Common Cancers Among Women

By

Rosemary Theroux, RNC, PhD, WHNP-BC

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Nurses: 5 Contact Hours*

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ABOUT THE AUTHOR

Rosemary Theroux, RNC, PhD, WHNP-BC, is a certified women’s health nurse practitioner and has practiced in a variety of clinical settings for more than 25 years. She is an associate professor in the Graduate School of Nursing at the University of Massachusetts-Worcester. She has conducted and published research in the area of women’s self-care decision making and women’s health practices in Africa. Dr. Theroux has a special interest in global women’s health. Along with other members of a non-profit group, she has developed a primary care setting with women’s health services in Ghana, Africa.

Rosemary Theroux has disclosed that she has no significant financial or other conflicts of interest pertaining to this course book.

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COURSE EVALUATION

COMMON CANCERS AMONG WOMEN

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<table>
<thead>
<tr>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agree</td>
<td>Agree</td>
<td>Disagree</td>
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</tr>
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<td>Strongly</td>
<td>Somewhat</td>
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<td>Strongly</td>
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</tbody>
</table>

OUTCOMES: After completing this course, I am able to:
1. Discuss the implications of human papillomavirus (HPV) testing and other cervical cancer screening strategies.
2. Describe the evaluation and treatment of breast cancer in women and the importance of follow-up in primary care for survivors.
3. Discuss the etiology, diagnosis, and treatment of gynecologic cancers in women.

COURSE CONTENT
4. The course content was presented in a well-organized and clearly written manner.
5. The course content was presented in a fair, unbiased and balanced manner.
6. The course content presented current developments in the field.
7. The course was relevant to my professional practice or interests.
8. The final examination was at an appropriate level for the content of the course.
9. The course expanded my knowledge and enhanced my skills related to the subject matter.
10. I intend to apply the knowledge and skills I’ve learned to my practice.

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16. My overall rating for this course is
   A. Poor     B. Below Average     C. Average     D. Good     E. Excellent

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# CONTENTS

Course Evaluation ................................................................. v
Figures and Tables ................................................................ xi
Pretest ............................................................................. xiii
Introduction ....................................................................... xv

**Chapter 1: Human Papillomavirus and Cervical Cancer Screening** ............................................ 1

- Learning Outcome .......................................................... 1
- Chapter Objectives .......................................................... 1
- Introduction ..................................................................... 1
- Human Papillomavirus Infection ........................................ 2
  - Types of Human Papillomavirus ........................................ 2
  - Risk Factors ................................................................ 2
  - Symptoms .................................................................... 2
  - Diagnosis .................................................................... 2
- Natural History of Human Papillomavirus ..................... 3
- Cervical Cancer ............................................................... 4
  - Risk Factors ................................................................ 4
  - Screening ..................................................................... 4
  - Anatomy of the Cervix ................................................ 5
- Cervical Cancer Screening: Cervical Cytology (Pap Smear) .................................................. 5
- Terminology for Cytologic and Histologic Reporting ..... 7

Management Guidelines ..................................................... 8
- Managing an Abnormal Cervical Cancer Screening .......... 8
- Evaluation of Abnormal Findings .................................. 8
- Treatment of Cervical Intraepithelial Neoplasia ............. 9
- Ablative Therapy ............................................................ 10
- Cone Biopsy and Conization Excisional Techniques .......... 11

Patient Education and Counseling .................................. 12
- Prevention of Human Papillomavirus Infection ............ 12
- Counseling Patients With Human Papillomavirus Infection .................................................. 12
- Notification and Follow-Up of Pap Test Results ........... 13
- Education for Women About Human Papillomavirus .... 13

Case Study 1-1 ................................................................. 14

Questions .......................................................................... 14
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chapter 2: Breast Cancer</td>
<td>23</td>
</tr>
<tr>
<td>Learning Outcome</td>
<td>23</td>
</tr>
<tr>
<td>Chapter Objectives</td>
<td>23</td>
</tr>
<tr>
<td>Introduction</td>
<td>23</td>
</tr>
<tr>
<td>Epidemiology of Breast Cancer</td>
<td>23</td>
</tr>
<tr>
<td>Etiology of Breast Cancer</td>
<td>24</td>
</tr>
<tr>
<td>Anatomy and Pathophysiology of Breast Cancer</td>
<td>24</td>
</tr>
<tr>
<td>Anatomy</td>
<td>24</td>
</tr>
<tr>
<td>Pathophysiology</td>
<td>24</td>
</tr>
<tr>
<td>Risk Factors and diagnosis</td>
<td>25</td>
</tr>
<tr>
<td>BRCA1 and BRCA2 Genes</td>
<td>26</td>
</tr>
<tr>
<td>Diagnosis of Breast Cancer</td>
<td>28</td>
</tr>
<tr>
<td>Indicators Associated With Disease Prognosis</td>
<td>32</td>
</tr>
<tr>
<td>Types of Breast Cancer</td>
<td>32</td>
</tr>
<tr>
<td>Noninvasive Breast Cancer: Lobular Carcinoma In Situ and Ductal Carcinoma</td>
<td>32</td>
</tr>
<tr>
<td>Invasive Breast Cancer: Invasive or Infiltrating Ductal Carcinoma</td>
<td>33</td>
</tr>
<tr>
<td>Atypical Cancers</td>
<td>33</td>
</tr>
<tr>
<td>Breast Cancer Treatment</td>
<td>34</td>
</tr>
<tr>
<td>Surgery</td>
<td>35</td>
</tr>
<tr>
<td>Adjuvant Therapy</td>
<td>35</td>
</tr>
<tr>
<td>Complementary Therapies</td>
<td>37</td>
</tr>
<tr>
<td>Psychosocial Aspects of Breast Cancer Treatment</td>
<td>38</td>
</tr>
<tr>
<td>Follow-Up After Breast Cancer Treatment</td>
<td>40</td>
</tr>
<tr>
<td>Breast Reconstruction After Mastectomy</td>
<td>40</td>
</tr>
<tr>
<td>Follow-Up Care</td>
<td>40</td>
</tr>
<tr>
<td>Chemoprevention</td>
<td>41</td>
</tr>
<tr>
<td>Ongoing Primary Care of Survivors</td>
<td>42</td>
</tr>
<tr>
<td>Breast Cancer Prevention</td>
<td>44</td>
</tr>
<tr>
<td>Estrogen and the Hormone Equation</td>
<td>44</td>
</tr>
<tr>
<td>Lifestyle Changes</td>
<td>45</td>
</tr>
<tr>
<td>Implications for Practice</td>
<td>45</td>
</tr>
<tr>
<td>During and After Diagnostic Testing</td>
<td>46</td>
</tr>
<tr>
<td>During and After Treatment</td>
<td>46</td>
</tr>
<tr>
<td>Survivors</td>
<td>46</td>
</tr>
</tbody>
</table>
Contents—
Common Cancers Among Women ................................................................. ix

Support Groups ......................................................................................... 47
Case Study 2-1 ........................................................................................... 47
Questions ....................................................................................................... 47
Discussion .................................................................................................... 47
Summary ....................................................................................................... 48

Exam Questions .......................................................................................... 49

References .................................................................................................... 51

Chapter 3: Gynecologic Cancers ................................................................. 57

Learning Outcome ...................................................................................... 57
Chapter Objectives ..................................................................................... 57
Introduction .................................................................................................. 57
Cervical Cancer ........................................................................................... 58
Types ............................................................................................................ 58
Etiology ......................................................................................................... 58
Risk Factors ................................................................................................. 58
Diagnostic Evaluation .................................................................................. 59
Symptoms ..................................................................................................... 59
Diagnosis ....................................................................................................... 59
Treatment ..................................................................................................... 60
Implications for Practice ............................................................................... 60
Ovarian Cancer ............................................................................................ 61
Types ............................................................................................................ 61
Etiology ......................................................................................................... 61
Risk Factors ................................................................................................. 62
Diagnostic Evaluation .................................................................................. 62
Symptoms ..................................................................................................... 63
Diagnosis ....................................................................................................... 63
Treatment ..................................................................................................... 63
Implications for Practice ............................................................................... 63
Uterine (Endometrial) Cancer ................................................................. 64
Types ............................................................................................................ 64
Etiology ......................................................................................................... 65
Risk Factors ................................................................................................. 65
Protective Factors ........................................................................................ 65
Diagnostic Evaluation .................................................................................. 65
Symptoms ..................................................................................................... 65
Diagnosis ....................................................................................................... 65
Treatment ..................................................................................................... 66
<table>
<thead>
<tr>
<th>Contents</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implication for Nursing</td>
<td>66</td>
</tr>
<tr>
<td>Vulvar Cancer</td>
<td>66</td>
</tr>
<tr>
<td>Types</td>
<td>67</td>
</tr>
<tr>
<td>Etiology</td>
<td>67</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>67</td>
</tr>
<tr>
<td>Diagnostic Evaluation</td>
<td>67</td>
</tr>
<tr>
<td>Symptoms</td>
<td>67</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>68</td>
</tr>
<tr>
<td>Treatment</td>
<td>68</td>
</tr>
<tr>
<td>Implications for Practice</td>
<td>69</td>
</tr>
<tr>
<td>Vaginal Cancer</td>
<td>69</td>
</tr>
<tr>
<td>Etiology</td>
<td>69</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>70</td>
</tr>
<tr>
<td>Diagnostic Evaluation</td>
<td>70</td>
</tr>
<tr>
<td>Symptoms</td>
<td>70</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>70</td>
</tr>
<tr>
<td>Treatment</td>
<td>70</td>
</tr>
<tr>
<td>Counseling</td>
<td>71</td>
</tr>
<tr>
<td>Summary</td>
<td>71</td>
</tr>
<tr>
<td>Exam Questions</td>
<td>73</td>
</tr>
<tr>
<td>References</td>
<td>75</td>
</tr>
<tr>
<td>Resources</td>
<td>77</td>
</tr>
<tr>
<td>Glossary</td>
<td>85</td>
</tr>
</tbody>
</table>
FIGURES AND TABLES

Chapter 1

Table 1-1: Low- and High-Cancer-Risk Human Papillomavirus Strains or Types .......................3
Figure 1-1: Anatomy of the Cervix..............................................................................................6
Figure 1-2: Low- and High-Grade Changes of Cervical Cells ....................................................8
Figure 1-3: Depth of Lesions in Cervical Intraepithelial Neoplasia ............................................10

Chapter 2

Table 1-2: Treatment of Cervical Intraepithelial Neoplasia .......................................................10
Table 2-1: Risk Indicators of Hereditary Breast and Ovarian Cancer Syndrome
   From a BRCA1 or BRCA2 Mutation .........................................................................................27
Figure 2-1: Sentinel Lymph Node Biopsy ..................................................................................31
Figure 2-2: Lymphatic Spread of Breast Cancer .......................................................................34
Table 2-2: Breast Cancer Risk Categories and Risk Reduction Strategies .................................41
Table 2-3: Breast Cancer Survivor Issues...................................................................................43
PRETEST

1. Begin this course by taking the pretest. Circle the answers to the questions on this page, or write the answers on a separate sheet of paper. Do not log answers to the pretest questions on the FasTrax test sheet included with the course.

2. Compare your answers to the pretest key located at the end of the pretest. The pretest key indicates the chapter where the content of that question is discussed. Make note of the questions you missed, so that you can focus on those areas as you complete the course.

3. Complete the course by reading the chapters and completing the exam questions at the end of each chapter. Answers to the exam questions should be logged on the FasTrax test sheet included with the course.

Note: Choose the one option that BEST answers each question.

1. Human papillomavirus (HPV) types that have been identified as high-risk are
   a. 6 and 11.
   b. 16 and 18.
   c. 31 and 33.
   d. 45 and 51.

2. The transformation zone of the cervix is the area in which the
   a. cells of the vaginal wall meet the cells of the cervix.
   b. columnar cells of the cervix meet the uterine lining cells.
   c. columnar cells of the cervix meet the cells of the vaginal wall.
   d. squamous cells of the cervix meet the columnar cervical cells.

3. After abnormal cervical cancer screening, a procedure that allows for close-up visualization of the vagina and cervix is
   a. cryosurgery.
   b. colposcopy.
   c. hysteroscopy.
   d. cervicography.

4. Breast cancer is the second leading cause of cancer deaths in women, exceeded only by
   a. lung cancer.
   b. uterine cancer.
   c. colorectal cancer.
   d. ovarian cancer.

5. Which type of breast cancer is not associated with any specific mammographic, palpable, or visual features?
   a. Lobular carcinoma in situ
   b. Ductal carcinoma in situ
   c. Invasive ductal carcinoma
   d. Inflammatory breast cancer

6. A woman who is diagnosed with breast cancer and is a carrier of a BRCA1 or BRCA2 mutation has an increased risk of developing
   a. internal bleeding.
   b. cancer in the contralateral breast.
   c. uterine cancer.
   d. bruising underneath the breast.
7. A practice or condition that increases a female patient’s risk of developing breast cancer is
   a. screening for heart failure.
   b. eating a plant-based diet.
   c. having extended hormonal exposure.
   d. adopting a physically active lifestyle.

8. A patient characteristic or action that decreases the risk of ovarian cancer is
   a. being nulliparous.
   b. taking evening primrose oil.
   c. taking oral contraceptives.
   d. eating a diet rich in meat.

9. Postmenopausal bleeding in women should initially be evaluated by
   a. dilatation and curettage.
   b. hysteroscopy.
   c. Pap smear and cervical biopsy.
   d. transvaginal ultrasound or endometrial biopsy.

10. A medical history factor that can decrease a woman’s risk of developing uterine cancer is
    a. anovulation.
    b. oral contraceptives.
    c. nulliparity.
    d. estrogen therapy.

PRETEST KEY
1. B Chapter 1 page 2
2. D Chapter 1 page 5
3. B Chapter 1 page 8
4. A Chapter 2 page 23
5. A Chapter 2 page 29
6. B Chapter 2 page 35
7. C Chapter 2 page 44
8. C Chapter 3 page 62
9. D Chapter 3 page 65
10. B Chapter 3 page 65
INTRODUCTION

COURSE OBJECTIVES

After completing this course, the learner will be able to:

1. Discuss the implications of human papillomavirus (HPV) testing and other cervical cancer screening strategies.
2. Describe the evaluation and treatment of breast cancer in women and the importance of follow-up in primary care for survivors.
3. Discuss the etiology, diagnosis, and treatment of gynecologic cancers in women.

The field of women’s health has greatly expanded beyond its original roots in reproductive health. It is an exciting time for women and for nursing professionals who work with women. Links are forming worldwide, and with a more global perspective, it becomes clear that the health of women is integrally tied to the social, economic, political, and religious forces that shape cultures and societies. With education, women become empowered to make better decisions about their health and the health of their families. Nurses and other healthcare providers play an important role in this educational process.

This course is intended to assist nurses in providing care for commonly diagnosed cancers in women. It is designed for nurses who wish to review, enhance, or expand their knowledge base and level of understanding of common cancers in women. This educational offering is intended to provide information that serves as either a comprehensive review or an enhancement to the nurse’s present knowledge base of HPV, breast cancer, and common gynecologic cancers. This course also provides information that nurses can use to educate female patients; support them in their decision-making concerning health matters; and assist them in feeling empowered as individuals, as mothers, as family members, and as valued members of our society.

Furthermore, this course is intended to expand the nurse’s understanding of current issues and controversies in common cancers among women and to enhance the nurse’s ability to knowledgeably approach these issues. The course is designed to assist nurses providing care to various populations of female patients.
CHAPTER 1

HUMAN PAPILLOMAVIRUS AND CERVICAL CANCER SCREENING

By Rosemary Theroux

LEARNING OUTCOME

After completing this chapter, the learner will be able to discuss the implications of human papillomavirus (HPV) testing and other cervical cancer screening strategies.

CHAPTER OBJECTIVES

After completing this chapter, the learner will be able to:

1. Describe the types, risk factors, symptoms, and natural course of HPV infection in women.
2. Identify cervical cancer screening methods and protocols.
3. Describe follow-up interventions after abnormal cervical cancer screening results.
5. Discuss patient education and counseling for the prevention and treatment of HPV infection.

INTRODUCTION

Human papillomavirus (HPV), a nonenveloped, double-stranded DNA virus, is the most common sexually transmitted infection (STI) in the United States (Centers for Disease Control and Prevention [CDC], 2016a). Most sexually active adults are at risk of infection; approximately 6.2 million Americans acquire new genital HPV infections each year (CDC, 2014). Most HPV infections occur in women younger than 25 years. The rates of HPV infections are highest in those aged 20 to 24 years (45%), and it becomes less prevalent with increasing age (Hoffman et al., 2016).

The past decade has brought advances in cervical cancer screening technologies and protocols for HPV testing of high risk (HR) strains and management of abnormal screening results. Currently three HPV vaccines are marketed in the United States. A vaccine for protection against nine types of HPV has been approved, and the number of doses has been decreased (Meites, Kemp, & Markowitz, 2016). Recent research has demonstrated a positive public health outcome from the HPV vaccine uptake rate among women (Audisio et al., 2016). During the first 8 years after the introduction of the HPV vaccine, the prevalence of vaccine-strain HPV decreased by 75% among all women and by 90.8% among vaccinated women (Kahn et al., 2016).
This chapter focuses on abnormal Pap smears, their association with HR HPV, and the far-reaching implications of HPV vaccine uptake for women and their families.

**HUMAN PAPILLOMAVIRUS INFECTION**

Human papillomaviruses (HPVs) comprise a family of more than 100 virus types. Manifestations of HPV infection range from plantar and genital warts caused by low-risk (LR) HPV strains to genital cancers and head and neck cancers (CDC, 2016b).

**Types of Human Papillomavirus**

HPV types are classified by their oncogenic (cancer-causing) potential. Clinically, HPV types are classified as high risk (HR) or LR based on their classification as causing cancer (see Table 1-1). Simultaneous or sequential infection with multiple HPV types is common. HPV 16 and 18 are considered oncogenic, accounting for the largest percentage (45%) of precancerous conditions and 55% of cervical cancers worldwide. HPV 16 is also dominant in other HPV-related anogenital and oropharyngeal cancers. HPV 16 accounts for more than 1 in 5 cervical HPV infections and is the most common HPV found among low-grade lesions (clusters of abnormal cells on the cervix) and in women without neoplasmia (Hoffman et al., 2016).

**Risk Factors**

The important risk factors for a woman’s acquisition of HPV infection are the number of lifetime and recent sexual partners, a history of unprotected sex, and early age of first intercourse. HPV is transmitted by direct skin-to-skin, usually sexual, contact with the genitals, mucous membranes, or body fluids of an individual with either warts or subclinical HPV infection. Cervical HR HPV infection generally requires penetrative intercourse. Oral-genital and hand-genital HPV transmissions are possible but are much less common than genital-genital transmission. Women who have sex with women have rates of HR HPV positivity, abnormal cervical cytology, and high-grade cervical neoplasia similar to those of heterosexual women (Reiter & McRee, 2016). Women with or without past sexual experiences with men have a similar risk, implying that digital, oral, and perhaps object contact predisposes them to HR HPV infection (Hoffman et al., 2016).

Congenital HPV infection from vertical transmission (mother to fetus or newborn) beyond transient skin colonization is rare. Conjunctival, laryngeal, vulvar, or perianal warts present at birth or that develop within 1 to 3 years of birth are most likely due to perinatal exposure to maternal HPV (Hoffman et al., 2016).

**Symptoms**

The presentation of HPV infection varies according to the anatomic areas involved. Conditions that are associated with HPV may include anogenital warts (condylomata acuminata), which are generally found near moist surfaces (e.g., the perianal area, vaginal introitus, vagina, cervix, labia, and vulva). Warts are generally not painful but may cause pruritus and bleeding.

**Diagnosis**

Diagnosis is confirmed by direct detection of HPV in samples using nucleic acid amplification testing (NAAT), polymerase chain reaction (PCR) testing, and biopsy of the cervix (Hoffman et al., 2016).
Natural History of Human Papillomavirus

The incubation period for HPV is probably weeks to months for genital warts and several months to years for cervical cellular abnormalities and cervical cancer. HPV is believed to access the basal cell layer and basement membrane through microabrasion of the genital epithelium during sexual contact. Once infected, these basal cells may become a viral reservoir (Hoffman et al., 2016).

The natural history of genital HPV infection varies between individuals and over time. Outcomes can be broadly grouped as latent (cells are infected but HPV infection remains unknown) or expressed infections. There are no detectable tissue effects in latent infection, as the virus is not actively replicating. The virus is present below detectable levels. It is uncertain whether apparent clearance of the HPV constitutes true eradication of HPV from infected tissues or whether it reflects latency (Hoffman et al., 2016).

Infection expression may be productive, creating infectious viral particles, or it may be neoplastic, causing preinvasive disease or malignancy (Schiffman & Kjaer, 2003). Productive infections are characterized by production of infectious viral particles. Most of these infections have little or no malignant potential. Most productive infections are subclinical (asymptomatic, unapparent, or unrecognized), but a smaller percentage yields clinically apparent genital warts. In both female and male genital tracts, productive HPV infections cause visible genital warts (condyloma acuminata; Hoffman et al., 2016).

An infection is considered subclinical when there is no evidence of genital lesions. The infectivity of subclinical HPV is assumed to be great. “Subclinical infections may be indirectly identified as low-grade cytologic, colposcopic, or histologic abnormalities” (Chisholm, 2016,

<table>
<thead>
<tr>
<th>TABLE 1-1: LOW- AND HIGH-CANCER-RISK HUMAN PAPILLOMAVIRUS STRAINS OR TYPES</th>
<th>HPV Types</th>
<th>Associated With</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk HPV</td>
<td>6, 11, 40, 42, 43, 44, 53, 54, 61, 72, 81</td>
<td>• Genital warts and benign or low-grade cervical cellular changes • Recurrent respiratory papillomatosis (a rare condition) • A minority of subclinical HPV infections</td>
</tr>
<tr>
<td>High-risk HPV</td>
<td>16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82</td>
<td>• Anogenital (cervical, vulvar, vaginal, anal, penile) and oropharyngeal cancers</td>
</tr>
<tr>
<td>High risk for cervical cancer</td>
<td>16, 18, 31, 33, 35, 45, 58</td>
<td>• Account for approximately 95% of cervical cancer cases worldwide, 68% of squamous cell carcinomas, and 85% of adenocarcinomas</td>
</tr>
<tr>
<td>High risk for cervical cancer and low-grade lesions</td>
<td>16</td>
<td>• Accounts for more than 1 in 5 cervical HPV infections and is the most common HPV found among low-grade lesions</td>
</tr>
<tr>
<td>High risk for cervical squamous cell carcinomas</td>
<td>18</td>
<td>• Occurs less commonly but is found in 13% of cervical squamous cell carcinomas</td>
</tr>
</tbody>
</table>

HPV-related infections may be detected by cervical screening or specialized testing. Cervical testing is reported as low-grade changes on the cervical cells, positive HPV, or HR HPV positive. No known therapy eradicates subclinical infection. Most HPV infection and related lesions, whether clinical or subclinical, spontaneously resolve, especially in adolescents and young women (Hoffman et al., 2016).

HPV infection can be transient or can become persistent. The clinical course of patients with HPV varies and is characterized by spontaneous regressions and/or recurrences. For most women, HPV infection resolves without intervention. Most infections are transient, asymptomatic, subclinical, and have no clinical consequences in immunocompetent individuals. In fact, 70% of infections clear in 1 year, and 91% of infected women do not have detectable levels of cervical HPV infection after 2 years. Thus most individuals acquire and clear HPV infection without knowing they were infected (Insinga et al., 2010).

Although the vast majority of cervical HPV infections (including those caused by the HR or oncogenic types) heal through the body’s natural immune response, some can persist and eventually progress to cervical cancer. Persistent HPV infection is an infection that is not cleared by the immune system and is characterized by persistently detectable HR-HPV DNA. Factors associated with persistent infection include older age, HR-HPV types, and immunodeficiency. The risk of progression to high-grade neoplasia increases with age; HPV infection in older women is more likely to reflect persistence (Viens et al., 2016).

**CERVICAL CANCER**

The causal link between HR HPV infection and the development of cervical cancer was first identified in 1984. Almost all types of cervical cancer – squamous cancer, adenosquamous cancer, and adenocarcinoma – are now believed to be associated with HR HPV (Goodman, 2015). The CDC estimated that approximately 30,700 new cancers were attributable to HR HPV, including 19,200 among females and 11,600 among males. HR HPV has a significant effect on morbidity, mortality, and cost in the United States and across the globe. Worldwide each year 530,000 women are diagnosed with cervical cancer and about 275,000 die (Viens et al., 2016). In the United States the overall incidence of cervical cancer is 7.5 cases per 100,000 women (Goodman, 2015).

Although there has been a drop in the overall incidence of newly diagnosed cervical cancers, minority populations continue to be disproportionately affected by cervical cancer. African American, Hispanic, and Asian American women reportedly demonstrate higher incidence and mortality rates than white women. Screening rates are also lower for Hispanic and African American women, at 77% and 82.13%, respectively. Thus the increased burden of the disease among minorities is closely tied to the lack of screening (Nardi, Sandhu, & Selix, 2016).

**Risk Factors**

The most common risk factors for the progression from HPV infection to cervical cancer are persistent HR HPV infection, smoking, immunodeficiency, high parity, long-term use of oral contraceptives, and chronic inflammation (Schiffman & Kjaer, 2003).

