Sjogren's syndrome may be present. The American College of Rheumatology estimates that 3 to 6 million Americans are affected. Allegations that a fibromyalgia diagnosis increases illness behavior and dependence on the medical system are not supported by research (White and Harth, 2001).

The treatment of fibromyalgia is directed toward the relief of symptoms (pain, sleep disturbance, mood disturbance, and fatigue), and should be individualized, while addressing physical fitness, work, and mental health (Barkhuizen, 2001). A variety of interventions involving pharmacological treatment of pain or depression, physical therapy, diet, meditation, cognitive therapy, and so on, have been helpful in some patients, but not all treatments may be covered by insurance. Examples of successful unusual treatments are the discontinuation of monosodium glutamate in the diet, which was theorized to excite neurotransmitters (Smith et al., 2001), and a randomized trial in which static magnetic fields in sleep pads brought improvement to fibromyalgia patients, though not significantly different than the improvement from placebo or usual care (Alfano et al., 2001). Participation in clinical studies and trials are ways to obtain potentially useful treatment or to contribute to knowledge about the causes of fibromyalgia. Fibromyalgia research is funded by the National Institutes of Health, especially the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

Understandably, many sufferers turn to untenable theories and unproven remedies. It is

important to avoid unproven remedies which are either expensive or dangerous, and it would seem prudent to seek treatments that have rational bases, and come from reputable sources.

In a study of 127 twin pairs, one twin with chronic fatigue syndrome (CFS) and one without, fibromyalgia was present in more than 70 percent of the twins with CFS, versus less than 10 percent in the twins without CFS (Aaron et al., 2001). Chronic fatigue syndrome, while it overlaps with fibromyalgia, is also different in certain ways. A substance P is elevated in the spinal fluid of fibromyalgia patients only (Natelson, 2001). Whether a cardiovascular response is abnormal in chronic fatigue syndrome, is controversial (Natelson, 2001; Naschitz et al., 2001).

Support organizations often emphasize that CFS has appeared prior to the twentieth century, under different names. The diagnosis requires at least 6 months of new-onset severe fatigue accompanied by infectious, rheumatologic, or neuropsychiatric symptoms such as intense headache, sore throat, tender lymph nodes, muscle and joint aches (without redness or swelling), unrefreshing sleep, and inability to concentrate (Natelson, 2001). The case definition for chronic fatigue syndrome reflects the assumption, as yet unproved, of a viral origin. An initial hypothesis linking CFS to Epstein-Barr virus has been abandoned. Some data support an immunologic origin to CFS, but allergies are the only consistent immune system abnormality among CFS patients (WebMD, 2000). While many patients have psychiatric co-morbidities, CFS does not have the same profile as depression or somatization disorder. Magnetic resonance imaging of the brain found subtle changes, but only in those CFS patients without a psychiatric co-diagnosis (Natelson, 2001). Reports of association with HLA genes were not confirmed in a recent study (Underhill et al., 2001).

In the United States, the prevalence of CFS has been estimated at 0.52 percent in women and 0.29 percent in men (Natelson, 2001). A large number of Gulf War veterans reported CFS symptoms. While investigations continue, the causes of CFS remain unclear.

As with fibromyalgia, chronic fatigue syndrome is treated individually and symptomatically. According to one web source, children have better prognosis than adults, and 95 percent recover within four years. Adults with a sudden onset appear to recover faster than those with no sudden beginning to their symptoms, although a multidisciplinary program helped most people (WebMD, 2000).

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20. SEXUALLY TRANSMITTED DISEASES

INTRODUCTION

Sexually transmitted diseases (STDs) are infections passed from person to person during sexual contact or from mother to child. More than 20 STDs, caused by organisms ranging from viruses to insects, have been identified. Of these, Connecticut physicians are required by law to report cases of five STDs—syphilis, gonorrhea, chlamydia, chancroid, and neonatal herpes—to the Connecticut Department of Public Health. No cases of chancroid or neonatal herpes have been reported in Connecticut in recent years, and new cases of syphilis have diminished to historic low levels. In contrast, thousands of new gonorrhea and chlamydia cases are still reported in Connecticut women each year.

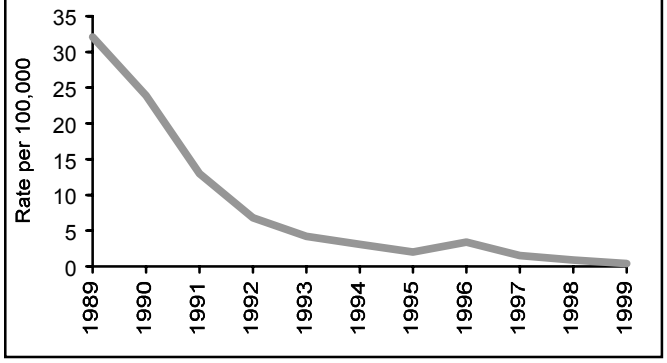
Because initial symptoms of gonorrhea and chlamydia typically are absent or transient in women, medical care is often sought only after serious complications have developed. Without treatment, gonorrhea and chlamydia infections can spread to the uterus and fallopian tubes, causing pelvic inflammatory disease (PID), other problems that may lead to infertility, or ectopic (tubal) pregnancy. PID occurs less frequently and is associated with milder pelvic lesions in women who use oral contraceptives (Henry Suchet, 1997). Ectopic pregnancy is the leading cause of maternal death during the first trimester of pregnancy, and nearly half of ectopic pregnancies have been attributed to STDs (Coste et al., 1994). In pregnant women, gonorrhea and chlamydia infections increase the risk of preterm birth, and newborns can become infected during delivery, resulting in eye infections and pneumonia. Furthermore, a chlamydia infection increases the risk of developing invasive cervical cancer (Anttila et al., 2001), and its presence can facilitate the acquisition and transmission of the human immunodeficiency virus (Chin, 2000).

