

# BREAST CANCER

— *overview of the disease*

■ By A. STANLEY, MRPHARMS

*The incidence of breast cancer is increasing, and it is the most common cause of death in women between the ages of 35 and 55. This article outlines the epidemiology, pathology, staging and prognosis of this disease*

*Coloured mammogram (X-ray) of a side view of a breast showing a cancerous tumour (blue, upper centre)*

**B**reast cancer is the most common form of cancer among women in westernised countries. It is responsible for 30 per cent of all cancer in women<sup>1</sup> and it is the third most common cancer in the world with 10 per cent of the global cancer burden.<sup>2</sup>

The incidence of breast cancer varies widely around the world, with North America and European countries having the highest rates.<sup>3</sup> In 2000, approximately 36,000 new cases of breast cancer were diagnosed in England and Wales and in 2002 there were 11,500 deaths from the disease.<sup>1</sup> The annual incidence is 114 cases per 100,000 of the population.<sup>1</sup> It is estimated that one in nine women in the UK will develop breast cancer at some point in their life.<sup>1</sup> Breast cancer is the most common cause of cancer death in women.<sup>1</sup>

Between two thirds and three quarters of all breast tumours are stimulated by oestrogen. The risk of breast cancer begins at

puberty and rises slowly until the perimenopausal years when it increases dramatically, levelling off at about the age of 75. A significant proportion of women with breast cancer will die of the disease and breast cancer is the most common cause of death in women aged 35 to 55.<sup>4</sup>

While the incidence rate has increased by 15 per cent in the 10 years to 2000, the death rate from breast cancer has been in steady decline since its peak in the mid-1980s. In 2002 the mortality rate stood at 30 per 100,000 women.<sup>1</sup> The five year age-standardised relative survival for women diagnosed between 1991 and 1995 in England and Wales was 73 per cent.<sup>1</sup> This rose to 78 per cent in the period 1996 to 1999.<sup>1</sup> These statistics demonstrate that advances in breast cancer prevention,<sup>5</sup> screening<sup>6</sup> and the treatment of primary breast cancer with appropriate surgery, ovarian ablation, anti-oestrogen therapy in women with the suitable receptor status and adjuvant chemotherapy<sup>7</sup> have dramatically improved the outlook for patients with this disease. Over 50 per cent of patients with early breast cancer survive for 10 years or more.<sup>4,7</sup> Indeed, there are a growing number of

women who have lived 30 years or more with breast cancer.

Breast cancer is a disease with a long natural course and, despite all the improvements in prevention and treatment, many women will continue to develop or present with locally advanced or widespread metastatic breast cancer. Patients presenting with stage III (locally advanced disease unsuitable for surgery) or stage IV (metastatic) disease cannot currently be cured. The aim of treatment for advanced breast cancer patients is thus palliation, firstly to control symptoms and sometimes also to prolong life.

**Breast cancer in men** Breast cancer can affect men as well as women. Male breast cancer accounts for approximately 1 per cent of the total cases.

## ■ RISK FACTORS

**T**he reported risk factors which have been proven to have some bearing on the likelihood of an individual developing breast cancer are listed in Panel 1 (p410). It is important always to remember that these are relative risks not absolute risk factors (ie,

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having one or more risk factors does not mean that a patient will develop the disease).

**Genetics** Some women carry the BRAC-1 or BRAC-2 genes. The presence of these genes can increase a woman's risk of developing breast cancer by 50–80 per cent over a lifetime. However, this genetic abnormality only accounts for approximately 5 per cent of all women with breast cancer.

**— PATHOLOGY**

Most breast cancers originate in the epithelia of the terminal ducts and lobes — only a small number involve the stroma (tissue at the back of the breast) or soft tissues.

About 80 per cent of breast cancers at presentation are invasive and invasive duct carcinomas account for over 90 per cent of these cancers. They generally present with hard and poorly defined lumps, dimpling and pitting of the skin and nipple inversion.

Invasive lobular carcinomas account for another 10 per cent of invasive breast cancers. These are relatively diffuse tumours and therefore far harder to detect without a mammogram. The majority occur at several sites or in both breasts.

Pre-invasive carcinoma accounts for the remaining cases of breast cancer although post-mortem studies have suggested that the incidence may be as high as 20 per cent (these are known as ductal carcinomas in situ [DCIS] or lobular carcinomas in situ [LCIS]). It is generally accepted that women with these conditions run an 11- or 12- fold increase in going on to develop invasive cancer.

**— STAGING**

As with the staging of all cancers the scheme works to describe the size and spread of the disease. A version of the tumour, node, metastases (TNM) system is used in breast cancer (Panel 2). The everyday working staging system in use in the UK is that described by the Union Internationale Contre Cancer (UICC) (Panel 3) but this is related to the more global TNM classification scheme.