**Screening**

Most cervical cancers are preventable with regular screening for precancerous lesions among women aged 21 to 65 years, with follow-up interventions for abnormal test results. However, most cervical cancers occur because screening was not performed rather than a failure of screening to detect the cancer. The Healthy People
2020 target for cervical cancer screening is 93%; however, in 2013 only 80.7% of women reported up-to-date cervical cancer screening, with even lower rates noted among Asians; Hispanics; women aged 51 to 65 years; and foreign-born, uninsured, and publicly insured women (Campbell, Menezes, Paskett, & Giuliano, 2012).

The goals of screening programs for cervical cancer include the identification and treatment of true precursors of cervical cancer. It is critical that the cervical cancer screening procedures and algorithms be effective at detecting precancerous changes while minimizing harm to the woman (Goodman, 2015; Lees, Erickson, & Huh, 2016). According to the American College of Obstetricians and Gynecologists (ACOG), “Protection from cervical cancer is the primary goal of screening, but as the prevalence of the disease decreases, other considerations may become equally important in the decision-making process. For example, the effects of invasive diagnostic workups (e.g., colposcopy and biopsy) and overtreatment of lesions likely to regress have adverse consequences related to costs and potentially to future reproductive outcomes in women” (2016b, p. e5).

Anatomy of the Cervix

To understand normal and abnormal Pap smear findings, nurses must be knowledgeable about cervical anatomy and cytology and the normal cellular changes that take place throughout a woman’s life.

The main parts of the cervix are the endocervix, the inner part leading into the uterus, and the ectocervix, the outer part of the cervix. The surface of the cervix and the canal that leads into the uterus (the endocervical canal) are made up of two types of cells – squamous epithelium and columnar epithelium. Squamous epithelium covers the vagina and ectocervix. It is smooth and pink in appearance.

Columnar epithelium cells line the endocervical canal. They are glandular cells that produce mucus. In young women, these cells can also be noted on the outer surface of the cervix around the external cervical opening (os). This glandular tissue has a rough texture and is dark pink. Women who take oral contraceptives often have columnar epithelial cells on the outer surface of the cervix due to the hormonal effects of the pills.

The area in which the squamous epithelium and the columnar epithelium come together on the cervix is called the squamocolumnar junction or the transformation zone (TZ; see Figure 1-1). In this area the cuboidal columnar cells are constantly being changed (or transformed) into flat squamous cells, as a part of a normal process. This cell turnover is influenced by the female hormones (Canadian Cancer Society, 2016).

Glandular cells are another type of cell that make up the thin layer of tissue that covers the inner canal of the cervix. Glandular cells also are present inside the uterus.

Most cervical cancers are squamous cell carcinoma. This type of cancer starts in flat, scaly cells covering the ectocervix. Cervical cancer develops from HR HPV-infected cells that typically originate in the squamocolumnar junction (Canadian Cancer Society, 2016).

Cervical Cancer Screening: Cervical Cytology (Pap Smear)

Sensitivity, Specificity, Positive Predictive Value

Three statistics evaluate the success of a cervical cancer screening test:

- **Sensitivity (also called the true positive rate):** The proportion of people with the disease who will have a positive result. In other words, a highly sensitive test is one that correctly identifies patients with a disease (Nicoll & McPhee, 2017).
- **Specificity (also called the true negative rate):** The proportion of people without the
disease who will have a negative result. In other words, the specificity of a test refers to how well a test identifies patients who do not have a disease (Nicoll & McPhee, 2017).

- Positive predictive value (PPV): The percent of patients with a positive test result who actually have the disease (Nicoll & McPhee, 2017).

Screening Guidelines

Cervical screening should be performed using conventional (slide) or liquid-based cytologic tests. Both cytology methods are associated with potential user errors: (1) the area of abnormal cervical cells may be missed or not sampled, (2) abnormal cells may not transfer from the smear applicator to the slide or vial, (3) preservation of the cells may be inadequate, or (4) a reading error may occur. Screening guidelines for cytology testing are effective in decreasing the incidence of cervical cancer. Screening guidelines have undergone substantial changes due to new evidence of disease pathogenesis and HPV natural history.

A major guideline change recognizes HPV testing combined with cervical cytology as more sensitive than cervical cytology alone at detecting high- or low-grade cervical histopathology (Saslow et al., 2012). Due to the deficiencies of cytology screening, HR HPV testing was developed as an adjunct to traditional cytology screening. Approved by the U.S. Food and Drug Administration (FDA) in 1999, HPV DNA tests evaluate for 14 HR HPV types. Results are reported as “not detected” or as “detected for high-risk HPV DNA type” without specifically identifying which ones. HPV testing was first recommended for the finding of
atypical squamous cells of undetermined significance (ASC-US) from the Pap (cytology) reading of women age 21 years or older. In 2006 clinical guidelines were expanded to include the use of HR HPV (cotesting) for screening of women age 30 years and older in conjunction with cytology (Pap test; Goodman, 2015).

The Pap test (also called a Papanicolaou test or Pap smear) or cervical cytology test has been the mainstay of cervical cancer screening for 60 years. The cytology screening test remains the current approach for women younger than 30 years. The advantages of cytology are its simplicity and low cost. Global epidemiologic studies have demonstrated its efficacy as a cancer prevention strategy. Traditional cytology has been shown to have a sensitivity of only 51% (30% to 87%) and specificity of 98% (86% to 100%). Annual screening has been able to overcome this low sensitivity (i.e., false-negative rate) of cervical cytology (Lees et al., 2016).

HPV tests are recommended for the triage of women aged 21 years or older who present with ASC-US Pap results. For women older than 30 years, the use of both HR HPV testing and cytology (cotesting) is recommended. HPV genotyping has been developed to determine appropriate follow-up for women who have a negative cytology with a positive HR HPV test and women who have an ASC-US cytology result with a positive HR HPV test. Genotyping determines the specific HR HPV and identifies the presence of HPV types 16 and 18 (Lees et al., 2016). The role of HR HPV in cervical cancer as well as the low sensitivity of cervical cytology has led to investigations regarding HPV testing as a primary screening method. There is evidence that shows the efficacy of HR HPV testing alone as a primary screening method for HPV in women older than 25 years, but no current protocol exists (Lees et al., 2016). HPV DNA testing to screen for primary cervical cancer as a stand-alone test is not recommended (Saslow et al., 2012).

Terminology for Cytologic and Histologic Reporting

The terms atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LSIL), and high-grade squamous intraepithelial lesion (HSIL) refer to cytology (Pap test) and cervical intraepithelial neoplasia (CIN). The numbers 1, 2, and 3 refer to the histology. Cytology and histology terms are synchronized – LSIL corresponds to CIN 1, and HSIL corresponds to CIN 2 or CIN 3:

ASC-US: Changes in the cervical cells have been found. Atypical squamous cells are present, and HSILs cannot be ruled out. The changes are almost always a sign of an HPV infection. ASC-US is the most common abnormal Pap test result.

LSIL: The cervical intraepithelial cells show changes that are mildly abnormal (CIN 1). A few of the cells on the surface of the cervix have changes in size and shape, but they are still somewhat similar to normal cells.

HSIL: The cervical intraepithelial cells show moderate to severe dysplasia (CIN 2/3). The cells look abnormal under the microscope, but they are still on the surface of the cervix. This suggests more serious changes in the cervix than occur with LSIL. It is more likely than LSIL to be associated with precancer and cancer.
MANAGEMENT GUIDELINES

Bethesda 2001 is currently the most commonly used classification terminology to report cytopathology findings. Developed by major medical groups in 1988, this system has undergone review a number of times in response to emerging data on the role of HPV in cervical cancer (Nayar & Wilbur, 2015).

Epithelial cells (squamous and glandular) are evaluated for abnormalities. A squamous intraepithelial lesion (SIL) is an abnormal growth of epithelial cells on the surface of the cervix, which are commonly called squamous cells. In the lower genital tract, these lesions are potential precursors of invasive cancer (see Figure 1-2). The newest Bethesda system (Nayar & Wilbur, 2015) uses a two-tiered nomenclature for cervical cytology abnormalities: low-grade and high-grade squamous intraepithelial lesion.

Managing an Abnormal Cervical Cancer Screening

Approximately 7% of U.S. women who undergo Pap testing will have an abnormal result (Lees et al., 2016). Algorithms created and updated by ASCCP provide a guideline for managing abnormal screening test results by assessing benefits and harms and include suggestions, taking into consideration both cytology and HR HPV types found in cotesting (Massad et al., 2013). The recommendations for interventions for abnormal findings have now been determined based on age groups. This follows the recommendations that cervical cancer screening not begin until age 21 years (ACOG, 2016a).

Evaluation of Abnormal Findings

The Pap test is a screening test. It cannot tell exactly how severe the changes are in cervical cells. A cervical biopsy is needed to find out whether precancer or cancer actually is present. Colposcopy is the accepted diagnostic...
test for evaluating abnormal cervical screening tests to determine the presence, location, grade, and extent of cervical intraepithelial neoplasia (CIN). It remains the gold standard for evaluation of the cervix to detect CIN (ACOG, 2016a).

The primary goal of this outpatient procedure is to identify invasive or preinvasive neoplastic lesions for directed biopsy and subsequent management. General colposcopy assessment has three components: cervical visualization, squamous columnar junction (SCJ) visibility, and TZ classification. The procedure examines the lower anogenital tract with a binocular microscope affixed to a stand. The colposcopy contains a stereoscopic lens or digital imaging system that has magnification settings ranging from 3- to 20-fold. The procedure is performed by healthcare providers (HCPs) with specialized training and skills that encompass lesion identification and grading and biopsy techniques. Sensitivity estimates range between 50% and 80% (Hoffman et al., 2016).

Application of acetic acid to abnormal epithelium results in the acetowhite change characteristic of neoplastic lesions and of some benign conditions. Under direct colposcopy visualization, abnormal tissue is identified, and biopsies are performed on the sites most likely to harbor the most severe neoplasia. A sample of tissue may be taken from areas of concern for evaluation by a pathologist.

Some women are highly anxious and distressed in anticipation of a colposcopy. They may express fear because they are unfamiliar with the procedure and are concerned about what will be discovered. They may also be worried about experiencing pain during the procedure. To increase female patients’ knowledge and improve satisfaction with the procedure, the nurse should thoroughly explain the process before the procedure. The presence of a support person can be helpful as well (Diaz, 2013).

After the colposcopy, the biopsy samples are examined for abnormalities (histology) by a pathologist. The CIN classification system is used to report the cervical biopsy evaluation. The numbers used (1 to 3) describe the actual depth of changes in the cervical lesion (cluster of cervical cells). In grade 1 (CIN 1), the abnormal cells infiltrate only the lower third of tissue. CIN 1 often goes away by itself without treatment and is now recognized as evidence of HPV infection, most of which is transient and unlikely to progress. In grade 2 (CIN 2), the cells penetrate to the second layer of tissue. In grade 3 (CIN 3), the abnormal cells penetrate the third layer of tissue and involve a fairly large area. Most CIN 2 and CIN 3 lesions are not separated or differentiated but are reported as CIN 2/3. Grade 4 is referred to as carcinoma in situ because the abnormal cells penetrate all epithelial layers. Grade 2 and 3 lesions are considered to be true cancer precursors (ACOG, 2016a; Hoffman et al., 2016; see Figure 1-3).

Treatment of Cervical Intraepithelial Neoplasia

Treatment and follow-up is determined by guidelines and the individual woman’s age and history (Hoffman et al., 2016). Counseling before the procedure should include the rationale, benefits and risks, details of how the procedure is performed, pain control strategies used during the procedure, what to expect after the procedure, and the schedule for posttreatment follow-up (Apgar, Kaufman, Bettcher, & Featherstone, 2013).

There are a number of ways to treat the lesions identified during the colposcopy procedure and biopsy. Treatment depends on the women’s age and the location and severity of the lesions (Chisholm, 2016; Wuerther & Avila-Wallace, 2016). Refer to Table 1-2 for a summary.
Ablative Therapy

Cryosurgery

The advantages of this therapy are that it is easy to perform in an outpatient setting, is inexpensive, requires minimal HCP training, and has minimal long-term fertility issues. Cryosurgery is generally not favored for the treatment of CIN 3 due to higher rates of disease persistence after treatment and lack of a histologic specimen to exclude occult invasive cancer.

Cryosurgery delivers a refrigerant gas, usually nitrous oxide, to a metal probe that freezes tissue on contact. This freezes the top layer of cervical cells and causes a destruction of the abnormal tissue. Before cryosurgery, women should be advised that discomfort may occur. Cramping can usually be controlled with ibuprofen taken before the procedure. Vasovagal reactions may also occur during cryosurgery. The woman is told to expect a foul-smelling, watery vaginal discharge (related to sloughing of the necrotic tissue) for 2 to 4 weeks after the
procedure. Women should be advised to postpone intercourse for 2 weeks until their follow-up examination (Hoffman et al., 2016).

During the procedure, excision or destruction of the entire epithelium in the transformation zone is required to prevent return of abnormal cells after treatment. As a result, the squamocolumnar junction (TZ) will not be visible in future colposcopy examinations, and there may be a need for a more invasive procedure in the future if lesions recur that are not visible with the colposcopy (Chisholm, 2016). Although rare, cryosurgery can also cause scarring of the cervix and lead to stenosis (narrowing or constriction) of the cervical opening, making future Pap testing difficult (Apgar et al., 2013).

**Laser Ablation**

Laser (high-energy light) ablation involves using a laser mounted on a colposcope to vaporize the abnormal cells (i.e., the TZ). The advantages of laser treatment are rapid healing (3 to 4 weeks) and minimal scarring. There is no risk of preterm labor unless the depth reaches 10 mm of the cervical canal. The disadvantages are cost and the need for specialized training. Sedation may be needed during the procedure (Apgar et al., 2013).

**Cone Biopsy and Conization Excisional Techniques**

If the lesion found on colposcopy extends into the endocervical canal and cannot be fully seen, a cone biopsy (excision of a conelike section of the cervix) is performed to ensure that the entire lesion is removed. Conization is removal of the entire TZ and endocervical canal. This procedure is reserved for cases of severe dysplasia (CIN 3) or cancer in situ, particularly in the case of endocervical extension. The procedure can be performed with a scalpel, a CO₂ laser, or large-loop excision (Hoffman et al., 2016).

**Cold-Knife Conization**

Cold-knife conization uses sharp excision with a scalpel to remove the cervical TZ and CIN lesion. It is performed in an operating room using general or regional anesthesia. Complications can include bleeding, infection, cervical stenosis, and cervical insufficiency. The need to perform the procedure in the operating room and a higher complication rate are distinct disadvantages of cold-knife conization (Hoffman et al., 2016).

**CO₂ Laser Conization**

CO₂ laser conization uses directed energy to cut and remove the cone-shaped biopsy specimen. This allows precise tailoring of the cone shape to minimize stromal excision and yields less blood loss. Disadvantages are its expense, some thermal compromise of specimen margins, and special training requirements. This procedure can be performed under local, regional, or general anesthesia. There is a higher rate of hemorrhage with laser conization than with other excision techniques because more tissue is removed. This procedure is also associated with prenatal complications such as extreme preterm labor and low birth weight (Apgar et al., 2013; Hoffman et al., 2016).

**Loop Electrosurgical Excision**

A loop electrosurgical excision procedure (LEEP) is commonly used to treat CIN 2 and CIN 3 because of its ease of use, low cost, and provision of additional tissue for histologic evaluation. LEEP uses a thin wire on an insulated handle through which an electrical current is passed. This creates an instrument that can simultaneously cut and coagulate tissue, ideally during direct colposcopic visualization. Because LEEP can be performed using local anesthesia, it has become the primary outpatient treatment modality for high-grade cervical lesions, including those that extend into the endocervi-
The advantage of this is that the tissue is removed, not destroyed. Thus the tissue is available for evaluation by a pathologist. After the procedure, healing is rapid, and only a mild discharge occurs. Possible complications include bleeding and cervical stenosis (narrowing or constriction of the cervix; Hoffman et al., 2016; Merk Manual, 2017). The relationship between preterm birth and previous LEEP remains uncertain (Apgar et al., 2013).

**PATIENT EDUCATION AND COUNSELING**

**Prevention of Human Papillomavirus Infection**

Vaccination against HPV is recommended to prevent HPV infections and HPV-associated diseases, including cancers. Routine vaccination at age 11 or 12 years has been recommended by the Advisory Committee on Immunization Practices (ACIP) since 2006 for girls and since 2011 for boys (Meites, Kemp, & Markowitz, 2016). Despite the fact that HPV vaccines are available for preteen girls and boys at low to no cost, they are underutilized in the United States. The HPV vaccines have demonstrated efficacy in the prevention of cancers and its precursors (Kahn et al., 2016), minimal systemic adverse reactions, positive safety profiles, a long-term immune response, and a reduction in the prevalence of HR HPV types, LR HPV types, and genital warts. However, HPV vaccines cannot prevent infection after the fact, which is why immunization is recommended before sexual debut. Testing for HPV is not indicated before vaccination (Wuerther & Avila-Wallace, 2016).

The latest HPV vaccine, Gardasil 9, is licensed for both sexes ages 9 through 26 years. It covers the HPV types included in the original vaccine and expands this protection by including five more HR HPV types (HPV 31, 33, 45, 52, and 58) that cause approximately 90% of cervical cancers globally along with a majority of vaginal, vulvar, and anal cancers. It is the only type of HPV vaccine now distributed in the United States. Based on clinical trials, the CDC and ACIP reduced the number of intramuscular doses of the 9-valent vaccine to two. It is recommended that 11 to 12 year olds receive two doses at least 6 months apart, rather than the previously recommended three doses. Teens and young adults who start the series later, at ages 15 through 26 years, will require the three doses (Meites et al., 2016).

**Counseling Patients With Human Papillomavirus Infection**

Receiving a diagnosis of HPV can create a significant emotional toll. Women who receive a positive HPV test result may experience feelings of stigma, anxiety, fear, or anger. The most common associated aspect of stigma is negative self-image (Barnack-Taularis, Serpico, Ahuwalia, & Ports, 2016).

Learning of abnormal cytology and positive HR HPV DNA results can be a distressing situation, and women may experience a host of unpleasant reactions. Some of these reactions may be due to lack of knowledge or familiarity with HPV, which may lead a woman to feel vulnerable because of fear, stigma, and confusion regarding her diagnosis (Diaz, 2013). A concern for many is disclosure about the virus. “Disclosing information regarding a sexually transmitted virus that is linked to lower genital tract cancers has the potential to instill fear, decrease self-esteem, provoke anxiety and depression, and negatively affect interpersonal relationships” (Diaz, 2013, p. 391). Reassuring the patient and removing the stigma associated with diagnosis of a sexually acquired viral disease can redirect the conversation toward the necessary next steps for evaluation.
Nurses can play a key role in support, counseling, and educating about HPV, testing, follow-up diagnostic evaluation, and treatment. In particular, the normal course of HPV infection should be discussed during all healthcare encounters. “It is paramount that the clinician have an excellent understanding of the natural history of HPV disease and is able to relay this information to the patient in a manner that is educational, timely, and understandable. It is equally important to relay this information in a manner that is supportive and reassuring” (Diaz, 2013, p. 399).

Notification and Follow-Up of Pap Test Results

Informing women of Pap test results is an essential role for the nurse. The clinical setting must have a system in place to provide timely patient notification of cancer screening and biopsy results and have a system in place to ensure that this happens. Each office or outpatient setting should establish priorities for tracking test results and follow-up ordered by the HCP. Computerized tracking and reminder systems are available with custom alerts, telephone reminders, and telephone numbers to call for automated test results using individual identifying numbers. Some practices are now using secure patient portals through which patients can receive their test results electronically and can receive electronic reminders about when their next test should be scheduled (ACOG, 2012).

Results of all Pap tests, consultations, and pathology reports are reviewed, initialed, and dated by an HCP who has been designated to perform this function. Patients report their preference for receiving lab results (telephone, text, patient portal) and receive an explanation of the office practice for notification of test results. They are instructed to call back for test results if they do not receive them in a timely fashion (ACOG, 2012).

Education for Women About Human Papillomavirus

- The human papillomavirus (HPV) vaccine can prevent disease and cancer caused by HPV. The vaccine is safe and effective.
- Women continue to need cervical cancer screening even if they are vaccinated against HPV.
- The development of cervical cancer is rare among women of any age receiving regular screenings.
- Condoms used consistently and correctly can lower the chances of acquiring and transmitting HPV and developing HPV-related disease (e.g., genital warts and cervical cancer). However, because HPV can infect areas not covered by a condom, condoms might not fully protect against HPV.
- Abstaining from sexual activity is the most reliable method for preventing genital HPV infections.
- Limiting one’s number of sexual partners can reduce the risk for HPV infection. However, even persons with only one lifetime sexual partner can acquire HPV.


Studies have shown that 46.6% of women do not return for follow-up testing after an abnormal cervical cancer screening or colposcopy (Tosteson et al., 2016). Patient education, telephone counseling, and written materials have been effective strategies in improving adherence to guidelines (Wuerther & Avila-Wallace, 2016). In one study, tailored counseling telephone messages, in conjunction with appointment reminders, resulted in higher adherence to follow-up recommendations after an abnormal Pap test result than use of print materials alone over a 1-year period. The use of telephone and print counseling interventions may be augmented by the design and implementation of short text messages to patients’ mobile phones because this mode of communication is common, attended to, and salient among the target population (Miller et al., 2013).

**CASE STUDY 1-1**

Emma is a 32-year-old gravida 3, para 3 (i.e., three pregnancies and three births) female patient of Hispanic origin who goes to a women’s health clinic in a small, rural community. Emma states that she would like a gynecologic examination because it has been 3 years since her last well-woman examination.

Emma’s past medical history and gynecologic history are unremarkable, and she has no current reports of medical problems. Emma was recently married and engages in sexual activity with her husband. She is considering having another child. Emma states that she is not currently using oral contraceptives or other birth control methods, and she does not smoke.

The women’s health nurse practitioner performs Emma’s gynecologic examination, which is also unremarkable. The nurse practitioner screens Emma for cervical cancer using a Pap test. Emma’s Pap test results reveal a high-grade squamous intraepithelial lesion (SIL). Emma is then scheduled for a colposcopy with biopsy of the identified lesion. The colposcopy determines that Emma has cervical intraepithelial neoplasia grade 2 (CIN 2/3). The nurse practitioner explains to Emma that this condition involves the growth of moderately abnormal cells on the thin layer of tissue that covers her cervix. When Emma asks if she has cancer, the nurse practitioner explains that the abnormal cells are not yet malignant but could become cancerous. The nurse practitioner recommends cryosurgery for Emma and contacts the gynecologist in the clinic to speak to Emma about performing this treatment.

**Questions**

1. When Emma asks the nurse practitioner for more information about her biopsy results, what should be the nurse’s response?
2. What specific information about the scheduled cryosurgery should the nurse share with Emma?
3. What other information about the posttreatment period should the nurse provide to Emma?

**Discussion**

1. The nurse practitioner should explain that CIN 2/3, or moderate cervical dysplasia, is considered a “preinvasive” condition. The term CIN 2/3 describes a condition in which there are moderate changes to the cervical cells from the human papillomavirus (HPV). CIN 2/3 is not cancer but may become cancer and spread to nearby normal tissue if not treated. Several methods of treatment are available for women who wish to continue childbearing. The treatment is aimed toward eradicating the abnormal cells while trying to preserve the structure of the cervix. All treatment methods have comparable rates for success in treating preinvasive lesions.
2. The nurse practitioner should explain that several methods of treatment are standard for CIN 2/3 in the United States. The physician will perform the procedure in an outpatient clinic or inpatient setting. The chosen option is cryosurgery, a technique used to freeze the abnormal cells on the cervix, which will then slough. New, healthy cells will replace the sloughed tissue. Emma can expect to experience a profuse, watery discharge for up to 4 weeks after the procedure. To prevent infection, she should not use tampons and should refrain from intercourse until her follow-up visit 2 weeks after the procedure. She is unlikely to experience discomfort, but she may take an over-the-counter analgesic, such as ibuprofen, if needed. She may experience vaginal spotting as the new tissue regenerates. Emma should have a support person accompany her on the day of the scheduled procedure if she feels it would be helpful.

3. The nurse should instruct Emma to telephone the clinic if she experiences fever, abdominal pain, or heavy bleeding after the cryosurgery. Emma should also be advised that cervical stenosis is a rare, but possible, complication of the procedure. The nurse should ensure that Emma understands that she will need follow-up cytology testing for high-risk human papillomavirus (HR HPV), which will be conducted at 6-month intervals.

**SUMMARY**

The prevalence of HR HPV and its link to cervical cancer has changed the way HCPs approach health care for women. HCPs now recognize that most women are at risk for becoming infected with HPV and thus must be educated and counseled appropriately. The major risk factors now known to influence cervical cancer can be modified by a woman’s personal behavioral choices. Although this information is essential for all women, it holds special implications for young women who are just beginning sexual activity. Education about HPV and cervical cancer, the risk factors for these conditions, and protective behaviors are central to the prevention of cervical cancer. In addition, women need information about cervical cancer screening guidelines, testing, and diagnostic studies. Nurses provide encouragement to women to undergo cervical cancer screening performed at appropriate intervals. It is also essential that nurses give accurate and up-to-date information about HPV infection and the possibility of prevention through vaccination. Nurses must continue to provide compassionate and sensitive care to women struggling with a new diagnosis of HPV infection or those dealing with ongoing life issues that have resulted from exposure to HR HPV types.
1. Human papillomavirus (HPV) types that have been identified as high-risk are
   a. 6 and 11.
   b. 16 and 18.
   c. 31 and 33.
   d. 45 and 51.

2. The important risk factors for HPV infection in women are the number of lifetime and recent sexual partners, a history of unprotected sex, and
   a. not being physically active.
   b. late or no pregnancy.
   c. early menstrual period history.
   d. early age at first intercourse.