SCOPE OF THE PROBLEM

Syphilis

Syphilis control is a success story in the recent history of public health in Connecticut. Since peaking in 1989, syphilis has nearly been eradicated. Although 543 newly acquired infections, termed "primary and secondary syphilis," were reported in Connecticut females

FIGURE 20-1
PRIMARY AND SECONDARY SYPHILIS
INCIDENCE RATES
Connecticut Females, 1989-1999



Source: Connecticut Department of Public Health, STD Control Program, 2000.
Rate calculations from Division of Policy, Planning, and Analysis.

in 1989, only 6 cases were reported in 1999, with case rates dropping from 32 to 0.4 cases per 100,000 females (Fig. 20-1). During the same interval, the number of congenitally acquired cases dropped from 25 or more per year between 1990 and 1992 to 0 in 2000 (Connecticut Department of Public Health, STD Control Program, 1999, 2000, 2001). Nationally, syphilis rates in males and females peaked in 1990 and in 1999 were at the lowest level since reporting began in 1941. In 1999, the Centers for Disease Control and Prevention launched the National Plan to Eliminate Syphilis in the United States (Centers for Disease Control and Prevention, 2000).

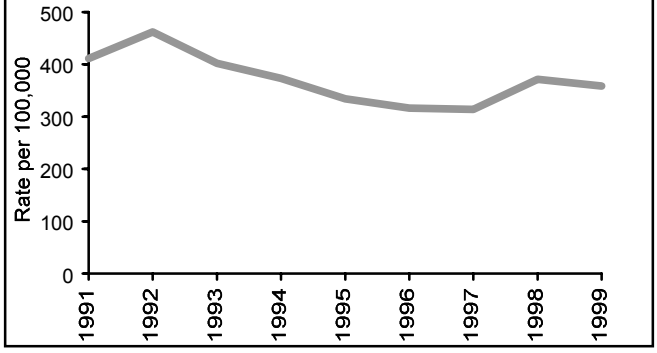
In the absence of HIV co-infection, untreated syphilis infections can remain clinically latent for many years, then re-emerge as serious, late-stage diseases of the heart and central nervous system. Although 12 Connecticut women died with late manifestations of the disease since 1990, there were no deaths from 1995 to 1998.

Chlamydia

Chlamydia is the most common of all STDs, with 5,000 to 7,000 new cases reported in Connecticut women each year. Chlamydia incidence peaked in 1992, declined through 1997, then rose again in 1998 (Fig. 20-2). In 1999 there were 6,056 new cases in Connecticut women (359 per 100,000 population), representing 82 percent of total cases.

Chlamydia is found in females more often than in males because, until the recent advent of urine-based screening, only women were routinely screened for the infection. No deaths attributable to chlamydia infection have been reported in Connecticut. Nationally it is believed that chlamydia infections have declined from over 4 million annually in the early 1980's to 3 million annually in the late 1990's, primarily due to increased screening and treatment of women (Centers for Disease Control and Prevention, 2000).

FIGURE 20-2
CHLAMYDIA INCIDENCE RATES
Connecticut Females, 1991-1999

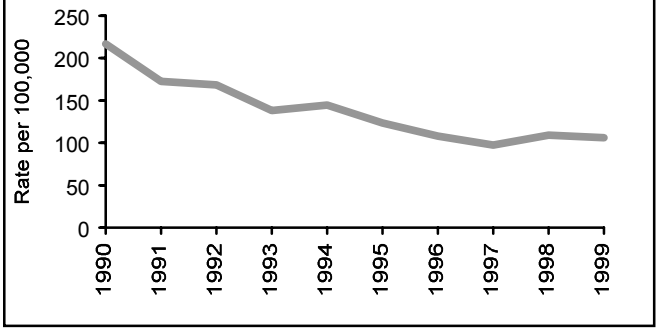


Source: Connecticut Department of Public Health, STD Control Program, 2000.
Rate calculations from Division of Policy, Planning, and Analysis.
Note: Chlamydia surveillance began 7/1/90, so 1990 data are not included.

Gonorrhea

Gonorrhea incidence among Connecticut women generally has been declining since peak levels were reached in the late 1980's (Fig. 20-3). In 1999 there were 1,796 reported new cases among Connecticut women (106 per 100,000 population), which was an historic low. Since 1992, slightly more cases have been reported in women than in men, whereas the opposite had been true previously.

