PRIMEVIEW

BREAST CANCER

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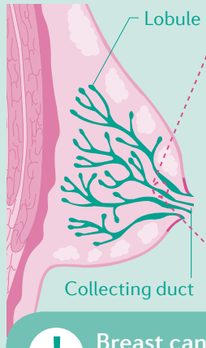
For the Primer, visit doi:10.1038/s41572-019-0111-2

Breast cancer is the most frequent malignancy in women. At the molecular level, it is a heterogeneous disease with molecular features that are used to guide treatment.

MECHANISMS

All breast cancers arise in the terminal duct lobular units (the functional unit of the breast) of the collecting duct. Dozens of genetic mutations have been identified in women with breast cancer, including amplifications, loss-of-function mutations, gain-of-function mutations and deletions. The clinically relevant molecular features are human epidermal growth factor receptor 2 (HER2), hormone receptors (oestrogen receptor (ER) and progesterone receptor (PR)) and *BRCA* mutations. Combining these features with histological characteristics guides treatment and is used for research purposes.



Luminal A-like
- ER and/or PR, no HER2 and low proliferation

Luminal B-like
- ER and/or PR, no HER2 and high proliferation

Triple-negative
- No ER, no PR and no HER2

HER+
- Luminal-like or nonluminal-like

! Breast cancer presents earlier in Asian women than in their western counterparts, potentially reflecting differences in genetic predisposition, lifestyle and environmental factors