3. A 33-year-old female patient is scheduled for a well-women examination. Her last cervical cancer screening was 5 years ago. Based on the latest cervical cancer screening guidelines, the nurse explains to the patient that today she will need
   a. a Pap test with HPV testing.
   b. a cervical biopsy.
   c. a histology test with high-risk HPV testing.
   d. an HPV and chlamydia test.

4. Cervical cancer screening for women age 21 through 29 is performed using
   a. a Pap test with HPV testing.
   b. a cervical biopsy.
   c. a Pap test.
   d. high risk HPV testing.

5. After abnormal Pap test results, a procedure that allows for close-up visualization of the vagina and cervix is
   a. cryosurgery.
   b. colposcopy.
   c. hysterectomy.
   d. cervicography.

6. A colposcopy is performed to direct a biopsy and
   a. perform subsequent management strategies.
   b. screen women who are at risk.
   c. prevent infection.
   d. freeze abnormal cells.

7. Advantages of laser therapy in treating cervical neoplastic lesions are rapid healing and
   a. low cost.
   b. need for minimal professional training.
   c. minimum scarring.
   d. no need for sedative medication.
8. A method of management for women with abnormal cervical histology results is
   a. cervicography.
   b. conization.
   c. SurePath.
   d. laparoscopy.

9. The HPV vaccine Gardasil 9 is
   a. administered orally.
   b. indicated for women between the ages of 35 and 50 years.
   c. administered in two doses for children of both sexes in the age range of 11 to 12 years.
   d. used to protect against four HPV types.

10. Nurse counseling for patients diagnosed with HPV infection includes reassuring the patient and
    a. avoiding discussion of the normal course of HPV infection.
    b. disclosing information about the diagnosis to the patient’s primary provider.
    c. relying on the patient to follow up on their own with diagnostic treatment.
    d. helping to remove any stigma associated with the diagnosis.


LEARNING OUTCOME

After completing this chapter, the learner will be able to describe the evaluation and treatment of breast cancer in women and the importance of follow-up in primary care for survivors.

CHAPTER OBJECTIVES

After completing this chapter, the learner will be able to:
1. Describe the epidemiology, etiology, pathophysiology, risk factors, and diagnosis of breast cancer.
2. Identify the different types of breast cancer.
3. Review the different treatment options for breast cancer.
5. Summarize breast cancer preventive strategies.
6. Discuss the nurse’s role during care of the patient through the different stages of breast cancer.

INTRODUCTION

Breast cancer is the second most common cancer in women after skin cancers and is the second leading cause of cancer deaths in women after lung cancer (Centers for Disease Control and Prevention [CDC], 2016). Women who live in North America have the highest rate of breast cancer in the world. Presently, there are about 2.5 million breast cancer survivors in the United States.

Breast cancer is a significant health problem for women. Breast cancer screening is practiced widely, which contributes to an increased diagnosis of ductal carcinoma in situ and invasive breast cancer. It is projected that over the next several decades, women born between 1946 and 1964 will face high risks for postmenopausal breast cancer (American Association of Cancer Researchers, 2015). However, with a decrease in postmenopausal hormone use, the incidence of postmenopausal breast cancer has declined (National Cancer Institute [NCI], 2016).

Epidemiology of Breast Cancer

Breast cancer represents 14% of new cancers in the United States. According to lifetime risk estimates for the general population, 12.3% of women will develop breast cancer during their lives (1 in 8 women), and 2.74% will die of it. Approximately 89% of diagnosed women survive 5 years (Moyer, 2014; NCI, n.d.c). Asians, especially individuals of Japanese and Chinese descent, have the best survival rates (American Cancer Society [ACS], 2016a).

Breast cancer is most commonly diagnosed in women ages 55 to 64 years; 95% of new cases occur in women older than 40 years; 97% of breast cancer deaths occur in women older...
than 40 years (DynaMed, 2016). Breast cancer incidence rates are higher in non-Hispanic White women than Black women for most age groups. Black women have a higher incidence rate before age 40 years and have a higher breast cancer mortality rate than women of any other racial or ethnic group in the United States at every age. The gap in mortality between Black and White women is wider now than it was in the early 1990s (ACS, 2015).

Etiology of Breast Cancer

A multitude of dietary, socioeconomic, and environmental factors may serve as causative or contributing influences in the development of breast cancer. It is now widely accepted that breast cancer is not caused by a single disease. Instead, malignancies of the breast are caused by many types of disease, all with distinct histologic, biologic, and immunologic characteristics. By their very nature, these diverse causations are difficult to isolate and study in human populations; thus interconnection is difficult to ascertain (Hunt, Robertson, & Bland, 2014).

A well-known theory interconnected to the cause of breast cancer is the shedding of cancer cells into cellular spaces. As the size of a primary breast cancer increases, some cancer cells are shed into cellular spaces and transported via the lymphatic network of the breast to regional lymph nodes, especially the axillary lymph nodes (Hunt et al., 2014). If cancer cells have spread to the lymph nodes, there is a higher chance that the cells have spread or metastasized to other sites. The more lymph nodes with breast cancer cells, the more likely it is that the cancer has spread to other organs. However, not all women with cancer cells in their lymph nodes develop metastases, and some women have no cancer cells in their lymph nodes and later develop metastases (ACS, 2015). The causes of most acquired factors that could lead to breast cancer are still unknown.

ANATOMY AND PATHOPHYSIOLOGY OF BREAST CANCER

Anatomy

The breast is made up of lobules (glands that produce milk), ducts (tiny tubes that carry milk to the nipple), and stroma (connective and fatty tissue that surrounds the lobules and ducts, including blood and lymph vessels). Most of the lymph vessels in the breast lead to lymph nodes under the arm (axillary nodes; Hunt et al., 2014). These nodes act to filter out particulate matter, especially bacteria and cancer cells, from entering the bloodstream. However, they may become the avenue through which cancer spreads to other parts of the body.

Pathophysiology

The lining of the ducts and lobules of a normal breast have two layers of cells. When an abnormal number of these cells are present, the organization is affected; when noncancerous, this altered pattern of cells is called hyperplasia. Hyperplasia is categorized as usual when the pattern of cell alignment still closely resembles that in a normal breast duct or lobule. More abnormal patterns of growth are referred to as atypical hyperplasia (ACS, 2015). Hyperplasia is further categorized as either ductal or lobular (ACS, 2015). Breast cancer normally arises in the epithelial cells that line the ducts and lobes of the breast, which undergo constant turnover. These cells are generated continuously by a basal membrane and normally divide, migrate, and differentiate in a tightly controlled process.

Clinical pathology is established when internal (genetic alterations) or external (e.g., environmental and hormonal) factors interfere and the cells undergo an abnormal spectrum of changes, from hyperplasia to preinvasive to invasive and metastatic cancer. More than 80%
of breast cancers show productive fibrosis that involves the epithelial and stromal tissues of the breast (ACS, 2015). Normal breast cells become pathologic because of changes (mutations) in DNA. Certain changes (mutations) in DNA that “turn on” oncogenes or “turn off” tumor suppressor genes can cause normal breast cells to become cancerous (ACS, 2015). Genes that speed up cell division and help cells grow are called oncogenes. When a proto-oncogene mutates, it can become permanently turned on or activated when it is not supposed to be, causing the cell to grow out of control (ACS, 2015).

Tumor suppressor genes are normal genes that slow down cell division, repair DNA mistakes, or keep the cell from dividing too quickly. When tumor suppressor genes do not work properly, cell division can grow out of control, which can lead to cancer. The HER2 gene makes HER2 proteins, which are receptors in the breast cells. Normally they help control how a breast cell grows. In 15% of invasive breast cancers, the HER2 gene does not work correctly and either makes too many copies of itself, known as HER2 gene amplification, or has an increased number of copies. This makes breast cancer cells grow and divide in an uncontrolled way.

Some DNA mutations are inherited. Inherited DNA mutations can dramatically increase the risk for developing certain cancers and are responsible for many of the cancers that run in families. For example, the BRCA genes (BRCA1 and BRCA2) are tumor suppressor genes. Under normal circumstances, these genes help to prevent cancer by making proteins that prevent cells from growing abnormally. A change in one of these genes can be inherited from a parent. When one of these genes changes, it no longer suppresses abnormal growth, and cancer is more likely to develop (ACS, 2015). However, most DNA mutations related to breast cancer occur in breast cells during a woman’s life rather than being inherited. These acquired mutations of oncogenes and/or tumor suppressor genes may result from other factors, like radiation or cancer-causing chemicals. Most breast cancers have several acquired gene mutations (ACS, 2015).

**RISK FACTORS AND DIAGNOSIS**

Risk factors for breast cancer are associated with demographics, lifestyle, medical history, reproductive and hormone exposure, and genetics. During diagnosis of a breast mass, a woman’s risk for breast cancer must be assessed. The National Cancer Institute has developed a Breast Cancer Risk Assessment Tool (available at www.cancer.gov/bcrisktool) that is based on the Gail model and estimates the 5-year risk of developing invasive breast cancer. Characteristics are entered into a risk calculator. Women with a 5-year risk of 1.67 or greater are considered high risk and are candidates for tamoxifen, which has been shown to reduce the risk of invasive and noninvasive cancer by approximately 50% (Stuckey & Onstead, 2015). Despite availability, genetic testing for hereditary breast and ovarian cancer syndrome (HBOCS) is underutilized. “In the United States, there are an estimated 220,000 BRCA mutation carriers and fewer than 10% have been identified” (Stuckey & Onstead, 2015, p. 4). According to Smith (2012), evaluation of a woman’s risk for HBOCS should be a routine part of every woman’s healthcare visit.

Of the anticipated 235,030 new cases of breast cancer that are diagnosed annually, approximately 10% are likely to be hereditary (ACS, 2015). The carrier frequency of HBOCS is approximately 1 in 500 individuals in the general population, but it has a prevalence of 1 in 40 individuals in the Ashkenazi Jewish population. Women with HBOCS have a 65%
to 74% lifetime risk of breast cancer (American College of Obstetricians and Gynecologists [ACOG], 2015).

**BRCA1 and BRCA2 Genes**

Although most cases of breast cancer and ovarian cancer in the United States occur sporadically, **BRCA1** and **BRCA2** mutations are present in 5% to 15% of all breast cancer cases. **BRCA1** and **BRCA2** genes are the most common inherited breast cancer mutations. Individuals who have inherited a mutated copy of either gene from a parent have an 80% chance of developing breast cancer during their lifetimes and thus are five times more likely than the general population to develop the disease. When breast cancer occurs, it is often at a younger age than in women who are not born with one of the gene mutations. Although **BRCA** mutations are most common in Jewish women of Ashkenazi (Eastern Europe) origin, they are also more common in Black women and Hispanic women, though they can occur in any racial or ethnic group (ACOG, 2015).

**BRCA** testing does not identify whether a patient has cancer but detects mutations in the **BRCA1** and **BRCA2** genes. Counseling and subsequent testing for the gene allows the patient to obtain important information that can assist with decisions about risk-reduction measures (Ko, Files, & Pruthi, 2012). **BRCA** testing is offered when a female patient has 1) either a strong family history or early onset of disease; 2) the test can be adequately interpreted; and 3) the results will affect medical management. Once the patient is identified as having increased risk for mutations in the **BRCA** genes, genetic counseling is provided by trained healthcare providers (HCPs). Genetic testing then follows for selected high-risk patients when indicated. Pretest and posttest genetic counseling are provided by an HCP experienced in cancer genetics and risk assessment (Smith, 2012). Conducting a comprehensive assessment of family history and obtaining informed consent for the right set of genetic tests takes expertise and time. When the primary care team is not comfortable or skilled with this level of detail, a genetic counseling referral allows for comprehensive care of the patient (Lynch, Venne, & Berse, 2015).

**Genetic Assessment**

Consideration of screening for potentially harmful **BRCA** mutations should begin once women have reached the age of consent (18 years). Primary HCPs should periodically assess all patients for changes in family history at least every 5 to 10 years (Moyer, 2014). During the encounter, primary HCPs should begin by conducting a cursory family history. This can help determine which patients should be referred for a genetic consultation before definitive genetic testing. Personal cancer history and a first- and second-degree relative cancer history should be elicited. If a positive history exists, the record should include a description of the type of primary cancer; the gender, age of onset, and lineage (paternal versus maternal) of the family member; and any relatives with multiple types of primary cancer (ACOG, 2015; Moyer, 2014).

After the brief screening, women who have at least one family member with breast, ovarian, or other types of **BRCA**-related cancer should be given one of several brief familial risk stratification tools to determine the need for in-depth genetic counseling. The Family History Screen-7 and the Breast Cancer Genetics Referral Screening Tool (B-RST) are validated and clinically useful for selecting patients who should be offered genetic counseling to further determine their candidacy for possible **BRCA** mutation testing (Moyer, 2014). While taking a woman’s history, the HCP should be alert for both personal and family factors that may indicate possible HBOCS (see Table 2-1). Women with positive
screening results should receive genetic counseling and, if indicated after counseling, BRCA testing. Adequate evidence suggests that the benefits of testing for potentially harmful BRCA mutations are moderate. This recommendation applies to asymptomatic women who have not been diagnosed with BRCA-related cancer (Moyer, 2014).

Women with at least one first-degree relative diagnosed with breast cancer before the age of 50 years are categorized as high risk (Ko et al., 2012). For a woman with a high familial risk but no personal history of cancer who desires BRCA testing, a close relative with a history breast cancer should be sought for testing to determine whether a familial BRCA gene mutation exists. If the family member does not have a BRCA mutation, other genes are likely the cause of the family pattern of breast cancer, and the patient will thus be considered high risk and receive screening and management on this basis. However, if the BRCA mutation is found in the relative but the patient has a negative result, the patient has only an average risk for breast cancer and continues following the typical screening recommendations. If testing of a family member with breast cancer is not possible, a negative test does not determine the true breast cancer risk for patients with a family history, and thus they should be managed as high risk (Research Committee of the American Society of Breast Surgeons, 2012).

Patients with breast cancer who are at significant risk for having a BRCA mutation may undergo testing before definitive surgery. The patient may await BRCA test results before surgical treatment or elect to proceed with lumpectomy, TABLE 2-1: RISK INDICATORS OF HEREDITARY BREAST AND OVARIAN CANCER SYNDROME FROM A BRCA1 OR BRCA2 MUTATION

<table>
<thead>
<tr>
<th>Personal history</th>
<th>Family history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast and/or ovarian cancer</td>
<td>Ashkenazi Jewish ethnicity</td>
</tr>
<tr>
<td>Breast cancer at age 50 years or younger</td>
<td>Close relatives with breast, ovarian, or pancreatic cancer</td>
</tr>
<tr>
<td>Two primary breast cancers (bilateral or ipsilateral)</td>
<td>Two or more family members with breast cancer</td>
</tr>
<tr>
<td>Triple-negative breast cancer (estrogen receptor negative, progesterone receptor negative, HER2/neu negative)</td>
<td>Close relative positive for BRCA1 or BRCA2</td>
</tr>
<tr>
<td>Breast cancer with Ashkenazi Jewish ancestry</td>
<td>More than one family member with two primary types of BRCA-related cancer</td>
</tr>
<tr>
<td>Breast cancer with a known mutation for a BRCA-susceptibility gene within the family</td>
<td>Male breast cancer</td>
</tr>
</tbody>
</table>


or unilateral mastectomy before results are available. Other patients may elect to defer testing until sometime in the future (Research Committee of the American Society of Breast Surgeons, 2012).

Women who have no first-degree relative with breast cancer— or who have a relative who was diagnosed with breast cancer after age 50 years—are at low risk. For women whose family history is not associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes, there is adequate evidence that the benefits of testing for potentially harmful *BRCA* mutations are few to none. The U.S. Preventative Services Task Force (USPSTF) recommends against routine genetic counseling or *BRCA* testing for women whose family history is not associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes (Moyer, 2014).

**Hereditary Breast and Ovarian Cancer Syndrome**

Once a patient is identified as having an increased risk of breast cancer because of a *BRCA* mutation, she can be counseled about guidelines for prevention and early diagnosis, including screening and options for risk reduction. These measures may include early surveillance; enhanced screening with breast mammography, ultrasound, or MRI; medication; or surgery. Women at high risk should undergo increased surveillance consisting of a clinical breast examination every 6 to 12 months beginning at the age of 25 years and imaging with annual MRI between the ages of 25 and 29 years and an alternating mammogram and MRI every 6 months for women 30 years of age and older (Stuckey & Onstead, 2015).

There are several surgical options for risk reduction and prevention of breast cancer. These options consist of prophylactic bilateral mastectomy with reconstruction, prophylactic bilateral salpingo-oophorectomy, and possible chemoprevention.

Prophylactic bilateral mastectomy has been shown to decrease the incidence of breast cancer by as much as 90% or more in patients at risk of hereditary breast cancer and in *BRCA1* and *BRCA2* carriers (Moyer, 2014). Women should be offered the preventive option of bilateral salpingo-oophorectomy after completion of childbearing, preferably before the age of 40 years. This procedure is associated with a 50% to 60% reduction in breast cancer risk and an 80% reduction in ovarian and fallopian tube or primary peritoneal cancers for women who carry *BRCA* mutations (ACOG, 2008; Research Committee of the American Society of Breast Surgeons, 2012). (See the section Chemoprevention for further information on the applicability to women with *BRCA* mutations.)

**Diagnosis of Breast Cancer**

In 30% of new cases of breast cancer, the woman discovers a lump in her breast. The most common sign of breast cancer is a painless, hard lump with irregular edges. Breast pain usually is associated with benign disease. Other less common presenting signs and symptoms of breast cancer include (1) breast enlargement or asymmetry; (2) nipple changes (retraction, erosion, inversion, or tenderness); (3) spontaneous discharge (especially if bloody); (4) ulceration, thickening, or erythema of the skin of the breast; (5) an axillary mass; and (6) musculoskeletal discomfort, breast pain, or heaviness. However, up to 50% of women presenting with breast complaints have no physical signs of breast pathology (DynaMed, 2016).

During clinical evaluation, diagnostic studies are directed toward the identification of breast cancer. A thorough, organized approach to the evaluation of a female patient with suspected breast cancer is necessary. The diagnostic process for breast cancer is based on a triple assessment method. The assessment considers
clinical, mammographic, and tissue sampling. Assessment findings may include

1. palpable breast mass, palpable lymph nodes, and skin and/or nipple changes on the clinical examination;

2. microcalcifications, spiculated opacities, non-palpable lesions in the ipsilateral or contralateral breast, solid masses that correlate with physical examination findings, adenopathy, or architectural distortion on mammography; and

3. histologic evidence of preinvasive or invasive cancer on tissue sampling cytology via core needle biopsy and/or fine needle aspiration or excisional biopsy.

(DynaMed, 2016)

The clinical, radiographic, and pathologic findings should be in concordance. If the biopsy findings do not concur with the clinical and radiographic findings, the multidisciplinary team (including clinician, radiologist, and pathologist) should review the findings and decide whether to recommend an image-guided or open biopsy to be certain that the target lesion has been adequately sampled for diagnosis (Hunt et al., 2014).

When possible, surgery should be delayed a few weeks after the outpatient biopsy results are received to allow the patient the chance to process the diagnosis, research treatment options, and obtain a second opinion if desired. In most cases waiting this short time for the operation poses no risk (Hunt et al., 2014). The diagnostic process also consists of determining clinical stage, evaluating histology, and determining molecular biomarkers.

Staging

Staging is a process of determining how far advanced the cancer process is to guide treatment decisions. Factors such as invasiveness, tumor size, spread to lymph nodes, and metastasis are considered in determining cancer stage on a scale of 1 to 4 (4 is the most advanced). Many breast cancers are now identified by stage 1 or 2. Stage 0 is defined as in situ cancer; in breast cancer this is typically ductal carcinoma in situ (DCIS). The most commonly used system is the American Joint Committee on Cancer (AJCC) TNM System for breast cancer. These stages include two classes: carcinoma in situ (noninvasive carcinoma, stage 0) if cancer cells are contained within a duct (DCIS) or lobule (lobular carcinoma in situ [LCIS]) and invasive breast cancer (infiltrating breast cancer, stages 1 to 4) if cancer cells spread beyond the basement membrane of the duct or lobule to adjacent breast parenchyma (DynaMed, 2016). The nationally accepted breast cancer staging guidelines are available through the AJCC.

Tumor Grade

Tumor grade is also determined during the pathologic examination of the breast tissue. The grade is based on how normal or abnormal the cells appear when examined microscopically. The lower the grade, the better the prognosis:

- Grade 1: Low-grade or well differentiated
- Grade 2: Intermediate-grade or moderately differentiated
- Grade 3: High-grade or poorly differentiated (NCI, n.d.d)

Molecular Markers

Molecular marker testing typically involves examination of preserved tissue specimens (usually formalin fixed or paraffin embedded) obtained during core needle biopsy or surgery. Tumor testing can determine whether treatment that involves hormonal or antibody therapy against specific receptors would be a beneficial adjunct to or alternative to traditional treatment options, such as chemotherapy. Three major
biomarkers are assessed – estrogen receptors (ERs), progesterone receptors (PRs), and human epidermal growth factor receptor type 2 (HER2) – in conjunction with other clinical findings (tumor grade, stage, lymph node involvement). These three markers have well-documented prognostic value as well as predictive value for specific treatments (Bearce & Lynch, 2015), and thus the results of biomarker testing guides treatment decisions and determines whether additional testing is indicated.

**Estrogen and Progesterone Receptors**

Normal breast tissue contains hormone receptors that respond to the stimulatory effects of estrogen and progesterone. Most breast cancers retain ERs, and for these tumors, estrogen retains proliferative control over the malignant cells. Thus an important component in the evaluation of a woman with early breast cancer is to test for the presence of hormone receptors (Bearce & Lynch, 2015). The ERs and PRs are proteins present in the cell cytoplasm and on the surface of some of the breast cancer cells. When the receptors are present, they bind to estrogen or progesterone, and the binding promotes growth of the cancer cells. A malignant tumor in the breast can have ERs or PRs or both. Knowing the patient’s hormone receptor status provides valuable information concerning her predicted response to hormone manipulation therapy. Tumors that lack hormone receptors will not respond to hormonal therapy (Bearce & Lynch, 2015). Postmenopausal women tend to be ER-positive; premenopausal women tend to be ER-negative. The majority (73%) of all breast cancers are ER-positive, of which more than 70% are also PR-positive. Hormone receptor status is an important indicator of cancer behavior; tumors positive for ERs and PRs have a better prognosis than those with negative receptors (Downes-Holmes & Silverman, 2012).

**Human Epidermal Growth Factor Receptor Type 2**

In 15% of invasive breast cancers, the HER2 gene doesn’t work correctly and either makes too many copies of itself, known as HER2 gene amplification, or is increased in amount. Breast cancer gene amplification is HER2-positive. These cancers are more high risk because they tend to grow faster and are more likely to spread. The Oncor INFORM HER-2/neu gene system is used to detect the HER-2/neu gene in human breast tissue. The test can be used to predict breast cancer recurrence as well as to determine the types of treatments that would be most effective. Drugs that block the HER2 gene to stop the growth of cells are called HER2-targeted therapies (Bearce & Lynch, 2015).

The pathology of “triple-negative phenotype” breast cancer (ER-negative, PR-negative, and HER2/neu-negative) has been strongly associated with BRCA1 mutations. When these three receptors are negative, the breast cancer is more aggressive and more likely to recur (Bearce & Lynch, 2015).

**Lymph Node Evaluation and Excision**

In addition to performing breast surgery, surgeons examine the lymph nodes for cancer cells using either an axillary lymph node dissection or sentinel lymph node biopsy to determine whether the disease has spread beyond the breast (see Figure 2-1). Lymph node assessment is performed for two reasons: (1) to determine whether the cancer has spread beyond the breast and (2) to remove any cancerous nodes. Oncologists use this information in staging the tumor and as a basis for planning optimal treatment (NCI, n.d.d). Axillary staging is generally not included in the management of DCIS (Hoffman et al., 2016).

Formerly a part of all breast cancer surgeries, axillary dissection has been replaced
in many cases by sentinel lymph node biopsy (SLNB), in which selected lymph nodes are removed and tested before any others are excised. SLNB is the preferred method of testing because it reduces the need for full axillary lymph node dissections among most women with no evidence of sentinel lymph node involvement (ACS, 2015). SLNB is most appropriate for women with early-stage breast cancer with clinically negative axillary nodes, because it results in less lymphedema postoperatively. The procedure is usually done at the same time as either lumpectomy or mastectomy. Approximately 1 hour before the tumor is removed, a radioactive substance is injected into the surrounding area. For the operation, radioactive dye is injected around the tumor and then tracked to the sentinel node or nodes (up to three) for removal through an incision in the axillary region. These sentinel nodes are the location where cancer cells from a breast tumor would reach first. The excised nodes are sent to the pathology laboratory for examination while the patient is still in surgery. If no cancer cells are found in the sentinel nodes, no further nodes are removed—only the tumor itself. If cancer

Sentinel lymph node biopsy of the breast. A radioactive substance and/or blue dye is injected near the tumor (left). The injected material is detected visually and/or with a probe that detects radioactivity (middle). The sentinel nodes (the first lymph nodes to take up the material) are removed and checked for cancer cells (right).

Note. From Winslow, Terese, Figure of Sentinel Lymph Node Biopsy (3-Panel Breast) as appeared in NIH Visuals Online. Copyright © 2010 by Terese Winslow LLC. U.S. Govt. has certain rights. Reproduced with permission of Terese Winslow LLC.
cells are found, however, the remaining nodes are removed and analyzed using standard axillary dissection technique (DynaMed, 2016).