FIGURE 20-3
GONORRHEA INCIDENCE RATES
Connecticut Females, 1990-1999



Source: Connecticut Department of Public Health, STD Control Program, 2000.

Age

Most chlamydia and gonorrhea infections are reported in adolescent and young adult females. In 1999, about 40 percent of the cases occurred in 15 to 19 year olds, and their infection rates exceeded those found in any other age group (2,446 and 684 per 100,000 females for chlamydia and gonorrhea, respectively).

Race and Ethnicity

Disproportionate numbers of Connecticut's black and Hispanic women are reported with gonorrhea and chlamydia infections, evidenced by high incidence rates (Table 20-1). Although blacks represented only 10 percent of Connecticut's female population, they accounted for 64 percent of gonorrhea cases and 47 percent

TABLE 20-1
GONORRHEA AND CHLAMYDIA INCIDENCE
BY RACE & ETHNICITY
Connecticut Females, 1999

	Gonorrhea		Chlamydia	
	Cases	Rate	Cases	Rate
All races	1,789	105.9	6,005	355.5
White	316	21.3	1,301	87.9
Black	1,136	701.5	2,822	1,742.2
Native American	0	0	0	0
Asian & PI	3	6.5	32	72.5
Hispanic	334	234.1	1,850	1,296.3

Source: Connecticut Department of Public Health, STD Control Program, 2000
Notes: Rates expressed as reported cases per 100,000 females.
Numbers and rates include data where race/ethnicity was not indicated on the case report. These data were distributed among the categories in proportion to known cases.

of chlamydia cases in 1999. Similarly, although only 8 percent of Connecticut women were Hispanic, Hispanics represented 19 percent of gonorrhea cases and 30 percent of chlamydia cases. Relative to white females, chlamydia rates were 20 times higher and gonorrhea rates were 33 times higher in black females; chlamydia rates were 15 times higher and gonorrhea rates were 11 times higher in Hispanic females.

Hospitalizations for STDs had similar patterns. Between 1993 and 1997, compared to white females, age-adjusted hospitalization rates of black females were 18 times higher for STDs and 4 times higher for PID, while rates for Hispanics were 5 times higher for STDs and twice as high for PID. All these differences were statistically significant (Connecticut Department of Public Health, Division of Policy, Planning, and Analysis, 2001).

Town of Residence

The incidence of syphilis, gonorrhea, and chlamydia is disproportionately high among women residing in urban areas. In 1999, four towns—Hartford, New Haven, Bridgeport, and Waterbury—accounted for 58 percent of gonorrhea cases and 50 percent of chlamydia cases. These towns represent only about 16 percent of the state's female population. Hartford residents accounted for four of the six Connecticut women reported with primary and secondary syphilis (Connecticut Department of Public Health, STD Control Program, 2000).

PREVENTION AND RISK REDUCTION

Sexually transmitted diseases can be prevented by abstaining from sex with a partner, and the risk of acquiring them or passing them to others can be reduced by using barrier protection (male or female condoms) consistently and properly (See Chapter 21, HIV Infection and AIDS, for a more detailed discussion of prevention or reduction of risky sexual behavior). A study from an STD clinic estimated that the relative risk of gonorrhea in women where a spermicide and condom, or spermicide and diaphragm were used, was 55-59% lower than in women where no spermicide, condom, or diaphragm were used (Austin et al, 1984).

The Connecticut Department of Public Health Abstinence-Only Education Initiative is designed to reach 9 to 14 year old children and to include parental or guardian involvement when possible. The initiative operates in five locations and is adding a sixth. The STD Control Program conducts urine-based STD testing through schools, correctional facilities, and Planned Parenthood clinics, and provides counseling, treatment, and public education.

Screening Tests

A simple and inexpensive blood-screening test exists for syphilis. Urine screening for chlamydia and gonorrhea, which costs about $38 per sample and $453 per case identified (Jones et al., 2000), is being used increasingly in Connecticut (Connecticut Department of Public Health, STD Control Program, 1999). Because gonorrhea and chlamydia often are asymptomatic, sexually active women—especially those with a new sex partner—should have regular check-ups for STDs performed by their doctors, even in the absence of symptoms. As STDs are highly infectious, the sex partners of infected women also should be tested.

Several analyses of cost-benefits indicate that the total cost of general testing for chlamydia in at-risk populations could save twice the cost of treating pelvic inflammatory disease and six times the cost of all the medical consequences of chlamydia infections, including tubal infertility and ectopic pregnancies (Henry Suchet et al., 1996). Therefore, programs designed to encourage or facilitate routine screening for STDs in high-risk populations (sexually active females between 15 and 24 years old, those who live in urban areas, and those with multiple sex partners) are likely to reduce costs in the healthcare delivery system.

TREATMENT

Syphilis, gonorrhea, and chlamydia can be treated successfully with antibiotics. The earlier a woman seeks treatment and warns her sex partners about the disease, the less likely it becomes that severe complications and passage to others, including her newborn, will occur.

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