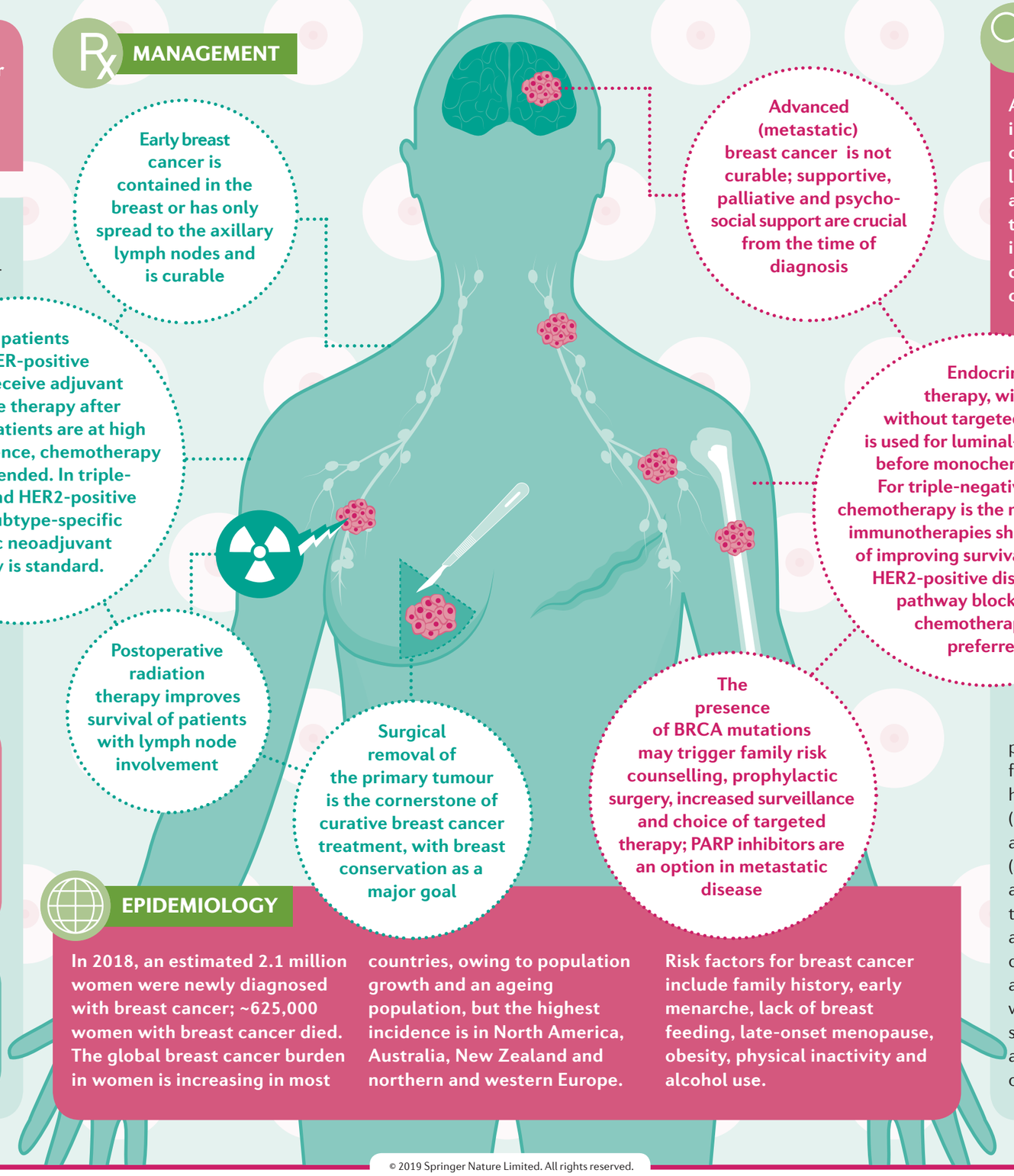
MANAGEMENT

Early breast cancer is contained in the breast or has only spread to the axillary lymph nodes and is curable

All patients with ER-positive disease receive adjuvant endocrine therapy after surgery. If patients are at high risk of recurrence, chemotherapy is recommended. In triple-negative and HER2-positive cancer, subtype-specific systemic neoadjuvant therapy is standard.

Postoperative radiation therapy improves survival of patients with lymph node involvement

Surgical removal of the primary tumour is the cornerstone of curative breast cancer treatment, with breast conservation as a major goal



Advanced (metastatic) breast cancer is not curable; supportive, palliative and psycho-social support are crucial from the time of diagnosis

Endocrine therapy, with or without targeted therapy, is used for luminal-like disease before monochemotherapy. For triple-negative disease, chemotherapy is the main treatment; immunotherapies show early signs of improving survival as well. For HER2-positive disease, HER2 pathway blockade and chemotherapy are preferred.

The presence of BRCA mutations may trigger family risk counselling, prophylactic surgery, increased surveillance and choice of targeted therapy; PARP inhibitors are an option in metastatic disease

DIAGNOSIS

A positive screening mammography (X-ray imaging of the breasts), or the development of breast symptoms or breast changes (lump, localized pain or skin changes), requires appropriate diagnostic evaluation. A 'triple test' — comprising clinical examination, imaging and needle biopsy — is used to confirm a diagnosis. Full characterization of the cancer requires assessment of the tumour histology; grade; ER, PR and HER2 receptor status; size; lymph node involvement; extent of vascularization; and surgical margin status (which is obtained once the tumour is excised). These details are indispensable for management.

OUTLOOK

Treatments are becoming more individualized based on tumour cell characteristics, with the promise of improved outcomes. However, the most pressing global challenge in the breast cancer field is to ensure patients in all parts of the world have access to high-quality standard diagnosis (imaging and pathology) and treatment (surgical, radiation and systemic therapy), avoid late diagnosis and are provided with adequate supportive and palliative care services.

EPIDEMIOLOGY

In 2018, an estimated 2.1 million women were newly diagnosed with breast cancer; ~625,000 women with breast cancer died. The global breast cancer burden in women is increasing in most countries, owing to population growth and an ageing population, but the highest incidence is in North America, Australia, New Zealand and northern and western Europe.

Risk factors for breast cancer include family history, early menarche, lack of breast feeding, late-onset menopause, obesity, physical inactivity and alcohol use.

doi:10.1038/s41572-019-0122-z; Article citation ID: (2019) 5:17

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