If abnormal axillary nodes are found or the axillary nodes are found to be positive for cancer cells with the SLNB, axillary lymph node dissection (ALND) is performed (NCI, n.d.c). ALND involves removal of a large number of axillary lymph nodes for examination by a pathologist. Breast cancer patients who undergo axillary lymph node dissection are about three times more likely to develop lymphedema compared with those who have SLNB (DynaMed, 2016).

**Indicators Associated With Disease Prognosis**

Many variables are associated with the likelihood of breast cancer recurrence. Identifying these factors is helpful in determining the best course of treatment for each woman. Axillary lymph node involvement is predictive of prognosis and is one of the best indicators for overall survival. Women with four or more positive nodes experience up to a 71% treatment failure rate at 10 years. Involvement of any regional nodes at diagnosis is predictive of worse prognosis and higher treatment failure rates (DynaMed, 2016). Apart from the stage, the primary tumor characteristics that most influence prognosis are hormone receptor status and HER-2/neu expression. Two thirds of breast cancers are ER- and PR-positive, which is associated with more treatment options and better prognosis (Hoffman et al., 2016).

**Types of Breast Cancer**

Many different kinds of breast cancer can arise in the various tissue types of the breast. Carcinoma of the breast is not a single disease but a group of different types of cancer that originate either in the ducts or the lobules of the breast. Each type has different effects on individual patients depending on age, general health, access to health care, comorbidities, and stage of the cancer at diagnosis (Hoffman et al., 2016).

Most breast cancers represent a type of adenocarcinoma, a cancer of the glandular tissue. There are two basic categories. If the cancerous cells are confined to the ducts or the lobules, the cancer is called noninvasive or in situ. Breast cancer that has spread through the walls of the ducts or lobules into the surrounding fatty and connective tissue is referred to as invasive or infiltrating (DynaMed, 2016). Each type can occur in either the ducts or the lobules of the breast and has the potential to eventually break through the cell wall and invade the surrounding tissues. Once invasion occurs, the cancer may metastasize to distant organs, becoming a potentially fatal malignancy (ACS, 2015). It is beyond the scope of this course to discuss all of the breast cancer types in detail.

**Noninvasive Breast Cancer:**

**Lobular Carcinoma In Situ and Ductal Carcinoma In Situ**

Of the 1 million benign breast biopsies, 10% are labeled atypical hyperplasia. These are examined microscopically and labeled either ductal or lobular. When these types of atypia are found after core needle biopsy, surgical excision of the site is recommended (Hoffman et al., 2016).

LCIS is not detectable by imaging studies or palpation. It is only diagnosed by biopsy. LCIS is considered an indicator of increased risk of breast cancer but not a precursor, because the incidence of eventual breast cancer development is approximately equal in both the side where LCIS was found and the other breast. In fact, LCIS is associated with an increased risk of subsequent invasive breast cancer in either breast. The risk of breast cancer for women with LCIS is approxi-
mately 1% per year; this increases in individuals who are diagnosed at an early age, have a significant degree of LCIS, or have a family history of breast cancer. Invasive breast cancer develops in 25% to 35% of women (Hoffman et al., 2016).

DCIS is a noninvasive cancer of the milk ducts that has not spread through the walls of the ducts into the fatty tissue or lymph nodes. This type of cancer can rarely be detected by clinical examination. Instead, it is usually identified by a finding of microcalcifications on mammography. In DCIS, cancerous cells are present in the ducts but do not spread into the tissues’ basement membranes, because the cellular mutations are not sufficient to allow extensive invasion outside the ducts. Thus DCIS is considered stage 0 breast cancer. The risk for invasive breast cancer is increased nearly five-fold for women with DCIS (Hunt et al., 2014).

Invasive Breast Cancer: Invasive or Infiltrating Ductal Carcinoma

Invasive or infiltrating lobular carcinoma (ILC) and invasive or infiltrating ductal carcinoma (IDC) are the two most common types of invasive breast cancers. ILC arises in the lobules, spreads into the fatty tissue, and can metastasize. ILC accounts for 10% of all breast cancers. Women with ILC are more likely than those with other cancers to have bilateral disease. This cancer type is difficult to detect by examination or mammography; breast MRI is often helpful in the diagnosis of ILC (Hunt et al., 2014).

IDC breaks through the duct wall and invades the surrounding fatty tissue, where it can also metastasize to other parts of the body by way of the lymphatic or circulatory systems (see Figure 2-2). IDC is the most common breast malignancy; 85% to 90% of invasive carcinomas originate in the milk ducts. Women with this type of tumor usually present with a discrete, solid breast mass (Hunt et al., 2014).

Invasive breast cancers can be of no special type (NST) or special type. Of the two, NST cancers typically have a worse prognosis. Approximately 80% of invasive breast cancers are NST IDC. Macroscopic or microscopic axillary lymph node metastases are found in up to 25% of women whose cancer is detected by routine screening and in up to 60% of women who present with symptoms. The tumor is a solitary, firm mass. NST IDC is more common in perimenopausal or postmenopausal women (Hunt et al., 2014). Approximately 95% of the women who die of breast cancer have distant metastases. Common sites of involvement, in order of frequency, are bone, lung, pleura, soft tissues, and liver (Hunt et al., 2014).

Atypical Cancers

Inflammatory Breast Cancer

Only 1% to 6% of all breast cancers are of the inflammatory type. Inflammatory breast cancer involves at least one third of the breast and is associated with diffuse skin and breast erythema. The skin appears thickened and edematous and resembles an orange peel (peau d’orange), and the underlying tissue is thickened, without a palpable mass. IBC is usually aggressive and metastasizes rapidly. It often makes the skin over the breast appear inflamed, red, and warm with peau d’orange characteristics. This type is associated with a poor prognosis (DynaMed, 2016).

Paget Disease

Paget disease can be associated with noninvasive disease (usually DCIS) or with invasive disease. This type of DCIS presents as a focal eczematous rash of the nipple with an exudate or crust on the nipple and areola caused by infiltration of the epidermis by noninvasive breast cancer epithelial cells (DynaMed, 2016). Dermal cells secrete chemoattractants that draw ductal carcinoma cells to the surface.
The characteristic skin breakdown of the nipple is indicative of a need for histologic examination of the area. Mammography reveals dense or calcified tissue in 21% of patients without a palpable tumor. An underlying DCIS is identified in about two thirds of cases (Hunt et al., 2014).

**Triple-Negative Breast Cancer**

Women whose tumors are found to be ER-negative, PR-negative, and **HER2/neu**-negative through molecular testing are said to have triple-negative breast cancer (TNBC), an aggressive form of breast cancer. TNBC is rare, but the incidence is higher in young women and in Black and Hispanic populations. Most **BRCA1**-mutation breast cancers are triple negative. A characteristic pattern of metastasis guides diagnosis. TNBC is treated with a combination of surgery, radiation, and chemotherapy; hormone and targeted therapy are ineffective (DynaMed, 2016).

**BREAST CANCER TREATMENT**

As technology becomes ever more sophisticated at detecting cancer cells, the view of breast cancer as a systemic disease gains more support. Thus the treatment of breast cancer today generally includes some combination of localized (surgery and radiation therapy) and systemic treatments (chemotherapy, hormonal therapy, targeted biologic therapies, or immunotherapy). It is beyond the scope of this course to discuss in detail the treatment options for each stage of breast cancer. Surgery followed by radiation, chemotherapy, or hormone therapy, depending on the stage of the cancer and its characteristics, is advised.
A woman who is diagnosed with breast cancer and is a carrier of a \textit{BRCA1} or \textit{BRCA2} mutation has an increased risk of developing a second breast cancer in the contralateral (opposite) breast. This often becomes important in decision making surrounding breast cancer management. Women who are younger at the age of diagnosis have been found to carry a higher risk of contralateral malignancy than women who are diagnosed with their first breast cancer at an older age (Stuckey & Onstead, 2015).

\textbf{Surgery}

Surgery is a cornerstone of treatment for breast cancer. Surgery remains the first treatment for tumors with a size that favors a good cosmetic outcome and without lymph node involvement. Women with breast cancer may have a lumpectomy or mastectomy (Hunt et al., 2014). Much progress has been made in the treatment of breast cancer since the days of radical mastectomy, which was the standard of care for many years. Currently, breast-conserving surgical procedures (which involve removal of the malignant tissue and a clear margin of normal tissue surrounding it) are commonly performed. This is also known as a lumpectomy. Surgery may also involve removal of lymph nodes, with a goal of preserving as much of the breast as possible.

Whether surgery precedes or follows systemic therapy, however, depends on a number of factors, including the stage of the cancer, the age of the patient, and the recommendations of the treatment team. The primary goals of breast cancer surgery are to remove the cancer from the breast and to determine the stage of disease.

In a lumpectomy, only cancerous tissue plus a rim of normal tissue are removed. This type of surgery allows as much of the breast tissue as possible to remain. Because tumors are now detected at an earlier stage and often are smaller in size, lumpectomy is a common procedure. However, a lumpectomy is not recommended if there is extensive tumor involvement, an inflammatory presentation, or multifocal disease (when there is more than one tumor that appear to have arisen from one original tumor; (Hoffman et al., 2016).

Mastectomy offers no survival advantage over lumpectomy followed by radiation therapy. A mastectomy may be performed when a lumpectomy is not possible or based on woman’s preference. There are three types of mastectomy: simple, modified radical, and radical.

1. Simple mastectomy: Removal of the breast tissue, skin, areola, and nipple, but not the lymph nodes. This procedure is generally used when axillary lymph nodes do not need to be removed, as evidenced by a negative sentinel node examination.

2. Modified radical mastectomy: Removal of the entire breast and lymph nodes under the arm; does not include removal of the underlying chest wall muscle, as with a radical mastectomy.

3. Radical mastectomy: Removal of the entire affected breast, the underlying chest muscles, the lymph nodes under the arm (axillary node dissection), and some additional fat and skin. Radical mastectomies are rarely used today, because in most cases removal of the underlying chest muscles is not needed to remove all of the cancer. This type of mastectomy is generally limited to cases in which the cancer has spread to the chest wall muscles (NCI, n.d.a).

\textbf{Adjuvant Therapy}

Adjuvant therapy for breast cancer is any treatment given after primary therapy to increase the chance of long-term disease-free survival. Adjuvant treatment of breast cancer is designed to treat micrometastatic disease (i.e.,
breast cancer cells that have escaped the breast and regional lymph nodes but which have not yet had an established identifiable metastasis). Adjuvant therapy for breast cancer can include radiation therapy, systemic treatment (chemotherapy, hormonal therapy, targeted drugs), or a combination of these treatments. The major benefit of biomarker-driven targeted therapy is the ability to customize treatment to the specific cancer subtype, provide treatment that is matched to the patient’s tumor, and potentially avoid treatment that may not be as effective (Bearce & Lynch, 2015).

**Radiation Therapy**

Radiation may be used after potentially curative surgery to destroy cancer cells remaining in the breast, chest wall, or underarm area. Breast cancer surgery is almost always followed by radiation therapy, because it has been shown to reduce the risk of cancer recurrence by about 50% and the risk of breast cancer death by about 20%. Radiation therapy may be administered internally or externally. Some patients are treated with both types of radiation in combination. The way the radiation therapy is given depends on the type, stage, and location of the tumor, as well as doctor and patient preference. Radiation therapy is typically given after surgical and chemotherapy regimens have been completed, but before initiating hormonal therapy. Standard whole breast radiation therapy consists of treatment 5 days per week for 5 weeks followed by a 1-week boost to the lumpectomy site (Downes-Holmes & Silverman, 2012).

**Systemic Treatment**

The goal of systemic treatment is to destroy any cancer cells that have moved beyond the breast to other areas of the body and to achieve long-term remission of the cancer. Medical scientists previously believed that a tumor had to reach a certain size before cancer cells moved into the bloodstream and traveled to other parts of the body. However, research has shown that cancer cells can migrate out of the breast very early in the development of a tumor. This is why systemic therapies are recommended for premenopausal women with breast cancer even if there is no evidence of cancer in the lymph nodes (ACS, n.d.).

Systemic therapy includes chemotherapy, hormone therapy, and targeted therapy, each of which works through different mechanisms. When systemic treatment is given to patients before surgery, it is called neoadjuvant therapy. It is often used to shrink the tumor enough to make surgical removal possible or allow for less extensive surgery (such as breast cancer surgery in women who would otherwise have required mastectomy). Systemic treatment given to patients after surgery is called adjuvant therapy. It is used to kill any undetected tumor cells that were left behind during surgery or had migrated to other parts of the body. The use of adjuvant systemic therapy is primarily determined by the tumor stage and histopathologic characteristics (hormone receptor and HER2 status; ACS, n.d.).

**Chemotherapy**

Chemotherapy for IBC reduces the chance of systemic recurrence and may be given as neoadjuvant (first-step) or adjuvant (postoperative) treatment. The benefit of chemotherapy is dependent on multiple factors, including the size of the cancer, the number of lymph nodes involved, the presence of ERs or PRs, and the amount of HER2 protein made by the cancer cells. Depending on the combination of drugs (such as taxanes and anthracyclines) used, chemotherapy is usually given for 3 to 6 months (ACS, n.d.).

**Hormonal and Endocrine Therapy**

Estrogen promotes the growth of many breast cancers, increasing the risk of recurrence or metastasis for these patients. In the
past oophorectomy was performed to eliminate estrogen production; this is still an option for metastatic ER-positive cancers, but the preferred therapy for ER- or PR-positive disease includes a drug regimen that blocks estrogen production or the effects of estrogen on the cancer cells. There are two classes of hormonal agents for breast cancer therapy. Selective estrogen receptor modulators (or SERMs) act against (or block) estrogen in some tissues of the body (such as breast cells) but act like estrogen in others. Tamoxifen and toremifene are drugs that prevent estrogen from binding to breast cancer cells and are effective in both postmenopausal and premenopausal women. Treatment of ER-positive breast cancer with tamoxifen for 5 years has been shown to reduce the rate of recurrence by 39% throughout the first decade and reduces breast cancer mortality by about one third throughout the first 15 years. The most common side effects are hot flashes, vaginal dryness, sexual dysfunction, depression, and mood swings. Although rare, tamoxifen can cause cataracts, fractures, blood clots in the lungs or legs, stroke, or endometrial (uterine) cancer (ACS, n.d.; DynaMed, 2016).

The second class of drugs are aromatase inhibitors (AIs), such as letrozole, anastrozole, and exemestane. They are used to treat both early and advanced hormone-receptor-positive breast cancer in postmenopausal women. AIs inhibit (block) the conversion of androgens to estrogens, thereby limiting the amount of estrogen that can reach cancer cells. This can lead to regression or stabilization of a tumor. However, AIs also act on other estrogen-sensitive tissues, which may account for some of the drugs’ side effects, such as muscle and joint pain and bone loss, which can increase fractures of the hip, spine, or wrist. AIs are not usually an effective treatment in women with functioning ovaries (including premenopausal women). AIs should be included in the treatment of postmenopausal women with hormone-receptor-positive breast cancer (DynaMed, 2016).

Two other drugs that act on hormone secretion may also be used. If SERMs are not effective or the disease progresses, fulvestrant (an antiestrogen drug given by injection once a month) can be used to block estrogen binding and reduce the number of estrogen receptors on breast tumors. For premenopausal women, potentially reversible ovarian ablation (medical castration) is achieved with a class of drugs called luteinizing hormone-releasing hormone (LHRH) analogs (e.g., goserelin or leuprolide). These drugs inhibit all ovarian function. Studies have shown that the addition of these drugs to tamoxifen and/or chemotherapy reduces the risk of breast cancer recurrence and death among premenopausal women with early stage, hormone-sensitive breast cancer (DynaMed, 2016).

Targeted Therapy

Approximately 15% to 20% of breast cancers overproduce the growth-promoting protein HER2. These tumors tend to grow faster and are generally more likely to recur than tumors that do not overproduce HER2. Trastuzumab is a monoclonal antibody that directly targets the HER2 protein and is approved for all HER2-positive breast cancers (DynaMed, 2016).

Complementary Therapies

Complementary and alternative therapies are generally defined as any medical system, practice, or product that is not part of conventional medical care. Integrative medicine is the use of evidence-based complementary practices in coordination with evidence-based conventional care. Integrative oncology refers to the use of complementary and integrative therapies in collaboration with conventional oncology care (Greenlee et al., 2014; Witt & Cardoso, 2016). Integrative therapies are commonly used
by breast cancer survivors for many indications, including managing the side effects of cancer therapy and improving quality of life. Women with breast cancer are among the highest users of such therapies and usage has been increasing. An estimated 48% to 80% of North American breast cancer survivors use complementary and integrative therapies following diagnosis (Greenlee et al., 2014).

There is strong evidence (grade A) on the use of behavioral therapies (e.g., meditation, mindfulness, and relaxation) and yoga for mood improvement in the context of depression and anxiety during cancer treatment. Meditation and hypnosis were also given a high grade for improving quality of life and physical functioning. Lower grades of recommendations (grade B) were made for acupuncture and acupressure, massage, music therapy, and stress management (Greenlee et al., 2014; United States Preventive Task Force Ratings, n.d.; Witt & Cardoso, 2016).

Clinicians and patients should adopt shared decision-making approaches when assessing the risk-benefit ratio for each therapy. It is important to initiate a discussion about the use of complementary and alternative therapies at each visit. Patients often seek information outside the medical system, which can result in a risk of interactions between herbs and anticancer therapies (Witt & Cardoso, 2016). The HCP should personalize the recommendations based on patients’ values and clinical characteristics. The integrative approaches being used alongside conventional medical care and should be fully communicated to all HCPs involved in the patient’s care. All modalities should be administered by qualified and experienced providers who have the appropriate training, licensure, and credentialing. Ongoing communication and exchange of treatment summaries among all clinicians are important (Greenlee et al., 2014).

All clinicians must obtain a complete list of the complementary therapies a patient is using to avoid possible detrimental action against conventional cancer treatments and maximize potential benefits of the integrative approaches.

**Psychosocial Aspects of Breast Cancer Treatment**

A breast cancer diagnosis and subsequent treatment can have a profound influence on a woman’s physical and psychosocial well-being, family life, career, and quality of life. Women with breast cancer experience emotional distress and mood disturbances, such as anxiety, confusion, and depression; worry about recurrence; and encounter a decreased sense of well-being (Lengacher et al., 2016). Some potential sources of distress occurring after the diagnosis of breast cancer include anticipation of suffering, taxing treatment regimens, difficulty coping with life changes, and adjusting to the inherent uncertainty and uncontrollability of the cancer. Breast cancer survivors report in the first 6 to 12 months that mood changes, feeling anxious and apprehensive, fear of recurrence, and challenges in managing everyday family life are emotionally distressful (Reich et al., 2017).

For most women, psychological distress will resolve with improvement in physical symptoms and time. In some survivors, persistent emotional distress may progress to maladaptive psychologic responses such as reactive anxiety or depression. Between 20% and 30% of women with breast cancer develop depression and anxiety in the year after diagnosis (Knobf, 2015). Breast cancer affects women almost exclusively, and because women have twice the baseline rate of depression as men, this might result in a higher rate of depression in patients with breast cancer compared with patients with other cancers. Specific treatments (antiestrogens such as tamoxifen, raloxifene, and letrozole; chemotherapy) may induce a menopausal state and may poten-
tially contribute to increased levels of depression (Mausbach, Schwab, & Irwin, 2015). Physiologic changes from the disease process itself, created by proinflammatory cytokine production, have also been correlated with depression (Fagundes, LeRoy, & Karunga, 2015).

Women with breast cancer have been found to be more at risk of developing long-term depression persisting more than 5 years after diagnosis (Maass, Roorda, Berendsen, Verhaak, & de Bock, 2015), particularly those who are older, have comorbid conditions, have node-positive disease, have a low educational level, and live alone (Suppli et al., 2014). Depression is a significant health concern for breast cancer survivors throughout the disease trajectory and can contribute to lower health-related quality of life (HRQOL; Jassim, Whitford, & Carter, 2015; Kenyon, Mayer, & Owens, 2013; Maass et al., 2015; Reyes-Gibby, Anderson, Morrow, Shete, & Hassan, 2012). Failure to identify and treat anxiety and depression increases the risk for poor quality of life and potential disease-related morbidity and mortality (Anderson et al., 2014). A critical part of care for women with breast cancer is the recognition of the presence of depression and determination of the appropriate level of intervention, ranging from brief counseling, mindfulness meditation, or support groups to medication and/or psychotherapy (Spiegel & Riba, 2014).

Up to 15% of survivors suffer symptoms of posttraumatic stress disorder (PTSD), some as many as 20 years after completion of treatment (Spiegel & Riba, 2014). PTSD is an anxiety disorder that develops in response to a traumatic event. In some persons, normal responses to trauma may develop into persistent mood changes and lead to chronic stress responses. Cancer-related PTSD is complex and may be a response to trauma associated with diagnosis, treatment, or therapy complications (Kangas, Milross, & Bryant, 2014). These symptoms can seriously impair their quality of life and well-being (Robins, Johnson, LoConte, & Brandt, 2017).

It is recommended that all patients with breast cancer be evaluated for symptoms of depression and anxiety throughout their care (initial diagnosis, start of treatment, regular intervals during treatment, end of treatment, at transition to survivorship, and upon recurrence or progression). Assessment should be performed using validated, published tools. Before screening, providers should have the appropriate resources for further evaluation and treatment available in their setting (Spiegel & Riba, 2014). A screening tool to assess for anxiety and depression in oncology patients is available: Patient Health Questionnaire (PHQ-9; National Comprehensive Cancer Network, 2016b). The initial screening consists of two items from the nine-item PHQ-9 (Kroenke, Spitzer, & Williams, 2001). Patients who report positive on the two-item questionnaire are encouraged to complete the remaining items of the PHQ-9.

In addition to the PHQ-9, a variety of other tools have been used in studies of women with breast cancer: the Hospital Anxiety and Depression Scale (HADS), the National Comprehensive Cancer Center Distress Thermometer, and the Profile of Mood States questionnaire (Agarwala & Riba, 2010).

Pharmacologic and nonpharmacologic interventions (e.g., psychotherapy, psychoeducational therapy, cognitive-behavioral therapy, and exercise) delivered by providers with expertise in these areas have been used for management of depressive or diagnosed mood disorders. Mindfulness-based stress reduction has shown to improve quality of life and decrease distress (Reich et al., 2017). The HCP should determine follow-up and compliance with individual or group psychological or psy-
chosocial referrals, as well as satisfaction with these services (Anderson et al., 2014).

**FOLLOW-UP AFTER BREAST CANCER TREATMENT**

**Breast Reconstruction After Mastectomy**

The decision to have, or not to have, breast reconstruction is very personal, shaped by many influences and emotions. Breast reconstruction usually involves additional surgery and pain as well as the dangers associated with major surgical procedures. Breast reconstruction also offers the potential benefit of much less alteration in appearance and body image.

Breast reconstruction is performed by a cosmetic surgeon rather than a breast surgeon (who performs mastectomy) and can be performed simultaneously with a mastectomy (called immediate reconstruction) or be delayed (called delayed reconstruction). There are benefits and drawbacks of each approach, but immediate reconstruction can only be performed if the tumor is not so far advanced that radiation is necessary. Chemotherapy is typically delayed for at least 2 weeks after immediate reconstruction. The reconstruction procedure often requires a longer recovery because the procedure is considerably more involved.

There are many different techniques and types of reconstructive breast surgery. The patient and the plastic surgeon must evaluate each option to determine its appropriateness and desirability for the specific circumstances. The goal of any reconstructive surgery is to achieve symmetry and preserve body image. The three basic types of breast reconstruction are (1) alloplastic reconstruction using a tissue expander with permanent implant; (2) autologous reconstruction using the woman’s own tissue; and (3) mixed autologous and alloplastic reconstruction using a flap with an implant (Lamp & Lester, 2015).

Reconstruction surgery involves many emotional and lifestyle factors. The decision for reconstruction must be considered thoroughly and carefully by each woman. Women facing unilateral or bilateral mastectomy should be referred to a plastic or reconstructive surgeon to discuss reconstructive options. Inclusion of family members, especially significant others, can help the patient process information and gain support during the reconstructive journey (Lamp & Lester, 2015).

**Follow-Up Care**

Women with a history of LCIS, atypical ductal hyperplasia, atypical lobular hyperplasia, or atypical papillomas are at a three- to five-times greater risk of breast cancer recurrence in their lifetime. These women should be referred to an oncologist for follow-up. If there is a strong family history, an annual MRI may be needed and chemoprevention may be indicated (Downes-Holmes & Silverman, 2012).

The first year after diagnosis, women should have a digital mammogram on the affected breast 6 months after the last breast conservation surgery, then again 6 months later. The timing of imaging on the affected breast should be coordinated with the contralateral annual mammogram at either 6-month follow-up. There are no recommended serum tumor markers that should be followed routinely for breast cancer survivors. Women with breast cancer who are at risk for bilateral disease (e.g., those with BRCA1 and BRCA2 mutations) should be considered candidates for annual breast MRI. Physical examinations should be performed every 3 to 6 months for the first 3 years, every 6 to 12 months for years 4 and 5, and annually thereafter (Khatcheressian et al., 2013).
Chemoprevention

Follow-up care for women at high risk of developing breast cancer has focused on the use of chemoprevention agents such as selective estrogen receptor modulators and aromatase inhibitors. Assessment of a woman’s potential risk for breast cancer needs to be conducted before the discussion of chemoprevention. Factors that identify potential candidates for chemoprevention and risk-reduction strategies appear in Table 2-2.