**— PROGNOSIS**

Approximate survival at 15 years post diagnosis is presented by stage of disease at presentation in Panel 4. Successful

*Panel 1: Risk factors for developing breast cancer in women*

	Highest risk	Increased risk	Low risk
Age	>50	30–50	<30
Relatives diagnosed with breast cancer	Two or more first degree	One first degree	No first degree
History of cancer in one breast	Yes		No
Place of birth	Northern Europe North America	Rest of Europe Australia South America	Asia Africa
Previous radiation (particularly to chest)	Yes		No
Ovarian ablation	Pre-35 years old	35 to menopause	No
Module density at mammogram	>75% of the breast	20–75%	<20% of the breast
Age at first full term pregnancy		>30	<20
Age at menarche		<12	>14
Age at menopause		>55	<45
Obesity (post-menopausal)		Obese	Thin
Parity (ie, given birth)		Nulliparous	Multiparous
Breast feeding		None	Longer the better
Contraceptive (<45 years)		Yes	No
Hormone replacement therapy		Yes	No
Social economic status		High	Low
Place of residence		Urban	Rural
Race or ethnicity:			
less than 40 years		Caucasian	Asian
more than 40 years		Black	Asian
Religion		Jewish	Seventh Day Adventist/Mormon
Height at age 14 (female)		>5 $\phi$ 6"	<5 $\phi$
Birth weight (female only)		>8lb 12oz	<7lb

*Panel 2: Tumour, nodes and metastases classification of breast cancer*

**Tumour status**

T0	No palpable tumour
T1	Tumour <2 cm with no fixation to underlying muscle
T2	Tumour >2cm but <5 cm with no fixation
T3	Tumour maximum diameter >5cm
T4	Tumour of any size with fixation to the chest wall or ulceration of skin

**Status of lymph nodes**

N0	No palpable axillary nodes
N1a	Palpable nodes not thought to contain tumour
N1b	Palpable nodes thought to contain tumour
N2	Nodes >2cm or fixed to one another and deep structures
N3	Supraclavicular or infraclavicular nodes

**Distant metastases**

M0	No clinically apparent distant metastases
M1	Distant metastases are present

"a" indicates no attachment to the underlying muscles; "b" indicates there is attachment; T=Tumour; N=Node; M=Metastases

*Panel 3: UICC staging system for breast cancer*

UICC stage	TNM classification
I	T1, N0, M0
II	T1, N1, M0; T2, N0-1, M0*
III	Any T, N2-3, M0; T3, any N, M0; T4, any N, M0
IV	Any T, any N, M1

\* Many expert groups include T2 tumours in stage 1. UICC = Union Internationale Contre Cancer

*Panel 4: Survival from breast cancer at 15 years after initial diagnosis*

Stage at diagnosis	Survival (%)
I	85
II	55
III	40
IV	<5

treatment of early stage breast cancer can result in relapse up to 30 years later, but it should be noted that irrespective of the disease-free interval the behaviour of the tumour at relapse is highly similar and predictable. The average survival at this point is about three years although highly variable from a few months to in excess of five years. The other patient group to bear in mind is young women with breast cancer. This is generally defined as those who are under the age of 34 when diagnosed. Less than half of this group will survive for five years and the majority will relapse in three.

**Nottingham prognostic index** A prediction of the prognosis following surgery is important information for the patient and for treatment planning. A prediction of the chances that a patient has been cured following surgery for breast cancer is provided by the Nottingham prognostic

### Panel 5: Nottingham prognostic index

**Prognosis = (0.2 x tumour size[cm]) + grade + stage**

index. This index (see Panel 5) uses the following clinical data on the tumour:

- The size of the tumour
- Whether or not the cancer has spread to the axillary lymph nodes and, if so, how many nodes are affected (an indication of the stage of the cancer)
- The grade of the cancer: this is based on the appearance of the tumour under the microscope and is an indication of how aggressive the cancer is

Using the formula means that patients can be advised whether they have a high, intermediate or low chance of a cure (the lower the score, the better the prognosis).

### SCREENING PROGRAMME

Early detection of breast cancer significantly improves prognosis. As a result, women between the ages of 50 and 64 are screened for breast cancer. This screening programme is currently being extended to all women between the ages of 50 and 70. Screening in women under the age of 50 is not thought to be effective because the higher density of breast tissue before the menopause makes it more difficult to detect abnormalities and the incidence of breast cancer in women under 50 is much lower.

### TREATMENT STAGES

The different stages of breast cancer are outlined in Panel 6. Treatment of early breast cancer is covered in detail in the second article in this special feature.

### Panel 6: Definitions of stages of breast cancer

#### Primary breast cancer

Refers to localised early breast cancer. Stage I refers to small (<2cm) tumours confined to the breast. Stage II and III includes larger tumours or those with ipsilateral (on the same side as the cancer) axillary node involvement.

#### Locally advanced breast cancer

Refers to breast cancer that has not spread to other parts of the body but is bigger than 5cm, has grown into the skin or muscle of the chest or is growing in the lymph nodes (ie, includes stage II or III cancers).

#### Secondary breast cancer

Refers to breast cancer that has metastasised to other parts of the body including the other breast (contralateral breast cancer) and is stage IV disease.

### REFERENCES

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#### British Oncology Pharmacy Association (BOPA)

BOPA exists to promote pharmaceutical care of patients with cancer through education, communication, research and innovation and has over 300 individual members. It runs an annual conference and provides a newsletter for its members. Further information is available from its website at [www.bopa.cix.co.uk](http://www.bopa.cix.co.uk)

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