The oral SERMs, tamoxifen and raloxifene, have been shown in randomized, controlled trials to reduce the risk for ER-positive breast cancer. Both of these drugs block estrogen in breast cells, which is why they can be useful in lowering the risk of breast cancer. The USPSTF found adequate evidence that treatment with these drugs can reduce the relative risk (RR) for invasive ER-positive breast cancer by 50% in postmenopausal women who are at increased risk for breast cancer (Moyer, 2013). They have been approved by the U.S. Food and Drug Administration (FDA) for this indication. When taken daily for 5 years, they substantially reduce breast cancer risk for women who are at increased risk due to family cancer history, reproductive risk factors, or personal history of atypical hyperplasia or LCIS. Moreover, this benefit is sustained for at least 5 years after ceasing tamoxifen (DynaMed, 2016).

For women at increased risk of breast cancer who are aged 35 years or older or who have LCIS, tamoxifen (20 mg daily) for 5 years should be discussed as an option to reduce the risk of ER-positive breast cancer. In postmenopausal women and women with atypical hyperplasia or LCIS, tamoxifen (20 mg daily) and raloxifene (60 mg daily) or, as an alternative, exemestane (25 mg daily) for 5 years should be discussed as

| TABLE 2-2: BREAST CANCER RISK CATEGORIES AND RISK REDUCTION STRATEGIES |
|----------------------------------|------------------|--------------------------|
| Risk Category             | Risk Factors                                                                 | Strategies                                                                 |
| High risk                 | • Gail model score >1.66  
• Age ≥60 years  
• Strong family history  
• Breast biopsy findings:  
  ◦ Atypical ductal hyperplasia  
  ◦ Atypical lobular dysplasia  
  ◦ Lobular cancer in situ | • Clinical breast examination every 6 months  
• Annual mammogram  
• Offer chemoprevention |
| Very high risk            | • Confirmed gene mutation (BRCA1 and BRCA2)  
• Strong family history suggesting genetic mutation  
• Irradiation of chest in youth | • Begin increased surveillance 5-10 years before the family member developed breast cancer, or by age 30 years  
• Clinical breast examination twice a year and alternate mammography or MRI annually  
• Prophylactic bilateral mastectomy with reconstruction, prophylactic bilateral salpingo-oophorectomy, and possible chemoprevention |

options for breast cancer risk reduction (Moyer, 2013; Visvanathan et al., 2013).

Discussions with women should include an assessment of individual risk of developing breast cancer, options for reducing risk (pharmacologic and nonpharmacologic), the effects of chemopreventative agents on the incidence of breast cancer, and the benefits and risks of using the medications (Visvanathan et al., 2013). Factors such as age, race, ethnicity, medications, and the presence of a uterus are considered balancing factors. Tamoxifen for 5 years in high-risk women reduces the risk of invasive breast cancer but increases risk of endometrial cancer, pulmonary embolism, cataracts, possible stroke, and hot flashes. Raloxifene for 3 to 4 years reduces breast cancer risk but increases risks for venous thromboembolic disease, hot flashes, and leg cramps (Moyer, 2013). Despite the evidence to support the use of SERMs as a breast cancer chemopreventive agent, uptake remains low because of concerns of toxicity. In addition, many women are not aware that they are at increased risk of breast cancer, and chemoprevention may not have been discussed as a risk-reducing strategy (Klemp, 2015).

Chemoprevention should be discussed with women who are positive for the BRCA mutations. Although tamoxifen has been shown to decrease the risk of breast cancer by 62%, BRCA1-mutation carriers have not been found to have the same benefit, which may be due to the fact that BRCA1-mutation carriers are more likely to develop ER-negative tumors (DynaMed, 2016). Clinical trials of tamoxifen and raloxifene have not been conducted specifically in women who are BRCA-mutation carriers (Moyer, 2014). The role of these chemoprevention medications in women with harmful BRCA1 or BRCA2 mutations without breast cancer is not yet clear, because high-quality studies have not examined the effectiveness of SERMs in BRCA1- and BRCA2-mutation carriers specifically. Thus there are no data on the efficacy of using chemoprevention medications (NCI, n.d.b). Until better targeted therapies are available, particularly for those who have not undergone premenopausal bilateral salpingo-oophorectomy, “the option of tamoxifen for breast cancer prevention should be discussed along with the evidence of benefits and potential side effects, thereby enabling an informed choice for women who wish to consider prevention therapy” (Phillips & Lindeman, 2014, p. 501).

Ongoing Primary Care of Survivors

When a woman has completed her treatment and early follow-up care, she is considered to be a breast cancer survivor, and the transition to primary care begins. A woman’s cancer experience does not end with the completion of therapy. Issues after treatment can involve several areas, both physical and emotional. See Table 2-3 for an overview of survivor issues that may be encountered.

Primary HCP involvement in cancer survivorship care is essential for promoting and overseeing healthy lifestyle adaptations to decrease the patient’s susceptibility to risk of cancer recurrence and postcancer treatment complications, as well as secondary illness unrelated to the cancer diagnosis (Cooper, Loeb, & Smith, 2010).

Standards of care for survivors should include the categories in the following sections (National Comprehensive Cancer Network, 2016c; Runowicz et al., 2016).

Surveillance for Cancer Recurrence

Because breast cancer can recur several years after the initial treatment, meticulous follow-up care is essential. Women are at a constant risk of relapse over the first 10 years after treatment. The most common sites of breast cancer metastasis are the bones, lungs, brain, and liver. Patients should report new or palpable
breast concerns, unusual neurologic symptoms, weight loss, headaches, cough, bone or abdominal pain, or unexplained respiratory symptoms. Breast cancer survivors also need to stay current with screenings for other types of cancer. For example, depending on age and family history, patients should also have a colonoscopy to screen for colon cancer (Downes-Holmes & Silverman, 2012).

### Prevention of Late Effects of Treatments

Surveillance of the patient for secondary complications needs to be integrated into the patient’s general primary care, because these sequelae may occur many years after cancer diagnosis and treatments. The nurse should determine the prior and current treatments for breast cancer. Aromatase inhibitors can cause bone loss and increased risk of osteoporosis, as well as joint pain and stiffness. Anthracycline therapy can cause cardiac toxicity and create a
risk of heart failure or cardiomyopathy. A thorough clinical screening for heart failure should be performed within 1 year after completion of anthracycline therapy.

**Prevention of New or Recurrent Cancers**

The focus of care after completion of therapy is on wellness. Women should be encouraged to participate in a regular exercise regimen and to lose weight if overweight based on body mass index. In the Nurses’ Health Study cohort, women with breast cancer who were moderately active and described at least 3 hours a week of exercise had a 50% reduced risk of recurrence and breast cancer death over inactive women (Klemp, 2015). Smoking cessation and consuming fewer than three alcoholic drinks per week are strongly encouraged. Women with a history of breast cancer increase their risk of recurrence and breast cancer death by 1.3- to 1.5-fold when regularly consuming three to four alcoholic drinks per week.

**Coordination of Care Between Specialists and Primary Care Providers**

Communication and cooperation among providers and survivors is critical. There should be clear communication regarding the roles of different members of the healthcare team. The primary HCP should serve as a general medical care coordinator throughout the woman’s care path of breast cancer detection and aftercare. The primary care setting should focus on assessment of the patient’s daily function, pain, presence of depression and anxiety, preventive care, and management of pre-existing comorbid conditions. It is critical to regularly address the patient’s overall physical and psychosocial status (Knobf, 2011; National Comprehensive Cancer Network, 2016c) see the previous section Psychosocial Aspects of Breast Cancer Treatment).

Referrals for specialist care should be made as needed; it is important to coordinate those components of survivorship care that are agreed upon with the oncology specialist (Runowicz et al., 2016). The continuity and coordination of cancer care is significantly enhanced when primary care nurse practitioners and oncology nurse practitioners are involved in patient care across settings.

**BREAST CANCER PREVENTION**

Ongoing research concerning the role of various modifiable lifestyle factors in the development of breast cancer provides direction for preventive measures for this disease. Women’s HCPs must remain up to date on the latest information so that they can share accurate information and teach their patients strategies to promote breast health and, hopefully, to lessen their risk of breast cancer and breast cancer reoccurrence. The medical community’s approach to breast cancer centers on early detection and prevention. Nurse practitioners and nurses who provide health care to women have the opportunity during encounters to address lifestyle modifications that can potentially reduce breast cancer risk.

Hormonal chemoprevention is suggested for women at increased risk for breast cancer, whereas lifestyle modification can be applied to all women, because all are at some risk of breast cancer. Recommended lifestyle changes are similar to those that help prevent other conditions such as cardiovascular disease and diabetes.

**Estrogen and the Hormone Equation**

Extended hormonal exposure associated with earlier menstruation, later menopause, or use of combined hormone replacement therapy beyond the average age of menopause places women at increased risk for breast cancer. Two studies examined the association of the use of estrogen replacement therapy and breast can-
Chapter 2—Breast Cancer

cancer. The Nurse’s Health Initiative study did not show a statistically significant increased risk of IBC associated with estrogen replacement therapy until after 15 years of use. This increased risk of IBC was associated primarily with ER- and PR-positive breast cancer (Downes-Holmes & Silverman, 2012).

Results from the Women’s Health Initiative (WHI) randomized controlled trial of conjugated estrogen and medroxyprogesterone acetate indicated that when given after menopause this combination increases breast cancer risk. However, the magnitude of these associations, as well as the question of whether a cause-and-effect relationship exists, remains controversial. In contrast, estrogen-only hormone replacement therapy using conjugated estrogen resulted in a reduction of the incidence and deaths from breast cancer in the second WHI trial performed in women with a previous hysterectomy (Howell et al., 2014). Women with atypical hyperplasia should be aware that their risk of breast cancer is substantially increased by the use of estrogen and progesterone (Kaunitz & Samiian, 2015).

Lifestyle Changes

According to the ACS (2016b), four lifestyle choices are recommended to reduce cancer risk: (1) achieve and maintain a healthy weight throughout life; (2) consume a healthy diet, with an emphasis on plant foods; (3) limit consumption of alcoholic beverages; and (4) adopt a physically active lifestyle.

Weight Gain Prevention and Diet

Cohort studies consistently link overweight, obesity, and adult weight gain to risk for post-menopausal breast cancer. Women who gain 20 kg or more during adulthood double their breast cancer risk. A Mediterranean dietary pattern and diets composed largely of vegetables, fruit, fish, and soy are associated with a decreased risk of breast cancer. Risk reduction may also be helped by appropriate intakes of dietary fiber, fruit, and vegetables. Studies investigating the possibility of a link between a high-fat diet and the development of breast cancer are ongoing. It is not known whether a lower-fat diet, fruits, and vegetables can lower one’s risk of breast cancer. Soy intake may be associated with reduced risk, but further research is needed. There is insufficient evidence that vitamins and herbal products are preventive (DynaMed, 2016). Breast cancer prevention interventions should therefore focus on preventing weight gain during the premenopausal years (Harvie, Howell, & Evans, 2015).

Alcohol

Consumption of an additional 10 g of alcohol (1 unit; e.g., 284 ml of 4% strength beer or cider, 25 ml of 40% strength spirits, or 80 ml of 12% strength wine) on a daily basis is estimated to increase risk by 2% to 12%. These studies suggest that women who want to minimize their breast cancer risk should not drink more than one unit daily and should probably have at least two alcohol-free days weekly (Harvie et al., 2015).

Physical Activity

Physical activity lowers the incidence of BC and improves prognosis compared with inactive women. Moderate exercise 5 or more days a week for 30 minutes a day can reduce the risk of breast cancer by 30% to 40%. Potential anticancer effects of physical activity include reductions in endogenous sex hormone concentrations, insulin resistance, and chronic low-grade inflammation (Downes-Holmes & Silverman, 2012; Harvie et al., 2015).

IMPLICATIONS FOR PRACTICE

In response to the likelihood that multiple factors play a role in the development of breast cancer, many HCPs have adopted a holistic
approach to care that hinges on health promotion. This strategy involves individualized patient education and counseling concerning diet, lifestyle habits, and environmental exposure— all aspects of health over which individuals have some control. Furthermore, the general health benefits of such changes have been proven in terms of improved quality of life. Prevention strategies such as these, when combined with early detection, are clearly the best approach (Harvie et al., 2015; Klemp, 2015).

Nurses can be a tremendous source of support and advocacy for women who are diagnosed with breast cancer. At every stage of the process, from the first discovery of a lump during breast self-examination or during a routine physical examination, a woman’s life is forever changed. All of her resources are important as she works her way through the diagnostic process, the necessary decision-making concerning treatment and possible breast reconstruction, the surgery and adjuvant therapies, and the future with its uncertainties. Women who are confronted with breast cancer often must find a depth in themselves that they may have never reached before. With this discovery can come a well of strength and self-acceptance.

**During and After Diagnostic Testing**

At the time of diagnosis, women are faced with a multitude of learning needs and knowledge deficits, yet are expected to learn all the information and make decisions about the local and systemic treatment of their cancer. They are often too shocked and may not process or remember the information given. Informational support in the form of education about the various types of treatment options can assist with decision-making and planning. If women have already established a comfortable relationship with their primary HCP, they will appreciate ongoing support and education during this time. Provider-initiated calls can be very therapeutic, because some women will not reach out on their own (Drageset et al., 2012).

Women should be encouraged to take the time they need to come to clarity about their decisions. They should also be encouraged to seek other opinions or other providers if they do not feel comfortable with recommendations. There are a number of excellent books available, written by women who have shared similar experiences. Many organizations exist nationwide that serve as clearinghouses for information and contact sources for individuals as well as groups. The Internet also serves as a rich source of information. (Refer to the Resource section.)

**During and After Treatment**

Only someone who has experienced breast cancer can truly understand the full impact associated with the diagnosis. Talking with other women who have experienced breast cancer surgery and reconstruction can be very beneficial for some women (Mollica & Nemeth, 2015). There are a number of organizations to help women identify and contact other women who have been through a similar experience. Nurses can assist women in locating local support groups and other breast cancer resources.

**Survivors**

Care for survivors should consist of evidence-based follow-up and surveillance, patient education on self-management of symptoms, health promotion, and monitoring and interventions for consequences and late effects from treatment (Knobf, 2011). Survivors need information that they can understand, advice for managing symptoms, and help integrating the breast cancer experience into their life (Knobf, 2011). There is a need for anticipatory guidance by providers and nurses to prepare survivors for the upcoming emotional challenges throughout the experience with breast cancer.
Support Groups

Support groups can supplement clinician contact. Given the increasing numbers of women with breast cancer, nurses need to develop alternative methods to provide education and support to women. Traditional face-to-face patient support groups are valuable and have been recommended by the National Accreditation Program for Breast Centers. As an alternative, many women use virtual support groups through various Internet and social media resources for medical information, advice, and support, such as blogs, chat groups, Facebook, and Twitter. “Social media is inherently bidirectional, interactive, and patient-driven in contrast with older models of health care education and decision making that are unidirectional and paternalistic” (Attai et al., 2015, p. 5).

Twitter has increasingly been embraced by patients as a way to share information and connect with other patients with similar concerns and conditions. The Breast Cancer Social Media tweet chat (#BCSM) was initiated by two breast cancer survivors. The goal was to provide credible, evidence-based information and support for anyone affected by breast cancer. The chats occur on a weekly basis and cover all aspects of breast cancer screening, diagnosis, treatment, and survivorship. An evaluation of this support modality by participants of the #BCSM chats revealed that (1) more than half of the followers did not participate in any other support group; (2) they experienced less anxiety related to their cancer and better understanding of many aspects of care; and (3) almost 90% of the participants considered the platform to be a “safe and comfortable” environment. Unlike other online groups, most #BCSM chats have physician leaders as well as patients, providing a more reliable resource for participants. See the Resources section for further information on support groups (Attai et al., 2015).

CASE STUDY 2-1

Marlene is a 54-year-old postmenopausal woman who underwent a lumpectomy 8 months ago followed by radiation therapy for early stage breast cancer. Marlene experienced no complications related to the surgery or radiation therapy and, according to her physicians, has an excellent chance for cure.

Today at the woman’s health center, Marlene confides to the nurse that she feels “down.” She states that she knows she has no reason to be depressed, but she just doesn’t feel that her body “looks like it did before.” Marlene has experienced a decrease in breast size in the affected breast, which is a complication of the surgery and radiation therapy, and this change in breast appearance is concerning her.

Questions
1. What is a priority nursing intervention for Marlene at this time?
2. What information should the nurse provide to Marlene?
3. What other actions should the nurse take?

Discussion

Using therapeutic communication, the nurse should provide ample opportunity for Marlene to express her feelings about her body image changes. This action both clarifies and validates Marlene’s feelings. Because breast cancer survivors are more at risk for depression, the nurse should screen for this with two questions from the Personal Health Questionnaire (PHQ)-9. If these are positive, the rest of the questions on the PHQ-9 should be completed. Based on the score from this tool, the nurse should discuss a referral with Marlene for continued care with a counselor or advanced practice nurse with expertise in psycho-oncology care. A priority would be to ensure that she is safe. Any positive reported plans for self-harm should be acted on immediately. Also,
the nurse can refer Marlene to support groups and social media resources that will allow her to verbalize her feelings and concerns with other women who have similar concerns.

If time constraints prohibit a lengthy discussion during this visit, the nurse should reschedule a return visit within a few days. The nurse can provide information about breast prostheses and other cosmetic devices to assist in promoting and maintaining a positive body image. If appropriate, Marlene should be encouraged to speak with her physician about the possibility of breast reconstruction surgery to provide additional resources for enhancement of her body image.

**SUMMARY**

Breast cancer, a problem worldwide, has reached epidemic proportions in both developed countries and developing nations. Nurses can encourage women to practice early detection by obtaining regular clinical breast examinations, practicing breast self-awareness, and choosing judicious use of mammography and other diagnostic techniques. Patients are educated and supported to make changes in dietary and exercise habits and lifestyle patterns that can have cancer-preventive effects. Nurses are in a unique position to provide informed, compassionate care for women who are diagnosed with breast cancer.
11. The most common sign of breast cancer is a painless hard lump
   a. with irregular edges.
   b. with defined edges.
   c. that is mobile.
   d. that appears bilaterally.

12. Carcinoma of the breast consists of a group of different types of cancer that originate either in the breast ducts or
   a. lymph nodes.
   b. lobules.
   c. fatty tissue.
   d. connective tissue.

13. Which type of breast cancer is not associated with any specific mammographic, palpable, or visual features?
   a. Lobular carcinoma in situ
   b. Ductal carcinoma in situ
   c. Invasive ductal carcinoma
   d. Inflammatory breast cancer

14. A woman who is diagnosed with breast cancer and is a carrier of a \textit{BRCA1} or \textit{BRCA2} mutation has an increased risk of developing
   a. internal bleeding.
   b. cancer in the contralateral breast.
   c. uterine cancer.
   d. bruising underneath the breast.

15. When arranging for a woman after mastectomy to discuss reconstruction surgery with a plastic surgeon, the nurse is careful to include
   a. a consumer product safety representative.
   b. a breast implant manufacturer representative.
   c. the woman’s primary healthcare provider.
   d. the woman’s family members.

16. A nurse caring for a female patient with breast cancer who was treated with tamoxifen should assess the patient for which side effects?
   a. Heart failure and cardiac toxicities
   b. Depression and menopausal symptoms
   c. Lymphoma and other blood cancers
   d. Decreased pulmonary function and cervical cancer

17. A practice or condition that increases a female patient’s risk of developing breast cancer is
   a. screening for heart failure.
   b. eating a plant-based diet.
   c. having extended hormonal exposure.
   d. adopting a physically active lifestyle.
18. To help prevent breast cancer, post-menopausal women should avoid
   a. all alcoholic beverages.
   b. plants foods.
   c. the use of hormonal therapy.
   d. any breast surgery.

19. Prevention strategies for breast cancer includes encouraging women to adopt a holistic approach to health for taking action for one’s health and
   a. using one-sided communication.
   b. screening by clinical breast examination only.
   c. ordering biannual mammography.
   d. promoting early detection with screening.

20. A role of the nurse in caring for a female patient who is newly diagnosed with breast cancer is to
   a. provide informational support and education about the various treatment options.
   b. encourage prompt decision-making about treatment options.
   c. support face-to-face peer support groups only.
   d. rely on the patient to initiate follow up and surveillance.


Chapter 2—Common Cancers Among Women


LEARNING OUTCOME

After completing this chapter the learner will be able to review the etiology, diagnosis, and treatment of gynecologic cancers in women.

CHAPTER OBJECTIVES

After completing this chapter, the learner will be able to:

1. Describe the etiology, risk factors, and symptoms of the common gynecologic cancers.
2. Discuss diagnostic and therapeutic modalities for women with gynecologic cancer.
3. Summarize appropriate assessment, education, and counseling to promote optimal psychological status and sexual function for women with gynecologic cancer.

INTRODUCTION

Gynecologic cancers, which include cervical, ovarian, endometrial, vulvar, and vaginal cancers, account for 11% of all new cancer cases in women. The most common are endometrial (54%), ovarian (24%), and cervical (13%; Stabile, Gunn, Sonoda, & Carter, 2015). Of the approximately 90,000 new gynecologic cancer cases diagnosed each year (American Cancer Society, 2015), more women are living and necessarily coping with stressors related to these cancers, which may become chronic. The ongoing stressors contribute to the higher levels of depression and anxiety in this population of women (Stabile et al., 2015).

The impact of gynecologic cancers is considerable. The increasing financial burden of gynecologic cancer care negatively affects the healthcare system and women’s quality of life. In addition, care for this population needs improvement. Women with gynecologic cancer generally do not receive care from the most knowledgeable providers, their care is not coordinated, and support services are not always available (Society of Gynecologic Oncology, 2013).

The risk and incidence of gynecologic cancer depends on which organs are affected. The major sites for malignancy are the vulva, vagina, cervix, uterus, and ovary. Each type of cancer is diagnosed and treated differently depending on the organ site. It is important that healthcare providers (HCPs) assess all women for risk factors, history, and symptoms related to gynecologic cancers at each encounter. Staying alert to key findings from a patient’s history and diagnostic studies will prevent missed opportunities for primary and secondary prevention and education and treatment. Unfortunately, screening tests for gynecologic cancer are only available for cervical cancer. Educating women about abnormal symptoms and when to seek care are important preventive interventions for nurses.
CERVICAL CANCER

Cervical cancer screening by Pap testing resulted in 11,955 women in the United States being diagnosed with cervical cancer and 4,217 dying from this disease in 2013 (Centers for Disease Control and Prevention [CDC], 2017). Cervical cancer is more common in women aged 30 to 45 years, and more than 85% of new cases are diagnosed in economically disadvantaged people (Hoffman et al., 2016). The majority of cervical cancer now occurs in developing countries and medically underserved populations because of a lack of access to Pap smear screening.

Types

The two most common subtypes of cervical cancer are squamous cell carcinoma and adenocarcinoma. Squamous cell carcinoma accounts for more than 70% of cervical cancer. Over the last 30 years, there has been a decline in the incidence of squamous cell carcinoma and an increase in the incidence of adenocarcinoma (Lea & Lin, 2012).

Adenocarcinoma constitutes 25% of cervical cancers and arises from the mucus-secreting glandular cells of the endocervix. Because of this origin within the endocervix, adenocarcinomas are often unrecognizable and may be advanced before becoming clinically evident. Traditional Pap smears are not reliable for screening for adenocarcinomas of the cervix (Lea & Lin, 2012).

Etiology

Human papillomavirus (HPV) can be detected in more than 99% of cervical cancers and is essential for malignant transformation. More than 40 subtypes of HPV have been identified, of which at least 15 are known to be oncogenic or high-risk. High-risk HPV is implicated as the major etiologic agent of cervical cancer. The most prevalent high-risk types are HPV-16 and HPV-18, which account for 70% of cervical cancer in the United States. Transient HPV infection is common, particularly in young women, but the development of cervical cancer is more rare. The persistence of an infection with high-risk HPV leads to increased risk of developing precancerous and cancerous lesions. Most cervical cancers are preceded by persistent infection with oncogenic types of HPV, cervical abnormalities, or adenocarcinoma in situ (AIS; Chisholm, 2016a).

Risk Factors

Several risk areas contribute to the development of cervical cancer:

- Past medical history: Abnormal cytology with high-risk HPV found on screening tests or treatment of cervical intraepithelial neoplasia (CIN; cervical lesions).
- Social factors: Lower education and income, obesity, poor health and living conditions, and limited access to screening all contribute to the risk of cervical cancer. The incidence of cervical cancer is 30% higher in Blacks than in Whites, and mortality is twice as high (Lea & Lin, 2012).
- Sexual activity: Unprotected sexual intercourse is a major risk factor. An increased number of sexual partners and early age at first intercourse have been shown to increase cervical cancer risk. Having more than six lifetime sexual partners imposes a significant increase in the relative risk of cervical cancer, as does an uncircumcised male partner with a history of multiple sex partners (Chisholm, 2016a).
- Smoking: Both active smoking and passive exposure are risk factors. There are increased rates of squamous carcinoma in smokers (Chisholm, 2016a).
• HIV infection: HIV-related immunosuppression inhibits regression of HPV infection and increases the risk of CIN (Chisholm, 2016a).

Long-term use (5 years or more) of combined oral contraceptives is associated with increased risk for cervical cancer, but risk may decrease after cessation. Diethylstilbestrol (DES) exposure in utero (in other words, DES-exposed daughters) also has conflicting evidence for cervical cancer risk (Chisholm, 2016a).

Diagnostic Evaluation

Diagnostic evaluation for cervical cancer and its premalignant lesions by Pap smear and HPV testing has led to a decrease in the incidence of cervical cancer in the United States. Squamous cell cervical cancer incidence and mortality have been reduced dramatically as a result of successful HPV testing and screening with Pap tests in many countries (Chisholm, 2016a). Precancerous lesions at the cervical transformation zone are captured at higher rates with cotesting. Abnormal findings are termed CIN (previously called cervical dysplasia). CIN is usually classified as CIN 1 (low-grade) or CIN 2/3 (high-grade; Hoffman et al., 2016). In general, progression from CIN 1 to invasive cancer requires several years, but wide variation exists.

Squamous cell carcinoma of the cervix may originate from the outer squamous cells on the surface of the cervix or the inner glandular cells of the squamocolumnar junction, or both. The origin is a preexisting lesion (cluster of abnormal cells), which in most cases follows infection with HPV (Hoffman et al., 2016). As it becomes invasive, the tumor breaks through the basement membrane and invades the cervical stroma. Diagnostic evaluation of cervical cancer may manifest as ulceration, a visible tumor, or extensive infiltration of underlying tissue. If not diagnosed and treated, cervical cancer may extend to the uterus, paracervical tissues, and pelvic organs. Cervical cancer may also spread to regional lymph nodes and metastasize to the lungs, liver, and skeleton (Lea & Lin, 2012).

Symptoms

Before a confirmed diagnosis of cervical cancer, women may be asymptomatic and have an abnormal Pap result. Others may present with a watery, blood-tinged vaginal discharge, which may be seen as postcoital, intermenstrual, postmenopausal, or spontaneous bleeding (Chisholm, 2016a). In women with suspected cervical cancer, a thorough external genital and vaginal examination is performed. With speculum examination, the cervix may appear normal. Lesions on the cervix may appear as exophytic (outward) or endophytic (inward) growths; as a polypoid mass, papillary tissue, or barrel-shaped cervix; as a cervical ulceration; or as necrotic tissue. During bimanual examination, a clinician may palpate an enlarged uterus resulting from tumor invasion and growth. Obstruction of the cervical canal by the tumor can result in hematometra (uterus fills with blood) or pyometra (infection) of the uterus (Lea & Lin, 2012).

Diagnosis

In response to an abnormal Pap smear with HPV testing, a colposcopically directed cervical biopsy is performed. During colposcopic evaluation, the entire transformation zone and all lesions must be visualized for the procedure to be considered adequate. The diagnosis is confirmed by cervical biopsy. The cervical biopsy and endocervical curettage (sampling) may reveal invasive cancer, premalignant lesions, or benign tissue. Premalignant lesions such as CIN 2, CIN 3, and AIS need to be evaluated further with cervical biopsy to evaluate for the possibility of microinvasive disease by microscopic examination of removed tissue.

One such biopsy is cone biopsy. During the conization procedure a cone-shaped section is
removed high in the cervical canal (transformation zone). A small amount of normal tissue around the cone-shaped wedge of abnormal tissue is also removed so that a margin free of abnormal cells is left in the cervix. Another option is when a scalpel is used to cut a section of the cervix; this is called cold-knife conization. By obtaining the entire lesion on conization, the maximum depth of invasion into the cervical stroma can be evaluated properly by the pathologist. Conization is also performed if colposcopy is inadequate. Either cold-knife conization or loop electrosurgical excision (LEEP) is acceptable. However, cold-knife conization is preferred because thermal artifacts can make interpretation of surgical margins difficult (Chisholm, 2016a; Hoffman et al., 2016; Lea & Lin, 2012).

**Treatment**

Clinical staging guides the treatment choice. Cervical cancer is staged by clinical criteria, using pelvic examination and biopsy findings. Early-stage cancers are confined to the cervix and are less than 4 mm in size. Advanced stages are based on whether the tumor has spread to surrounding tissues. Radiologic modalities such as CT and MRI can supplement staging. Treatment is based on staging and can range from watchful waiting with cotesting to LEEP, modified hysterectomy, or radical hysterectomy with lymph node dissection. If the tumor is larger than 4 cm or there is evidence of metastasis, radiation therapy and chemotherapy are used (Chisholm, 2016a).

If CIN 1 is found, women can be monitored with more frequent cotesting (HPV and cytology). For CIN 2 or 3, treatment consists of excision or destruction of the epithelium in the squamocolumnar zone to prevent progression to cancer. Removal of tissue is accomplished by two procedures:

- Ablation (destruction of some of the outer layers of the cervix) consists of performing cryotherapy, laser, electrocautery, or cold coagulation.
- Excision (removal of tissue) is accomplished through LEEP or one of the three techniques of conization (i.e., cold-knife, laser, or electrosurgery needle).

LEEP has the advantage of collection of a tissue sample during the procedure. Postprocedure follow-up consists of cotesting (cytology and high-risk HPV testing) at 12 and 24 months. Women aged 21 to 24 years may be observed with colposcopy and cytology every 6 months (Chisholm, 2016a).

AIS of the cervix, although uncommon, is increasing in incidence and typically diagnosed at a younger age. Cervical AIS may be considered a high-grade CIN or preinvasive (stage 0) form of cervical cancer. AIS and adenocarcinoma are not easily identified by colposcopy. Lesions can be multifocal and extend farther into the endocervical canal, above the transformation zone. Diagnostic excision is required to exclude invasive cancer, usually with cold-knife conization. AIS is treated with hysterectomy or an excisional procedure if preservation of fertility is desired. Treatment for invasive adenocarcinoma follows the same guideline as squamous cervical cancer (Chisholm, 2016a).

**Implications for Practice**

Nurses can improve care for women with gynecologic cancers by providing counseling during patient encounters and assisting in navigating primary care services by helping women understand the importance of cancer screening and follow-up after abnormal results. As an example, nurse navigation services demonstrated an increase in women’s follow-up colposcopy attendance after abnormal cytology screening (Luckett, Pena, Vitonis, Bernstein, & Feldman,
Because care for women has been found to be fragmented (Society of Gynecologic Oncology, 2013), nurses can act as care coordinators across settings (e.g., prehospitalization and posthospitalization, survivor care) and serve as a central communication point for the multiple providers and services women may need.

Models of care delivery for women who have survived gynecologic cancer include primary care, gynecologic care, oncologist-led care, and survivorship clinics offering multidisciplinary services. Although the appropriate implementation of survivorship care plans is still being explored, nurse navigators can coordinate care as women transition back to primary care after active treatment. “Nurses can have an enormous impact on improving and expanding access to oncology care as clinicians, designers, and leaders of initiatives to improve care” (Murphy & Mollica, 2016, p. 1).

**OVARIAN CANCER**

Ovarian cancer is the fifth most common cancer in women in the United States. It ranks fifth among causes of cancer death in women and has the highest mortality rate. Although the incidence of ovarian cancer is relatively low, overall survival is only 35%. In 2013, 22,240 new cases of ovarian cancer were diagnosed and 14,000 women died of the disease (CDC, 2017). About two thirds of women with ovarian cancer are age 55 years and older, and the disease is slightly more common in White women than in Black women. A woman’s lifetime risk for ovarian cancer diagnosis is estimated at 1 in 48 to 54 women (Levine, 2017).

Close to 70% of women have already experienced cancer spread outside of the pelvis at the time of the initial diagnosis of ovarian cancer. Earlier diagnosis has been linked to an increased survival rate (Crull, Mayer, & Jessup, 2014). The challenge to early diagnosis is the fact that symptoms can be subtle and not specific to the gynecologic system. They are most often gastrointestinal, abdominal, and urinary and can resemble common conditions such as irritable bowel syndrome, gastroenteritis, and urinary tract infections. Because of this, women are misdiagnosed initially and are treated for other conditions (Slatnik & Duff, 2015).

**Types**

About 90% of primary malignant ovarian tumors are epithelial carcinomas. Epithelial ovarian cancer is most commonly detected in an advanced stage, when the overall 5-year survival rate is 20% to 30%. Ovarian epithelial tumors may arise within either endometriosis or cortical inclusions. These include low-grade endometrioid carcinomas, clear-cell carcinomas, borderline and low-grade serous carcinomas, and mucinous carcinomas. These tumors are believed to evolve slowly from lower-grade precursor conditions (endometriotic cysts, cystadenomas, etc.) and are classified as type I. Nonepithelial ovarian cancer is a group of uncommon histologically and clinically distinct tumors. Type II ovarian tumors are considered high grade and include endometrioid carcinomas and carcinosarcomas. These tumors are extremely rare with an aggressive clinical course and a generally poor prognosis (Levine, 2017).

**Etiology**

Although the cause is unknown, age and gender are the most important factors associated with the development of ovarian cancer. About 90% of cases have been reported in women older than 45 years (Levine, 2017). Because the pelvis contains major components of the gastrointestinal and urinary tracts in addition to the reproductive organs, determining the cause of any pelvic symptoms requires careful assessment, including an evaluation for ovarian can-
Any of the various cell types in the ovaries can give rise to cancerous growth.

**Risk Factors**

Other risk factors for ovarian cancer include nulliparity, early menarche, pregnancy later in life, a personal history of breast cancer, a family history of breast or ovarian cancer, endometriosis, infertility, early menarche, late menopause, or hormone therapy use for more than 5 years. Genetic predisposition is seen in approximately 10% to 15% of patients with ovarian cancer; the majority of these women possess a *BRCA1* or *BRCA2* gene mutation. The term hereditary breast and ovarian cancer syndrome (HBOCS) is used to describe the tendency to develop breast or ovarian cancer because of an inherited *BRCA1/2* gene mutation (Slatnik & Duff, 2015).

Several associative causes have been found, although no studies have proved causation. These include the use of fertility medications and androgens, use of unopposed estrogens after menopause, exposure to asbestos, genital exposure to talc, a high-fat diet, dairy product consumption, and childhood mumps infection (Crull et al., 2014).

Several factors can be protective. Pregnancy, breastfeeding, tubal ligation, and suppression of ovulation (oral contraceptive use) provide some protection against ovarian cancer. Oral contraceptives can decrease risk by 40% to 80%. This begins within 1 year of use, increases with duration of use, and persists nearly 20 years after they are stopped. Five years of use by nulliparous women reduces the risk to that of parous never-users, and 10 years of use by women with a family history reduces the risk to a level below that of a never-user with a negative family history (Crull et al., 2014; Levine, 2017).

**Diagnostic Evaluation**

Reproductive health history is a critical area of diagnostic evaluation for ovarian cancer. During the physical examination, the HCP examines the abdomen for distension, masses, and ascites. A pelvic examination is performed to detect ovarian (adnexal) masses. A mass found on examination that is solid, fixed, or irregular could be malignant. An adnexal mass in a post-menopausal woman has an increased likelihood of malignancy. Palpable ovaries 3 to 5 years after menopause should be evaluated, because ovaries normally decrease in size and become nonpalpable after menopause (Levine, 2017).

Several procedures are used to assist in the diagnosis of ovarian cancer:

- **Ultrasound:** Transvaginal ultrasound can be used to determine the size, location, and quality (e.g., fluid-filled, solid, complex) of the mass. Current imaging standards support the use of transvaginal ultrasonography for initial evaluation of ovarian masses (American College of Obstetricians and Gynecologists [ACOG], 2016). A CT scan of the pelvis and abdomen can also be performed to establish the extent of disease before surgery (Crull et al., 2014).

- **Serum CA-125 antigen levels:** The test to determine the serum CA-125 antigen level was originally used to monitor the course of epithelial ovarian cancer. It is used currently for diagnostic workup of suspected ovarian cancer in women with symptoms or physical examination findings and is also used with ultrasound in preoperative decision making about the surgical approach for evaluating pelvic masses. False-positive results can be caused by other conditions, including non-gynecologic cancers and active endometriosis (Levine, 2017).
• Imaging: Abdominal and pelvic CT and MRI scans are performed to assess indeterminate lesions and to evaluate for metastases (Levine, 2017)

• Laparotomy: Laparotomy or laparoscopic biopsy is performed for surgical confirmation and clinical staging, which provides direction to the treatment and prognosis of the cancer.

• Genetic testing: Factors known to increase the risk of ovarian cancer include an identified BRCA1/2 gene mutation and a family history of ovarian cancer, or Lynch syndrome, which is suggestive of a hereditary cancer syndrome. These women should be considered for genetic counseling to further evaluate their risk and determine the need for genetic testing (Moyer, 2014). If a woman has a BRCA1/2 mutation, her lifetime risk of developing ovarian cancer is 65% to 74%, placing her in a high-risk category. These women may benefit from regular screening ultrasonography and CA-125 evaluations. Women with a strong family history of epithelial ovarian, fallopian tube, or peritoneal cancers, particularly if there is a documented germline mutation, are advised to have a risk-reducing bilateral salpingo-oophorectomy after appropriate counseling and at the completion of childbearing (Levine, 2017).

Symptoms

Ovarian cancer has been called “the silent killer” because of the misconception that symptoms do not manifest until late in the disease. However, ovarian cancer is not always silent and does have symptoms. Most symptoms of ovarian cancer are nonspecific, but nearly all women will report at least one symptom that is pelvic, abdominal, or menstrual in nature. Women also commonly experience abdominal, gastrointestinal, and urinary symptoms. Complaints often include nausea and anorexia, constipation, abdominal pain and bloating, urinary pressure and frequency, pain with intercourse, and back and pelvic pain. Symptoms are likely to be progressive, persistent, frequent, and severe (Levine, 2017). Although the majority of women experience symptoms, many do not take the symptoms seriously and attribute them to other factors such as menopause, aging, or urinary tract infections (Slatnik & Duff, 2015).

Diagnosis

A definitive diagnosis is confirmed by histologic evaluation of ovarian tissue obtained during primary surgery or laparoscopic or image-guided biopsy. If that is not feasible, peritoneal washings are sent to pathology for evaluation (Levine, 2017).

Treatment

The treatment is planned according to the stage of the disease at the time of surgery. Most often, surgical removal by a gynecologic oncologist of as much of the tumor as possible constitutes the initial step. A total abdominal hysterectomy with debulking of the tumor and removal of the ovaries and fallopian tubes is common as well, followed by some combination of platinum-based chemotherapy. Combination immunotherapy and chemotherapy is also used in some protocols. Five-year survival rates are approximately 90% for stage 1, 80% for stage 2, 15% to 20% for stage 3, and less than 5% for stage 4. Surgery can be curative if the disease is confined to the ovaries (Levine, 2017).

Implications for Practice

Recent research has shown that certain symptoms are more likely to occur in women with ovarian cancer than in the general population. Goff and colleagues (2007) have developed an ovarian cancer symptom index (the Goff Symptom Index) for early identification of women with potential ovarian cancer. This
tool focuses on symptoms most commonly seen among women who were subsequently diagnosed with ovarian cancer. Although not yet standard of care, the easy-to-administer symptom index has been recommended as a possible tool to aid in screening. Use of the symptom index with at least four of the following symptoms (occurring at least 12 times per month but present for less than 1 year) was reported to have 64% to 69% sensitivity and 88% to 97% specificity in four case-controlled studies for ovarian cancer:

- Pelvic/abdominal pain
- Urinary urgency or frequency
- Increased abdominal size/bloating
- Difficulty eating or early satiety

(Levine, 2017)

Women should be informed about symptoms of ovarian cancer during their visits. This may encourage women to report symptoms that have not resolved, have worsened, or have become more frequent and seek evaluation sooner. HCPs should encourage women to use symptom diaries.

Studies examining the effectiveness of various screening strategies, alone or in combination, are ongoing, and several clinical assessment tools are being evaluated for the earlier assessment of ovarian cancer. Until these methods are validated, early detection will depend on early symptom recognition by women and prompt workup by providers. Nurses should be aware of the factors that put some women at higher risk for ovarian cancer (e.g., certain genetic mutations, family history) and factors that lower risk, such as oral contraceptives. If a woman has familial and other risk factors, HCPs should offer the option of genetic counseling (Slatnik & Duff, 2015).

**UTERINE (ENDOMETRIAL) CANCER**

Cancer of the endometrium is the most common gynecologic malignancy in the United States (CDC, 2017). There are 40,000 cases a year diagnosed in the United States (CDC, 2017), and women have a 2.6% lifetime risk of endometrial cancer (ACOG, 2015a). Uterine cancer is rare in women younger than 45 years; about 70% of all cases occur in women between the ages of 45 and 74 years, and the highest number of cases are diagnosed in the 55- to 64-year-old age group. Although the incidence of this type of cancer is higher for White women than for Black women, Black women have mortality rates that are nearly two times higher (ACOG, 2015a).

**Types**

Uterine (endometrial) cancer is slow growing; most of the neoplasms are adenocarcinomas that develop from endometrial hyperplasia. Uterine cancer can be categorized broadly into two types that differ in epidemiology, genetics, prognosis, and treatment. Type I, or endometrioid adenocarcinoma, is the most common type of uterine cancer and accounts for more than three fourths of all cases (Chisholm, 2016b). Type I is estrogen-related and occurs most often in women who are obese and postmenopausal, and occasionally in women who are premenopausal but anovulatory. Most cases of type I cancer are low grade and confined to the uterus when diagnosed, with relatively low-grade features, and carry a good prognosis (ACOG, 2015a).

Type II tumors may be estrogen-independent, and they are often accompanied by surrounding endometrial atrophy. Type II endometrial cancer is characterized by clear-cell and papillary serous tumors and is considered to be high grade, with a significant risk of extrauterine disease. These tumors are often locally advanced or metastatic, and they carry a poorer prognosis than type I.
Patients with type II tumors are more likely to be older, nonwhite, multiparous, current smokers, and nonobese and to have had breast cancer treated with tamoxifen (Chisholm, 2016b). Uterine papillary serous carcinoma accounts for only approximately 10% of all cases of uterine cancer, but it is responsible for the deaths of almost 40% of patients with endometrial cancer (ACOG, 2015a).

**Etiology**

Most uterine malignancies arise within the inner lining of the uterus (endometrium) and are adenocarcinomas that develop from overgrowth of the endometrium (hyperplasia). Endometrial hyperplasia refers to abnormal proliferation of endometrial glands and stroma associated with excess estrogenic stimulation. Long periods of unopposed estrogen caused by chronic anovulation (e.g., polycystic ovary syndrome) or estrogen-producing tumors stimulate the endometrial lining. This stimulation promotes endometrial atypical hyperplasia (excess growth), which increases the risk of uterine cancer.

**Risk Factors**

Risk factors for uterine cancer include those factors that expose the endometrium to estrogen. Unopposed estrogen therapy, nulliparity or low parity, early menarche (before age 12 years), late menopause (after age 55 years), therapy with tamoxifen, infertility, polycystic ovarian disease, chronic anovulation, diabetes, gallbladder disease, thyroid disease, metabolic syndrome, hypertension, obesity and a high-fat diet (which increases the levels of circulating estrogen), and breast cancer are risk factors for uterine cancer. Genetic factors such as Lynch syndrome (hereditary nonpolyposis colon cancer) and a first-degree relative with endometrial cancer also increase the risk for uterine cancer (ACOG, 2015a; Chisholm, 2016b).

**Protective Factors**

Factors associated with a lower risk of endometrial cancer include having multiple children, use of combination oral contraceptives, and menopausal estrogen replacement therapy that is combined with progesterone therapy for women who have a uterus (ACOG, 2015a).

**Diagnostic Evaluation**

During the pelvic examination, the clinician observes for bleeding and palpates uterine size and position. Pelvic examination may reveal a uterine enlargement or mass. The adnexa (ovaries, fallopian tubes, and ligaments holding the uterus in place) are also palpated for masses (Chisholm, 2016b).

**Symptoms**

Most women are symptomatic in the early stages, a factor that leads to early diagnosis and, commonly, successful treatment. For postmenopausal women, the cardinal symptom is vaginal bleeding; perimenopausal women may have heavy or prolonged menstruation or spotting or bleeding between menses. Other symptoms of endometrial cancer include chronic vaginal discharge, pelvic pain, dyspareunia, and weight loss (Chisholm, 2016b).

**Diagnosis**

Diagnosis is made by an endometrial biopsy. Endometrial cells (atypical glandular cells) found on Pap smears of postmenopausal women who are not taking hormone replacement therapy should prompt further investigation to rule out cervical or endometrial abnormalities (ACOG, 2015a). An evaluation of any vaginal bleeding in postmenopausal women needs to be initiated (ACOG, 2015a). Initial testing to evaluate the uterine lining for diagnosis can be with transvaginal ultrasound or endometrial biopsy (EMB). Classically, dilatation and curettage (D&C) has been the procedure used to diagnose endometrial
cancer. Outpatient endometrial sampling with disposable devices is reliable and accurate and is the method of choice for histologic evaluation of the endometrium (ACOG, 2015a; Chisholm, 2016b). If insufficient tissue is found on EMB, further studies are warranted and ultrasound may be performed. If ultrasound is initially performed to measure the endometrium, and the thickening is less than 4 mm, endometrial sampling is not required. If endometrial thickening is greater than 4 mm, alternative evaluation, such as hysteroscopy or EMB, should be performed (ACOG, 2015a). If both tests are negative and bleeding continues, D&C or hysteroscopy may be performed (Chisholm, 2016b).

Treatment

Uterine cancer is staged and treated at the time of surgery, based on its location and extension into surrounding tissue and distant metastases (ACOG, 2015a; Chisholm, 2016b). Treatment involves total abdominal hysterectomy (removal of the uterus, cervix, both fallopian tubes, and ovaries, as well as selective pelvic and para-aortic lymphadenectomy). This procedure is followed by radiation, chemotherapy, or both, depending on the individual case. The most common uterine cancer, adenocarcinoma, is slow growing and usually remains localized for a long time. When diagnosed and treated early, survival rates are good. For all cases of endometrial cancer, the relative 5-year survival rate is 84%; for cancer found at an earlier stage, the survival rate is much higher. The survival rates for White women are at least 18% better at every stage than for Black women (Chisholm, 2016b). Referral to a gynecologic oncologist should be made at the time of diagnosis for treatment planning (ACOG, 2015a).

Implication for Nursing

During encounters with women, the nurse should discuss the need to report any bleeding after menopause or any change in menstrual patterns (e.g., midcycle spotting). For women who have not had a hysterectomy, combined postmenopausal hormone therapy with both estrogen and progesterone prevents development of endometrial hyperplasia. Taking progesterone, either alone or in combination with estrogen, as is found in combined birth control pills, lowers the risk for endometrial cancer. Women with a family history of uterine cancer should consider genetic counseling (Chisholm, 2016b). Nurses should inform women of how to lower their personal risk by preventing obesity to decrease exposure to excessive estrogen. Exercising regularly, keeping blood sugar and blood pressure under control, and maintaining a healthy weight are important primary prevention practices (Chisholm, 2016b).

VULVAR CANCER

Vulvar cancer represents 3% to 5% of gynecologic malignancies in the United States and less than 1% of all cancers. The mean age of diagnosis is 65 years, but incidence in younger women is rising because of an increase in human papillomavirus infections. Most studies show approximately 40% HPV DNA positivity in patients with vulvar cancer. Late diagnosis is common because of patient and clinician delay. Ninety percent of vulvar cancer is squamous; in some cases, it develops slowly through precancerous epithelial changes called vulvar intraepithelial neoplasia (VIN; Hoffman et al., 2016). There are several other types of vulvar cancer. Melanoma is the second most common cause of vulvar cancer, representing 2% to 9% of vulvar tumors. Rare types of vulvar cancer include Paget disease, basal cell carcinoma, adenocarcinoma, and verrucous carcinoma (Fedorowicz, 2016).
Types

Noninvasive Vulvar Disease

VIN is a high-grade squamous lesion on the vulvar skin. These lesions are a cancer precursor. HPV DNA has been found in up to 80% of VIN lesions. VIN typically affects women ages 35 to 55 years. The incidence of VIN appears to be increasing, particularly in women in their 40s. There are two types of VIN: (1) HPV-associated (warty, basaloid, and mixed) and (2) VIN, differentiated type, which is seen particularly in older adult women and is often associated with lichen sclerosis or squamous hyperplasia (Chisholm, 2016c).

Invasive Vulvar Cancer

There are two types of vulvar squamous cell carcinoma (VSCC), often categorized by the presence or absence of HPV in the tumor. HPV-negative VSCC affects older adult women (aged 55 to 85 years) and is associated with lichen sclerosis and vulvar inflammation. The second type, HPV-associated VSCC, with a reported range 20% to 60% of vulvar cancers, typically affects younger women. The incidence of both types increases with advancing age, with peak incidence range in women aged 70 to 80 years (Fedorowicz, 2016).

Etiology

The etiology of vulvar cancer is unknown. For the HPV-negative VSCC, it is hypothesized that the itching and scratching of the vulva leads to lichen sclerosis. This evolves into squamous cell hyperplasia. This lesion advances to squamous cell carcinoma. For HPV-associated VSCC, infection with HPV (type 16 is the most common type, followed by HPV types 33 and 18), smoking, and impaired immune system (e.g., infection with HIV) are the main causes of cancer (Fedorowicz, 2016).

Risk Factors

There are several risk factors for vulvar cancer related to infection, other skin conditions, and lifestyle. Infectious factors consist of HPV infection (condyloma acuminatum), VIN, and HIV. Other skin conditions such as chronic irritation of the vulva, lichen sclerosis, or lichen simplex chronicus can evolve into vulvar cancer. Lifestyle practices increasing the risk for vulvar cancer may include poor hygiene, smoking, multiple partners (Fedorowicz, 2016).

Diagnostic Evaluation

All women with persistent vulvar complaints should undergo a pelvic examination, with careful examination of the vulva and the entire perianal area, by the clinician. The clinician checks for lesions and notes any white or brown lesions or erythema of the vulva. The abdomen is also palpated for inguinal lymph node adenopathy. Any lesions should be biopsied. This is particularly true of pigmented lesions, genital warts in women who are postmenopausal or immune compromised, or warts that persist despite topical therapies. The selection of the best location to biopsy is aided by magnification of the vulva and perianus, usually with a colposcope. This examination is termed vulvoscopy. Colposcopy of the cervix and vagina is performed because of the common association with other squamous intraepithelial lesions. Cervical cancer screening is performed if the cervix is still present (Fedorowicz, 2016).

Symptoms

VSCC may be asymptomatic. In 50% of women, VIN is discovered on a routine gynecologic examination or during evaluation of abnormal cervical or vaginal cytology. Pruritus and burning are the most common symptoms. These can persist for weeks or months before diagnosis because many patients may be embarrassed or may not recognize the significance
of their symptoms. There may be tenderness and pain. Bleeding or discharge is an occasional presenting symptom, and patients with advanced disease may present with a lump in the groin caused by metastases to groin lymph nodes (Fedorowicz, 2016).

Lesions may be present, sometimes with bleeding. Lesions may be white, raised, or flat with a warty or ulcerated appearance. A lesion may appear as an ulcer, warty papule, or hyperkeratotic plaque. Many women have reported symptoms for up to 6 months, and 30% have had up to three medical consultations and have used prescribed topical medications before a tissue diagnosis of cancer is made (Fedorowicz, 2016).

**Diagnosis**

Diagnosis (VIN or squamous cell cancer) is confirmed by the vulvar biopsy. Multiple directed biopsies may be needed.

These are further classified into low-grade squamous intraepithelial lesion of the vulva (vulvar LSIL), high-grade squamous intraepithelial lesion of the vulva (vulvar HSIL), or differentiated-type VIN (ACOG, 2016a). If positive for squamous cell carcinoma, tumor staging is performed. The status is determined by inguinal-femoral node involvement (Hoffman et al., 2016). The patient’s prognosis depends on lymph node spread. If nodes are negative, the survival rate is 90%; if nodes are positive, the survival rate may be from 24% to 75% (ACOG & American Society for Colposcopy and Cervical Pathology [ASCCP], 2016). Early-stage vulvar cancer has a favorable prognosis. The most important prognostic factor for survival is groin node status (Carter & Downs, 2012).

**Treatment**

**Vulvar Intraepithelial Neoplasms**

Treatment is recommended for all women with vulvar HSIL. Because of the potential for occult invasion, wide local excision is performed if cancer is suspected, even if biopsies show vulvar HSIL. Surgical excision is the standard treatment of choice for VIN because it allows for thorough histologic examination to rule out invasive carcinoma (ACOG & ASCCP, 2016). The goals of treating VIN are to prevent progression to invasive cancer, to relieve symptoms, and to preserve normal anatomy. Medications are limited to women with no sign or suspicion of invasive cancer on clinical examination and biopsy.

Imiquimod, a topical immune-response modifier, is the most commonly used topical agent for the treatment of VIN. Imiquimod results in at least a partial response in approximately 80% of patients after treatment for 16 weeks. The application of topical imiquimod 5% is effective for the treatment of VIN, although it is not approved by the FDA for this purpose. Recommended treatment regimens include three-times-weekly application to affected areas for 12 to 20 weeks, with colposcopic assessment at 4- to 6-week intervals during treatment (ACOG & ASCCP, 2016).

Carbon dioxide laser ablation is useful in the treatment of multifocal VIN; a large area of the vulva can be treated with this modality, resulting in proper wound healing and a good cosmetic outcome. Laser ablation (laser vaporization) is limited to younger women with no sign or suspicion of invasive cancer on clinical examination and biopsy (Chisholm, 2016c).

**Invasive Squamous Cell Vulvar Cancer**

Imaging, along with ultrasound and fine needle aspiration of lymph nodes or MRI, can determine the metastasis and stage of vulvar cancer. Management of vulvar cancer must be individualized. The stage of disease dictates the type of treatment. There is no standard surgical procedure, and the emphasis is on performing the most conservative treatment consistent
with cure of the disease. To decrease psycho-sexual morbidity, a more conservative operation than radical vulvectomy usually is indicated. The procedure may be called a radical wide local excision, and for localized lesions, this operation is as effective as radical vulvectomy in preventing local recurrence. Advanced disease with lymph node involvement may require disfiguring and debilitating surgery (vulvectomy). Radiation and chemotherapy may be indicated for women with stage 3 or 4 cancer (Fedorowicz, 2016).

Vulvar melanoma disproportionately affects the elderly and develops more commonly among Whites than other races. Vulvar melanoma has an overall poor prognosis, and 5-year survival rates range from 8% to 55%. A radical local excision with 2-cm margins appears to be adequate for most well-circumscribed lesions (Fedorowicz, 2016).

**Implications for Practice**

Nurses should counsel patients, family, and support members to monitor for depression. Evaluation for depression during diagnosis and recovery is part of the care for women with gynecologic disorders, because these symptoms can adversely affect women’s quality of life, function, and self-care (Stabile et al., 2015). Nurses can serve as resources for women in such areas as where to go for support and how to deal with emotions such as sadness, depression, anxiety, and a feeling of a lack of control over the outcome of the disease and treatment (Murphy & Mollica, 2016).

According to Stabile et al. (2015), 90% of patients with gynecologic cancer experience sexual dysfunction at some point in their treatment. It is important to acknowledge the potential for sexual side effects due to treatment and to provide patients the opportunity to discuss their sexual health in a comfortable setting. Nurses can offer support and education around discussions about sexual health (Murphy & Mollica, 2016).

**VAGINAL CANCER**

Vaginal carcinomas can be primary, secondary, or related to in utero DES exposure. Extremely rare, vaginal carcinomas account for only 1% to 2% of gynecologic malignancies. Vaginal cancer is primarily found in women who are postmenopausal. Because of recent increases in HPV infection of the lower genital tract, vaginal intraepithelial neoplasia (VaIN) is now also diagnosed in younger women. Cervical and vulvar neoplasia may also increase the risk for VaIN and vaginal squamous cancer (Peiser, 2015).

**Etiology**

The vagina can be a common site of metastatic cancer from cervical or vulvar tumors and possibly the anus because of the close proximity of anatomy in women (Peiser, 2015). Specifically, 80% of vaginal cancers are caused by secondary carcinomas from other sites (Peiser, 2015). Vaginal cancer is mostly related to precancer cells left untreated. DES, an endocrine-disrupting chemical, is known to cause cancer if exposure occurred in utero. Exposure has also been linked to cancer of the vagina of female offspring of women who received DES during pregnancy.

In noninvasive vaginal disease, precancerous epithelial changes are called VaIN. The cellular changes may be either low or high grade. VaIN has histopathology similar to CIN and VIN. It is rarely found as a primary lesion and most often develops as an extension of CIN, mainly in the upper third of the vagina. Abnormal cytology most often is the first indication of VaIN. Patients with a history of cervical or vulvar cancer are at a higher risk for this type of cancer (Peiser, 2015). Invasive squamous cell vaginal carcinoma accounts for
approximately 90% of vaginal cancers. Invasive vaginal cancers are squamous and appear to develop slowly from VaIN (Peiser, 2015).

**Risk Factors**

There are many risk factors associated with vaginal cancer, including age older than 60 years; smoking; HPV infection; history of abnormal cytology, CIN, or cervical cancer; and chronic irritant vaginitis from douching or foreign bodies such as a vaginal pessary. Associated conditions include condyloma (genital warts), and spread of cancers of the cervix, vulva, and endometrium (Peiser, 2015).

DES is a nonsteroidal synthetic estrogen that was used between 1940 and 1971 to prevent miscarriage in high-risk pregnant women. It was taken off the market when study results revealed that adenocarcinoma of the vagina, formerly a rare disease, was seen in young women who were exposed to DES in utero. Structural alterations and changes in the tissue of the vagina and cervix are often seen in women exposed prenatally to DES, and DES exposure has also been linked to infertility (Hoffman et al., 2016).

**Diagnostic Evaluation**

A complete evaluation is performed that includes information from risk assessment, symptom presentation, speculum examination, digital palpation, colposcopy, cytology, and biopsy of any visible lesions. Vaginal cancer is typically asymptomatic. Therefore a thorough vaginal evaluation is critically important to diagnostic evaluation. During the pelvic examination the speculum should be rotated as it is slowly withdrawn to ensure that the entire vaginal mucosa is visualized (Carter & Downs, 2012).

**Symptoms**

On evaluation, primary vaginal carcinoma may present as ulcerated erythematous patches (Peiser, 2015). The ulcerated erythematous patches may not present as symptoms. If present, symptoms may include vaginal spotting, discharge, and odor. Most female patients with invasive vaginal carcinoma present with painless vaginal discharge and bleeding (Peiser, 2015).

**Diagnosis**

Diagnosis may be initiated by evaluation of cytologic abnormalities noted during a screening Pap test. Any lesions must be evaluated histologically for confirmation of cancer cell growth. If the cervix is surgically absent (from previous hysterectomy or after a normal cervical colposcopy and biopsy), an enhanced colposcopy should specifically be performed to evaluate for lesions through complete visualization of the vaginal wall. After application of acetic acid and Lugol solution, vaginoscopy (an examination of the entire vagina using a colposcope) is performed. Abnormal findings should be biopsied. Biopsies of the cervix should be performed to rule out a primary cervical tumor (Carter & Downs, 2012).

**Treatment**

VaIN is believed to be a precancerous lesion, and high-grade lesions require eradication. Various treatment modalities for VaIN include surgical excision, topical agents, laser ablation, and radiation therapy. Before treatment with laser or topical therapy, biopsies should be performed to rule out invasive disease (Carter & Downs, 2012).

After a diagnosis of squamous cell carcinoma, an MRI or CT scan is used to determine tumor stage, size, and involvement and to identify metastatic disease for guiding treatment (Peiser, 2015). Because vaginal cancer is rare, there is no standard treatment. Radiation therapy is the treatment of choice for most patients with vaginal cancer, but treatment depends on the stage of disease at the time of diagnosis.
Patients with selected stage 1 to 2 (early stage) disease can be treated with surgical resection (Peiser, 2015).

Whenever possible, patients should be referred to tertiary referral units because of the rarity of these lesions and the limited experience of most practitioners with the specialized techniques used to treat these cancers effectively (Society of Gynecologic Oncology, 2013).

Counseling

Some vaginal cancers appear to have a relationship with high-risk HPV. Nurses should counsel women about the use of prophylactic vaccines against HPV. The current HPV vaccines provide protection against HPV types 16 and 18, which account for about 70% of cervical, vaginal, and anal cancers. Vaccines are most effective when administered in sexually naïve individuals. The vaccines are indicated for females 9 to 26 years of age for prevention of cervical and other lower genital tract cancers. Women who have received HPV vaccines must continue to receive Pap smear screening, because current vaccines do not provide protection for other high-risk HPV subtypes that can cause cervical and other lower genital tract cancers (ACOG, 2015b; Lea & Lin, 2012).

Women with precancerous conditions (CIN, VIN, VaIN) should be considered at risk for cancer. Careful follow-up, monitoring, and retesting should be performed based on protocols for each type of condition.

SUMMARY

The diagnosis of gynecologic cancer has a dramatic impact on the physical, emotional, social, and sexual domains of a woman’s life. The nature of gynecologic cancers may require invasive treatment procedures on the female reproductive system, with potential loss of fertility. Psychological and sexual issues are a major concern for women diagnosed with gynecologic cancer. Nurses have an important role to provide education and support to women with gynecologic cancers during the phases of screening, diagnosis, treatment, recovery, and follow-up.
Note: Choose the one option that BEST answers each question.

21. A possible symptom of cervical cancer is a
   a. watery, blood-tinged discharge.
   b. bloated feeling immediately after eating a meal.
   c. thick, yellow vaginal discharge between periods.
   d. fullness or pressure in the abdomen.

22. A patient characteristic or action that decreases the risk of ovarian cancer is
   a. being nulliparous.
   b. taking evening primrose oil.
   c. taking oral contraceptives.
   d. eating a diet rich in meat.

23. A nursing intervention to promote early identification of ovarian cancer in women is
   a. providing counseling for the patient’s symptom index.
   b. recommending a vegan diet.
   c. explaining that only female patients older than 50 years have a need for concern.
   d. suggesting screening tests for all female patients.

24. Postmenopausal bleeding in women should initially be evaluated by
   a. dilatation and curettage.
   b. hysteroscopy.
   c. transvaginal ultrasound or endometrial biopsy.
   d. Pap smear and cervical biopsy.

25. A 65-year-old patient calls the office reporting intermittent, external vaginal itching over the past several months. Appropriate nurse counseling is to recommend the patient
   a. use over-the-counter, topical antifungals.
   b. obtain a prescription for a mild corticosteroid cream.
   c. monitor for symptoms related to new detergents or other products.
   d. schedule a pelvic examination with the clinician.

This concludes the final examination. Please answer the evaluation questions found on page v of this course book.
REFERENCES


Chapter 3 — Common Cancers Among Women


RESOURCES

BIRTH CONTROL/SEXUALLY TRANSMITTED INFECTIONS/ABNORMAL PAP SMEAR FINDINGS

AIDS Clinical Trials Information Service
1-800-874-2572
P.O. Box 6421
Rockville, MD 20849-6421
http://www.actis.org

The Alan Guttmacher Institute
Sexual and reproductive health research, policy analysis, and public education
(212) 248-1111
120 Wall Street
New York, NY 10005
http://www.guttmacher.org

American Foundation for AIDS Research (AmFAR)
(212) 682-7440
733 Third Avenue, 12th Floor
New York, NY 10017
http://www.amfar.org

American Sexual Health Association (ASHA)
(919) 361-8400
P.O. Box 13827
Research Triangle Park, NC 27709-3827
info@ashasexualhealth.org
http://www.ashastd.org

American Society for Colposcopy and Cervical Pathology
1530 Tilco Drive, Suite C
Frederick, MD 21704
info@asccp.org

Association of Reproductive Health Professional (ARHP)
(202) 466-3825
1300 19th Street, NW, Suite 200
Washington, DC 20036
ARHP@arhp.org
Centers for Disease Control and Prevention (CDC)
https://www.cdc.gov/nchhstp/

Centers for Disease Control and Prevention (CDC)
*U.S. selected practice recommendations for contraception use, 2013*
http://www.cdc.gov/mmwr/preview/mmwrhtml/rr6205a1.htm?s_cid=rr6205a1_w

Centers for Disease Control and Prevention Sexually Transmitted Disease Guideline (APP)
https://www.cdc.gov/std/tg2015/default.htm

**Hepatitis Foundation International**
1-800-891-0707
8121 Georgia Avenue, Suite 350
Silver Spring, MD 20910
info@hepatitisfoundation.org
http://www.hepfi.org

**National Cervical Cancer Coalition (NCCC)**
1-800-685-5531
PO Box 13827
Research Triangle Park, NC 27709
http://www.nccc-online.org

**National Network of Libraries of Medicine**
*Access to online databases on HIV and other topics*
1-800-338-7657
http://nnlm.gov

**Project Inform**
*Information, inspiration, and advocacy for people living with HIV/AIDS*
1-800-822-7422
205 13th Street, No. 2001
San Francisco, CA 94103
http://www.projectinform.org/

**BREAST CANCER EDUCATION AND RISK ASSESSMENT**

**American Cancer Society**
1-800-ACS-2345 (1-800-227-2345)
http://www.cancer.org

**Breast Cancer Action**
415-243-9301
657 Mission Street, Suite 302
San Francisco, California 94105
info@bcaction.org
http://www.bcaction.org
Resources—Common Cancers Among Women

Breast Cancer Risk Tool (Gail Model)
http://www.cancer.gov/bcrisktool/

Breast Cancer Surveillance Consortium Risk Calculator
https://tools.bcsc-scc.org/BC5yearRisk/calculator.htm

Cancer Information Service, National Cancer Institute
1-800-4-CANCER (1-800-422-6237)
BG 9609 MSC 9760
9609 Medical Center Drive
Bethesda, MD 20892-9760
http://www.cancer.gov

Decision Aids (Breast and Ovarian Cancer)
Ottawata Hospital Research Institute

International Gynecologic Cancer Society
http://www.igcs.org

MammaCare Foundation
Breast models and teaching tools
(352) 375-0607
930 NW 8th Avenue
Gainesville, FL 32601
http://www.mammacare.com

National Alliance of Breast Cancer Organizations (NABCO)
1-800-80NABCO (1-800-806-2226)
9 East 37th Street, 10th Floor
New York, NY 10016

National Cancer Network
Guidelines for breast and gynecologic cancer care
http://www.nccn.org/

National Coalition for Cancer Survivorship
info@canceradvocacy.org
http://www.canceradvocacy.org

Social Media
Breast Cancer Chat (Support on Twitter)
#BCSM

Society of Gynecologic Oncology (Guidelines)
https://www.sgo.org/clinical-practice/guidelines/
DIET AND NUTRITIONAL GUIDELINES

Dietary Guidelines for Americans
http://www.health.gov/dietaryguidelines/

MyPlate & Food Pyramid Resources
http://www.nutrition.gov/smart-nutrition-101/myplate-food-pyramid-resources

Office of Dietary Supplements (ODS), National Institutes of Health
http://ods.od.nih.gov

U.S. Food and Drug Administration (FDA), Center for Food Safety and Applied Nutrition
http://www.fda.gov/Food/

GENERAL INFORMATION ON WOMEN’S HEALTH ISSUES

Alzheimer’s Disease Education and Referral (ADEAR) Center
1-800-438-4380
adear@nia.nih.gov
http://www.alzheimers.gov

Center for Women Policy Studies
(202) 872-1770
1776 Massachusetts Avenue, NW Suite 450
Washington, DC 20036
cwps@centerwomenpolicy.org
http://www.centerwomenpolicy.org
Healthy People 2020
  http://www.healthypeople.gov/

Institute for Women’s Policy Research
  Status of women in the United States (reproductive and health reports)
  http://statusofwomendata.org

National Institute of Women’s Health Office of Research (ORWH)
  (202) 682-2640
  1413 K Street NW, 4th Floor
  Washington, D.C. 20005
  nwhn@wwhn.org
  http://www.womenshealthnetwork.com

National Women’s Health Resource Center
  1-877-986-9472
  157 Broad Street, Suite 200
  Red Bank, NJ 07701
  info@healthywomen.org
  http://www.healthywomen.org

North American Menopause Society (NAMS)
  (440) 442-7550
  5900 Landerbrook Drive, Suite 390
  Mayfield Heights, OH 44124
  info@menopause.org
  http://www.menopause.org

Office on Women’s Health
  1-800-994-9662
  200 Independence Avenue, S.W.
  Washington, DC 20201
  http://www.womenshealth.gov/

Ovarian Cancer National Alliance
  (202)-331-1332
  (866) 399-6262 (toll free)
  ocna@ovariancancer.org
  http://www.ovariancancer.org

Society for Women’s Health Research
  http://swhr.org
INTEGRATIVE/COMPLEMENTARY MEDICINE

National Certification Commission for Acupuncture and Oriental Medicine (NCCAOM)
(904) 598-1005
76 South Laura Street
Suite 1290
Jacksonville, FL, 32202, USA

Natural Standard Database
https://naturalmedicines.therapeuticresearch.com/databases.aspx
National Center for Complementary and Integrative Health
1-888-644-6226
nccih-info@mail.nih.gov
nccih.nih.gov

Therapeutic Touch NH-PAI, Inc.
Nurse healers: Professional Associates International
(518) 325-1185
TTIA Box 130
Delmar, NY 12054
info@therapeutic-touch.org
http://www.therapeutic-touch.org

OSTEOPOROSIS

Foundation for Osteoporosis Research and Education (FORE)
510-832-2663
888-266-3015
1814 Franklin Street, Suite 620
Oakland, CA 94612
info@americanbonehealth.org

National Osteoporosis Foundation (NOF)
1-800-231-4222
1150 17th Street, NW Suite 850
Washington, DC 20036
http://nof.org/

Osteoporosis Risk Calculators
https://riskcalculator.fore.org/default.aspx

University of Washington’s Osteoporosis Risk Assessment (OsteoEd)
http://depts.washington.edu/osteoed/tools.php?type=orai

World Health Organization’s Fracture Risk Assessment Tool
http://www.shef.ac.uk/FRAX/
SEXUALITY

National Vulvodynia Association
(301) 299-0775
P.O. Box 4491
Silver Spring, MD 20914
http://www.nva.org

Sexuality Information and Education Council of the United States (SIECUS)
(212) 819-9770
90 John Street, Suite 402
New York, NY 10038
http://www.siecus.org

The Women’s Health Foundation
(773) 305 8200
32 W. Deming Place
Chicago, IL 60614-2676

WOMEN WITH DISABILITIES

Center for Research on Women With Disabilities
(832) 819-0232
Baylor College of Medicine
One Baylor Plaza, BCM 635
Houston, TX 77030
crowd@bcm.edu
http://www.bcm.edu/crowd

Health Promotion for Women With Disabilities
(610) 519-6828

Villanova University College of Nursing
800 Lancaster Avenue
Villanova, PA 19085
http://www1.villanova.edu/villanova/nursing/community/womendisabilities.html

Initiative for Women With Disabilities
(212) 598-6429
iwd@nyumc.org
TIPS ON INTERNET RESOURCES

- Check the date of information or data you find on the Internet. Some may be outdated, especially for fast-changing research topics, such as human papillomavirus, hormone replacement therapy, or abnormal Pap smear findings.
- Be aware that some sites have more reliable information than others. Some sites are juried, or reviewed by organizations to control content; others are not.
- Surf at your own risk. Be discriminating about the information you receive, and confirm it with a health practitioner. Look at other sites for confirmation as well.

In addition to the Internet sites previously listed in this guide are the following:

**Division of STD Prevention, Centers for Disease Control and Prevention (CDC)**
http://www.cdc.gov/nchstp/dstd/dstdp.html

**Mayo Clinic Health Oasis**
(507) 284-2511
200 1st Street SW
Rochester, MN 55905
http://www.mayohealth.org

**U.S. National Library of Medicine**
8600 Rockville Pike
Bethesda, MD 20894
http://www.nlm.nih.gov/
adenocarcinoma: A malignant tumor originating in the epithelial cells of glandular tissue forming glandular structures.

adenocarcinoma in situ: A group of malignant cells that may become cancer and spread to nearby normal tissue.

adjuvant: Cancer treatment that is not the primary form of treatment for removal of cancerous tissue. It is instead a systemic treatment that is initiated after surgery to prevent return of the cancer by killing cells that may have traveled elsewhere in the body.

agglutination: Clumping together. An abnormal sign in evaluation of sperm function that could indicate an immune response.

alternative and complementary therapies: Nontraditional approaches to healing and health care. Frequently, these therapies are philosophically different from Western medicine. They often involve interventions believed to induce healing from within to allow the body, mind, and spirit to heal.

Alternative therapy: Modalities used in place of conventional health care.

Complementary therapy: Modalities used in conjunction with conventional health care.

amenorrhea: Absence of menstruation.

anovulatory cycle: Menstrual cycle in which no egg is released from the ovary.

artificial menopause: A condition brought on by surgical removal of the ovaries, radiation therapy, or chemotherapy treatment that renders the ovaries nonfunctional.

aspiration: Withdrawal by gentle suction.

assisted hatching: A micromanipulation technique used in assisted reproductive technology interventions in which a hole is made in the outer covering of the egg to assist the sperm to penetrate and fertilize it.

assisted reproductive technologies (ARTs): The various new technologies for assisting infertile couples to conceive.

asymptomatic: Absence of symptoms in the presence of a disease.

atherosclerosis: Buildup of fatty plaque on the walls of an artery, stiffening the artery and reducing blood flow.

basal body temperature (BBT) charting: Method to determine when ovulation has occurred; used in natural family planning and fertility.

basal thermometer: Specially calibrated instrument to measure body temperature in relation to ovulation.

benign: Noncancerous.
bimanual examination: Part of the standard examination of the female pelvic organs in which the examiner inserts two fingers into the vagina, pressing with the opposing hand on the abdomen. In this way, the ovaries and uterus are palpated for abnormalities.

biopsy: A procedure to remove a small piece of tissue for microscopic analysis by a specialist.

bisphosphonates: Synthetic forms of a class of compounds found in the body that inhibit the process of bone resorption; used to prevent and treat postmenopausal osteoporosis.

bone density screening: Measurement of bone mass by using low-dose x-ray procedures.

**BRCA1 and BRCA2:** Human genes that produce tumor suppressor proteins. These proteins help repair damaged DNA and, therefore, play a role in ensuring the stability of the cell’s genetic material. When either of these genes is mutated or altered, such that its protein product either is not made or does not function correctly, DNA damage may not be repaired properly. As a result, cells are more likely to develop additional genetic alterations that can lead to cancer. Specific inherited mutations in **BRCA1** and **BRCA2** increase the risk of female breast and ovarian cancers, and they have been associated with increased risks of several additional types of cancer.

breast self-examination (BSE): Monthly examination advised for all adult women in which women examine their breasts for any changes by using both visual inspection and palpation.

carcinoma: Cancer of the tissue that covers body surfaces, both internal and external.

carcinoma in situ (CIS): Carcinoma that has not yet invaded surrounding tissue.

cervical intraepithelial neoplasia (CIN): Also known as cervical dysplasia; abnormal changes in the cells on the surface of the cervix.

cervicitis: Inflammation of the cervix caused by infection, injury, or irritation.

cervicography: Diagnostic technique in which photographs are taken of the cervix.

cholesterol: A substance that is manufactured by the liver as well as derived from animal fat. Hormones such as estrogen and progesterone are made from cholesterol. It is also a part of cell membranes. Cholesterol is transported through the bloodstream attached to lipoproteins.

chronic fatigue syndrome: A constellation of symptoms characterized by debilitating fatigue and flu-like symptoms. The cause is not well understood but is thought to be multifactorial.

climacteric: The period, which can last from months to years, when the menstrual cycle of women becomes irregular, hormone levels fluctuate and eventually decrease, and periods cease altogether. During this time, the woman passes from a reproductive to a nonreproductive state.

clinical breast examination (CBE): A breast examination performed by a licensed professional trained to do breast examinations.

clitoris: A small, pea-sized, hooded, erectile structure located on the vulva above the vagina. It is the anatomic homologue of the penis in the male and is highly responsive to sexual stimulation.

Colles’ fracture: A fracture of the radius that occurs when a person extends a hand to break a fall.

colposcopy: Technique for viewing the cervix under magnification, making it possible to see structures not visible to the naked eye. Used to evaluate the cervix and vagina.

columnar epithelium: Glandular tissue of the cervix that is composed of tall, narrow cells.
cone biopsy: Surgery to remove a sample of abnormal tissue from the cervix.

congenital: Existing at or dating from birth, but not due to heredity.

conization of the cervix: A surgical procedure in which a part of the cervix surrounding the cervical canal is removed.

core biopsy: Also known as core needle biopsy (CNB). Involves using a hollow needle to withdraw small cylinders (or cores) of tissue from an abnormal area in the breast. A CNB is most often done in the healthcare provider’s office with local anesthesia using ultrasound to guide the needle into the right place.

corpus luteum: A structure formed after ovulation by the remaining tissue of the follicle. Its main function is secretion of progesterone, which prepares the uterine lining for implantation by a fertilized embryo. The corpus luteum helps support the developing embryo, or it disintegrates if fertilization has not occurred.

cryopreservation: Use of a medium, usually liquid nitrogen, to store something in a frozen state. Refers to preservation of embryos in assisted reproductive technology.

cryosurgery: Use of a cold source to freeze abnormal tissue.

cryotherapy: A treatment that involves freezing of abnormal tissue; commonly used to remove abnormal cervical cells as well as genital warts from the vagina and external genitalia.

Depo-Provera: A synthetic progesterone (medroxyprogesterone acetate) used as an injectable method of birth control.

diethylstilbestrol (DES): A synthetic estrogen that was once given to women early in pregnancy to prevent miscarriage. It was taken off the market because of its multiple effects on the offspring of women who took it, including increased risk of a rare type of vaginal cancer and increased rates of infertility in male and female offspring.

dilatation and curettage (D&C): A vaginal procedure in which the cervical canal is stretched enough to permit the passage of a sharp instrument (a curette). The curette is used to scrape the endometrium to empty the uterine contents or to obtain tissue for examination.

dysmenorrhea: Painful menstrual cramps.

dyspareunia: Pain with sexual intercourse.

dysplasia: Abnormal cell growth that can be a precancerous condition.

dysuria: Painful urination.

ectopic pregnancy: A pregnancy that implants and develops outside the uterus, most often in the fallopian tube. This can be life-threatening and requires immediate intervention.

embryo: Fertilized egg. The developing human organism is an embryo from approximately week 1 of development through week 8.

emergency contraception pill (ECP): Also known as the morning after pill, this type of pill is used to deter pregnancy in case of an accidental method failure or unprotected intercourse. Specific birth control pill formulations are used to interrupt fertilization and implantation.

endocervical canal: Canal that runs down the center of the cervix and opens into the vagina on one side and into the uterus on the other.
endometrial biopsy: A test done to sample the uterine lining. Used in infertility evaluation for evidence that ovulation has occurred. Also used to diagnose abnormalities of the uterine lining, such as uterine cancer.

Procedure: Usually done about 10 days after a rise in basal body temperature. A small cannula is inserted through the cervical canal into the uterus, where a sample of the lining is gathered by suction or curettage. Mild to moderate cramping can be expected. Use of a nonsteroidal anti-inflammatory drug beforehand is helpful. A vasovagal response may occur; having the patient elevate the legs and take time to come to an upright position usually abates this response. Nausea and vomiting or fainting may occur if the reaction is more pronounced.

endometrial hyperplasia: Abnormally rapid and extensive growth of the uterine lining.

endometrioma: Implant of endometrial tissue outside the uterus; found in endometriosis.

endometriosis: Tissue that closely resembles the endometrial tissue is located outside of the uterus in the pelvic cavity. Symptoms may include pelvic pain or pressure, dysmenorrhea, dyspareunia, and infertility.

endometrium: Inner lining of the uterus that responds to the cyclic influence of hormones during the menstrual cycle.

endorphins: Hormones found in the brain that give a sensation of well-being and affect pain perception and emotion.

energy healing: A variety of techniques and disciplines that are believed to augment, modulate, stimulate, or improve certain deficiencies or blocks in the human energy system.

enzyme: A protein that is needed for specific chemical reactions in the body but is not changed by the reaction and therefore can be used again.

epithelial cells: Cells that make up the type of tissue that covers the surfaces of the body and its internal organs.

estrogen: Group of similar hormones that stimulate the maturation of egg follicles, leading to ovulation.

Three forms of estrogen are found in the human body: estradiol, estriol, and estrone. Synthetic forms are used in formulations of the birth control pill and standard hormone replacement therapy.

estrogen replacement therapy (ERT): Use of a form of the hormone estrogen to create a state of hormone balance in a woman who has stopped menstruating, similar to her hormonal state before menopause. ERT is given to women during and after menopause to prevent hot flashes, mood changes, osteoporosis, and genitourinary symptoms. Use of estrogen alone by a woman who still has a uterus increases the risk of uterine cancer.

expedited partner therapy (EPT): The clinical practice of treating the sex partners of patients diagnosed with chlamydia or gonorrhea by providing prescriptions or medications to the patient to take to her or his partner without the healthcare provider first examining the partner.

false-negative: Failure of a test to detect an existing abnormality.

false-positive: Indication of abnormality when none exists.

fertility awareness methods (FAMs): Birth control methods that identify the beginning and end of the fertile period of the menstrual cycle.
fibroadenoma: A benign tumor that contains glandular and fibrous elements and is commonly found in the breast.

fibrocystic breast disease: Not really a disease but rather a condition in which fluid-filled cysts enlarge in conjunction with the second half of the menstrual cycle, causing discomfort and swelling of the breasts.

fibroid: Fibrous, encapsulated connective tissue tumor, especially of the uterus (leiomyoma).

fine-needle aspiration (FNA): Technique for evaluating breast masses thought to be fluid-filled (cysts) by attempting to remove fluid with a fine needle.

folic acid: One of the B vitamins; involved in normal cell growth.

follicle: Group of tissues in the ovary that develop around an immature egg and are responsible for producing hormones and growth-promoting factors. Rupture of the follicle from the ovary is ovulation.

follicle-stimulating hormone (FSH): Hormone produced by the pituitary gland that targets the ovary and promotes growth of ovarian follicles.

fomite: An object, such as clothing or towels, that can provide a location for transmission of infection.

galactorrhea: Spontaneous discharge of milk from the breasts not associated with breast-feeding; may be a symptom of a pituitary tumor.

gamete: A reproductive cell (egg or sperm).

gamete intrafallopian transfer (GIFT): Transfer of a retrieved egg, along with prepared sperm, into the fallopian tube of a woman.

genitourinary syndrome of menopause (GSM): A collection of signs and symptoms associated with a decrease in estrogen and other sex steroids involving changes to the labia majora/minora, clitoris, vestibule/introitus, vagina, urethra, and bladder.

genetic counseling: Education and assessment of heritable risk factors provided by specially trained health professionals to help people make informed decisions based on genetic knowledge.

gland: Organized group of cells that secretes substances such as hormones.

gonadotropin: Substance produced by the pituitary gland that stimulates the gonads (ovaries or testes).

gonadotropin-releasing hormone (Gn-RH): Hormone produced by the hypothalamus that stimulates the pituitary gland to release gonadotropins.

gravidity: Total number of a woman’s pregnancies.

health promotion: The motivation to increase well-being and actualize health potential.

her2 gene: The her2 gene makes HER2 proteins. HER2 proteins are receptors on breast cells. Normally, HER2 receptors help control how a healthy breast cell grows, divides, and repairs itself. However, in about 25% of breast cancers, the her2 gene does not work correctly and makes too many copies of itself (known as her2 gene amplification), resulting in too many HER2 receptors (HER2 protein overexpression) and uncontrolled breast cell growth and division.

high-density lipoprotein (HDL): A protein that carries fats and cholesterol through the bloodstream. Referred to as good cholesterol because it transports cholesterol out of tissues and allows it to be excreted.
hormone: Glandular secretion that controls the activity of tissues and organs.

hormone replacement therapy (HRT): Use of estrogen and progestin to replace hormones no longer produced after menopause.

hot flash (flush): The transient sensation of warmth, redness, or perspiration experienced by some women during or after menopause. It results from autonomic vasomotor disturbances that accompany the changes that are taking place in the neurohormonal activity of the ovaries, the hypothalamus, and the pituitary gland. A hot flush is a visible red flush of the skin and perspiration; a hot flash is a sudden warm sensation in the neck, head, and chest.

human chorionic gonadotropin (hCG): Hormone secreted in the urine and into the bloodstream of pregnant women. Its detection is the basis of both urine and serum pregnancy tests.

hyperplasia: An increase in the number of cells.

hypothalamus: Part of the brain that regulates a number of different body processes – including body temperature; appetite; thirst; and hormonal stimulation to the ovaries, thyroid gland, and adrenal glands – by way of its action on the pituitary gland.

hysterosalpingogram: A procedure used to indirectly visualize the reproductive tract of a woman and can be used to achieve patency of a blocked tube.

Procedure: A radiopaque iodine-based dye is injected through the cervix and follows the normal pathway into the uterus, fallopian tubes, and abdominal cavity. The procedure should be scheduled for the first half of the menstrual cycle. It can be a very uncomfortable procedure, especially if the tubes are blocked. Vasovagal reactions may occur after the dye is injected. This is an outpatient procedure.

Results: It reveals abnormalities of the internal configuration of the uterus, such as fibroids or bicornate uterus. It also determines patency of the tubes, and it can sometimes clear an obstruction.

hysteroscopy: A procedure in which contrast medium, usually iodine-based, is used to distend the uterine cavity. Visualization of the structures is possible by using a hysteroscope, a lighted scope that is inserted through the cervix into the uterus. With hysteroscopy, one can perform a simple biopsy or remove a small polyp in the office setting. It can also be used for more complex operative procedures on the uterine lining, such as electrocautery, laser, and fibroid removal. These procedures would be performed in the operating room. Mild to moderate cramping often accompanies hysteroscopy.

insemination: Introduction of sperm into the female reproductive tract.

in situ: Used in this course in reference to carcinoma in situ, an early stage of cancer that is confined to the immediate area in which it began. In breast cancer, it means that the cancer remains confined to the ducts or lobules and has not invaded the surrounding fatty tissue or spread to other organs.

intracytoplasmic sperm injection (ICSI): A micromanipulation technique used during assisted reproductive technology interventions in which a single sperm is injected into an egg, bypassing the egg’s outer coating.

intraductal: Abnormal breast cells involving only the lining of a milk duct. These cells have not spread outside the duct into the normal surrounding breast tissue.

in vitro: “In glass” or outside the human body; usually refers to fertilization of an egg in assisted reproductive technologies.
in vitro fertilization/embryo transfer (IVF/ET): The oldest of the assisted reproductive technologies in which eggs are harvested from the ovary through the vaginal wall, placed in a laboratory environment, and fertilized. Then the fertilized eggs are transferred to the uterus for implantation.

**Kegel exercises:** Exercises performed to strengthen the muscles of the pelvic floor and control urination.

**laparoscopy:** Surgical procedure in which a fiber-optic scope and instruments are inserted through a small incision near the umbilicus to view pelvic structures and remove abnormal tissue. It is also used as one method of evaluating the fallopian tubes.

**laparotomy:** Abdominal surgery.

**laser:** An electro surgical instrument in which electricity is converted to light, which is concentrated and thereby produces heat. The light of a laser is ordinary light that has been controlled and organized to emit one wavelength. The light travels through space in a beam, which can be finely focused to intensify its effects. Laser light can be used to cut, vaporize, coagulate, or fulgurate (superficial charring of surface) tissue. Heat is created when the tissue absorbs the radiation.

**lesion:** Any abnormal tissue.

**libido:** Sexual drive.

**low-density lipoprotein (LDL):** A protein that carries cholesterol and tends to promote deposits on arterial walls. Also known as bad cholesterol.

**luteinizing hormone (LH):** One of the hormones secreted by the pituitary gland that is essential to the development of the ovarian follicle and ovulation.

**lymph nodes:** Glands of the lymphatic system that supply white blood cells to the general circulation and filter out bacteria and foreign particles from the lymph fluid.

**macrocalcifications:** Calcium deposits in the breast tissue detected by mammography; they often result from degenerative changes within the breast tissue following old injuries, inflammations, or aging of the breast arteries and are usually not related to malignancy.

**malignant:** Cancerous.

**mastalgia:** Painful breasts. Also termed mastodynia.

**medical abortion:** Use of drugs to induce abortion, rather than surgical termination of pregnancy.

**menarche:** Initiation of menstrual cycles with the first menstrual period.

**menopausal hormone therapy (MHT):** Hormonal therapy, usually estrogen and progestin, prescribed for menopausal symptoms.

**menopause:** The actual permanent cessation of menstrual cycles, which is diagnosed after 1 year without menses.

**menses:** Periodic vaginal discharge of bloody fluid from a nonpregnant uterus; occurs from the age of puberty to menopause.

**metastasis:** Spread of cancer from the original site (referred to as the primary cancer) to a lymph node or distant organ.
**microcalcifications:** Detected by mammography, specks of calcium in the breast tissue that may be found in areas of rapidly dividing cells. When many microcalcifications are present in a cluster, they may indicate a small cancer; approximately one half of the cancers detected appear as these clusters.

**micromanipulation:** Procedure used to manipulate the tiny sperm or egg to improve chances of fertilization.

**minilaparotomy:** Female sterilization procedure in which the fallopian tubes are cauterized or blocked through a small abdominal incision.

**mittelschmerz:** Abdominal pain in the region of an ovary during ovulation that usually occurs midway through the menstrual cycle.

**myometrium:** Smooth muscle layer of the uterine wall.

**natural progesterone:** A manufactured form of progesterone derived from plant sources, whose chemical structure is identical to that of the progesterone produced by the female body.

**neoplasm:** A new and abnormal formation of tissue.

**node negative:** Results of the biopsy of lymph nodes reveal that the lymph nodes are free of cancer. This is an indication that the cancer is less likely to recur.

**node positive:** Results of the biopsy of lymph nodes reveal that cancer has spread to the lymph nodes under the arm on the same side as the original tumor.

**nullipara:** Woman who has never been pregnant.

**oophorectomy:** Excision of an ovary.

**oocyte:** Developing ovum or egg.

**open biopsy:** Surgical removal of all or a portion of an abnormal breast mass, usually with the patient under general anesthesia.

**oral micronized progesterone:** A specially formulated type of progesterone that has the same structure as the progesterone produced by women’s bodies. The particles are very finely ground. This form of progesterone is better absorbed into the bloodstream than other oral forms of progesterone.

**os:** Opening of the cervical canal.

**osteoblasts:** Bone cells that are responsible for laying down new bone.

**osteoclasts:** Bone cells that are responsible for breaking down old bone in a process called remodeling.

**osteoporosis:** A condition in which a large amount of bone mass is lost, leading to brittle, porous bone that can be easily fractured.

**ovarian follicle:** See “follicle.”

**over-the-counter (OTC) drugs:** Medications sold without the need for a prescription.

**parity:** The number of past pregnancies that have reached viability, regardless of whether the infant or infants were alive or stillborn.

**pelvic inflammatory disease (PID):** A serious infection of the reproductive organs, often caused by infection with sexual pathogens. Tissue destruction can occur without symptoms. Infertility is a major long-term consequence.

**perimenopause:** A period of transition of changing ovarian activity before menopause and through the first few years of amenorrhea.
**pessary**: A device placed inside the vagina to function as a supportive structure for the uterus.

**phytoestrogens**: Plant-derived compounds that have a weak estrogenic effect in the human body. They are found naturally in whole plant foods and herbs and sometimes used in the management of menopause as an alternative or complement to conventional hormone replacement therapy.

**pituitary desensitization**: Medical intervention in which drugs are used during assisted reproductive technology interventions to suppress the release of hormones from the pituitary gland, which would result in ovulation, before all the multiple eggs are matured.

**pituitary gland**: Structure at the base of the brain that receives instructions by means of hormones from the hypothalamus and sends hormonal messages to a number of glands and organs, including the ovaries.

**postcoital test (PCT)**: Part of infertility workup that is used to evaluate aspects of sperm function and cervical mucus.

*Procedure*: The test must be timed carefully with the immediate preovulatory phase; basal body temperature should not yet show an increase. Sexual intercourse should have taken place at home either the night before or morning of the examination. A sample of mucus from the exocervix and endocervix is obtained with a small syringe during a pelvic examination. Evaluation under the microscope reveals the type of mucus present and the number and motility of sperm. A normal sperm count is a minimum of 5 to 10 motile sperm per high-power field. Conducive mucus should be present.

*Results*: If the mucus is favorable and the semen analysis reveals normal findings, more specialized testing is needed to determine sperm-mucus incompatibilities or sperm capacitation problems.

**precursor lesion**: Change in the appearance or nature of a cell before it becomes cancerous.

**pre-exposure prophylaxis** (PrEP): A way for people who do not have HIV, but are at substantial risk for it, to prevent HIV infection by taking a pill every day.

**pre-exposure vaccination**: The administration of antigenic material to stimulate an individual’s immune system to develop adaptive immunity to a pathogen. Vaccines can prevent or ameliorate morbidity from infections.

**premenstrual dysphoric disorder (PMDD)**: A severe form of premenstrual syndrome that is characterized by heightened emotional symptoms, such as depression, anxiety, anger, and persistent irritability.

**premenstrual syndrome (PMS)**: Also called premenstrual tension, a collection of symptoms that occur during the second phase of the menstrual cycle that improve with the onset of menses. Causes are not well understood.

**primary tumor**: Original site of a cancer.

**prodromal symptom**: An early sign of an outbreak of disease. It most typically refers to the itching or skin sensitivity that often precedes an outbreak of herpes.

**progestin/progestogen**: Synthetic forms of the naturally occurring hormone progesterone, which is produced by the ovaries. Used in hormone replacement therapies and hormonal birth control methods.

**proliferation**: Rapid and repeated cellular reproduction.
**prostaglandin inhibitors**: A group of drugs, used to treat inflammatory diseases, that inhibit synthesis and activity of prostaglandins. These drugs have been approved by the U.S. Food and Drug Administration for treatment of menstrual pain. These drugs do have side effects. Although many are over-the-counter drugs, they should be used intelligently and monitored by the patient and healthcare practitioner. Ibuprofen (Motrin), indomethacin (Indocin), and mefenamic acid (Ponstel) are examples.

**prostaglandins**: Local substances produced by the tissues and found in many parts of the body. Prostaglandins play an important role in menstrual cramps. They may cause vasodilation and pain in breast tissue. They also play a role in body water content, appetite, and body temperature.

**receptor**: Part of the molecular structure of a cell. Substances circulating in the bloodstream whose molecular shape fits a receptor’s shape can bind to the cell membrane and activate reactions in the cell. This is the process by which hormones produce their effects. Certain tumors also have hormone receptors that recognize estrogen or progesterone. If a tumor has receptor sites for hormones, this information is used in making decisions about treatment options.

**recommended dietary allowances (RDAs)**: Recommended nutrient intakes estimated to meet the needs of almost all of the healthy people in the population.

**refractory period**: The period after orgasm during which another orgasm cannot occur. This period varies between men and women, and it can change with age and other factors.

**relaxation**: The absence or alleviation of mental, physical, and emotional tension through purposeful activities that quiet the mind and the body.

**rugae**: Folds in the vaginal mucosa.

**safer sex**: A commonly used way of acknowledging that there is no such thing as totally safe sex. Safer sex describes practices designed to minimize transfer of any body fluids (semen, blood, vaginal secretions) between partners.

**selective estrogen receptor modulators (SERMs)**: A classification of drugs that act as estrogen agonists or estrogen antagonists and are commonly used in place of estrogen by postmenopausal women.

**semen evaluation**: At least two semen samples are collected on separate days by masturbation. Each sample should be collected after abstaining from ejaculation for a minimum of 48 hours but not longer than 3 to 4 days. The ejaculate should be collected in a sterile container and should be examined within 1 hour of collection. Analysis involves a complex array of tests to evaluate many aspects of sperm health, including count; motility; shape; clumping; presence of bacteria, antibodies, or other elements; and biochemical analysis.

**seropositivity**: The presence of a certain antibody in a blood sample.

**sexual history**: Past and present health conditions, lifestyle behaviors, knowledge, and attitudes related to sex and sexuality.

**sexually transmitted infection (STI)**: Also termed sexually transmitted diseases. Such infections are spread primarily by intimate contact between partners, through either skin-to-skin or bodily fluid contact.

**sexual response cycle**: The phases of physical changes that occur in response to sexual stimulation and sexual tension release.
sonogram: Also called ultrasound, a procedure that uses sound waves to form an image of internal structures. Hollow or fluid-filled structures appear black, and more solid structures appear white.

sonohysterography: A procedure in which saline solution is inserted into the uterine cavity, distending the cavity. Ultrasound is then used to observe structures such as polyps, submucous myomas, and adhesions.

speculum: Instrument used during a pelvic examination to allow visualization of the cervix and vaginal lining by holding the vaginal walls apart.

sperm penetration assay (SPA): Part of a semen evaluation for male factor infertility that tests the ability of sperm to shed their protein coating and release enzymes that are needed to penetrate the coating of an egg.

squamocolumnar junction: Area on the cervix where the squamous tissue of the outer aspects of the cervix and the glandular tissue arising in the cervical canal meet. Also called the transformation zone. This area is characterized by rapid cell turnover and is a common site for development of cancerous or precancerous cells.

squamous cell carcinoma: Any of various carcinomas that arise from a kind of flat, scaly epithelial cell found in organs such as the skin, cervix, oral cavity, larynx, and vulva.

squamous epithelium: Flat, platelike epithelial cells that cover the internal and external surfaces of the body. They are one of two types of cells that make up the cervix; there, they cover the outer surface of the cervix.

squamous metaplasia: A normal process of cell growth and replacement in which squamous tissue slowly replaces the glandular tissue that arises in the cervical canal.

squamous tissue: A type of tissue that lines many internal and external body surfaces. It is a smooth, flat, and nonglandular type of tissue.

staging: A system of defining how widespread a cancer is by using information learned through diagnostic techniques. This information is used to determine appropriate treatment.

steroid: A group name for chemicals that have a particular molecular configuration and contain cholesterol as part of their structures. A number of hormones, including the sex hormones, are steroids.

stress urinary incontinence (SUI): A loss of urine that occurs with increased intra-abdominal pressure, such as from sneezing, laughing, or coughing.

suppressive therapy: Daily antiviral medication taken by someone with a viral infection to stay symptom-free longer or reduce the frequency of recurrent symptoms. Often used for patients with genital herpes.

surrogate: A substitute.

thromboembolic disease: A disorder in which blood clots can travel to various organs, causing blockage of the circulatory system. Sites of blockage can include the heart (myocardial infarction), the brain (stroke), the lungs (pulmonary embolism), and other organs.

toxic shock syndrome (TSS): A severe, acute disease most often caused by Staphylococcus aureus that has been associated with high-absorbency tampon use during menstruation.

transformation zone: See “squamocolumnar junction.”
transvaginal: Through the vagina, referring to the current methods of retrieving eggs from the ovary. This route is also used for hysterectomy.

**tubal embryo transfer (TET):** A variation of the gamete intrafallopian transfer procedure in which the egg is fertilized before being placed in the fallopian tube.

**tubal patency:** Unobstructed fallopian tubes.

**tubal reanastomosis:** A surgical procedure in which the cut ends of the fallopian tubes are brought together to reverse a previous sterilization.

**ultrasound:** Use of high-frequency sound waves to obtain images of internal structures. Used in conjunction with other diagnostic and surgical procedures to guide probes and instruments. Used for diagnosis of breast disease and pelvic reproductive abnormalities and to assist in monitoring women undergoing assisted reproductive technologies. (*See also* “sonogram.”)

**vacuum aspiration:** Removal of tissue by the creation of negative pressure through the removal of air.

**vaginal flora:** Microorganisms normally found in the vagina, including *Staphylococcus epidermidis*, *Lactobacillus*, *Streptococcus mitis*, and *Corynebacteria*.

**vaginismus:** Painful, unintentional muscle spasms in the thighs, pelvis, and vagina that lead to constriction of the pelvic muscles, often making sexual intercourse and pelvic examination impossible. Usually occurs when a woman senses that something is about to penetrate the vagina and is typically associated with prior emotional or physical trauma.

**vas deferens (ductus deferens):** Tube in the male reproductive system through which sperm pass from the testes to the ejaculatory duct and then into the urethra.

**vasectomy:** Surgical removal or blockage of the vas deferens, resulting in male sterilization.

**vulvar self-examination (VSE):** A systematic examination of the vulva by the woman.

**zygote:** Term for an early fertilized egg before implantation.

**zygote intrafallopian transfer (ZIFT):** An assisted reproductive technology technique in which fertilization of the egg is accomplished before transfer to the fallopian tube. Also called tubal embryo transfer.