

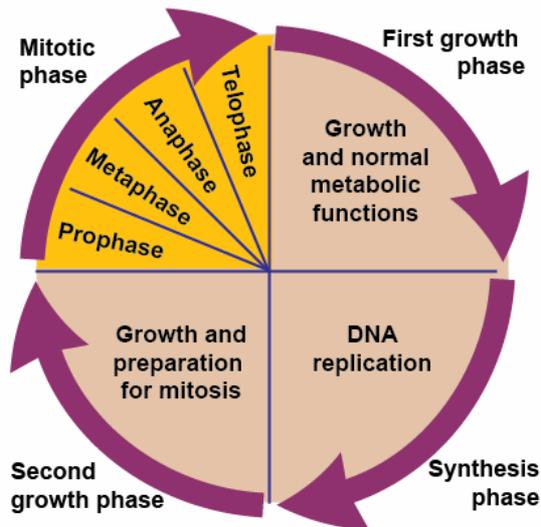
Teva

Understanding Breast Cancer

What is Cancer?

One in three of us will get cancer in the course of our lives. About half of all cancers are thought to be caused by factors associated with diet and lifestyle and can be avoided by following the Code Against Cancer. Enormous advances have been made in the treatment of cancers and many of them can be cured if *diagnosed* early and so it makes sense for us to become better informed.

The process of growth and division of cells (the cell cycle) has two main stages – *interphase*, when the cell grows and *chromosomes* are replicated, and *mitosis* when the *nucleus* and then the whole cell divides. These stages can be subdivided into a number of phases, as seen above, that are regulated by *control genes* and *growth factors*.

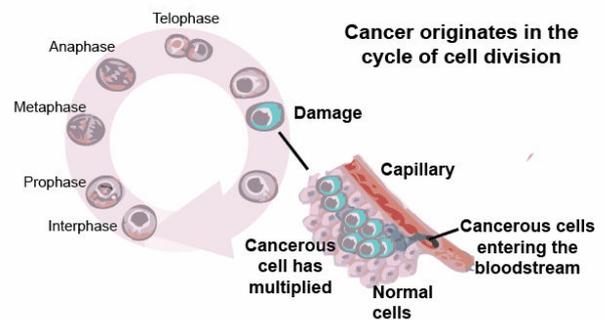


Cancer occurs when *mutation* occurs in a cell cycle control gene or a gene producing growth factors or *receptors* so that they become overactive; they are then called *oncogenes*, or cancer causing genes. Normal cell cycle control is then lost.

The cancerous cell divides in an uncontrolled way, passing on its oncogenes and forming a cluster of similar cells called a *tumour*. If the cells remain together, it is called a *benign tumour* but if the cells break away and are transported in the blood or lymphatic system to invade and cause cancers in other tissues, it is a *malignant tumour*.

Breast Cancer

Breast cancer arises in a million women around the world each year, making it the most common female cancer. In men, the breasts are composed of the same tissues and so they can also suffer from breast cancer. The incidence is lower but survival rates are about the same as for women. In Ireland, about one in nine women will develop breast cancer during their lifetime. The disease is more common in older women because genetic damage, which causes oncogenes to develop, accumulates over time. Breast cancer is more common and increasing in 'Western' countries and much less common in Japan for reasons not fully understood.



Genes and Breast Cancer

A small number, 5-10%, of breast cancers are thought to be caused by an inherited faulty gene. Two breast cancer genes have been identified: *BRCA1* and *BRCA2*. Both genes code for *proteins* that normally play a role in the repair of damaged *DNA*. However the mutated *BRCA1* and *2* genes code for proteins that are shorter and do not function as well in repairing *DNA* damage. This causes increased risk of breast, *ovarian* and *prostate* cancer.

What are the Symptoms of Breast Cancer?

In most women, breast cancer is first noticed as a painless lump in the breast. There may or may not be other symptoms. The symptoms of breast cancer are:

- a painless lump in the breast
- change in size/shape of a breast
- dimpling of the skin of the breast
- a rash/ thickening/ discharge from the nipple
- a swelling or lump in the armpit

Many healthy women find that their breasts feel tender and lumpy before their period. Women should examine their breasts once a month, at least a week before or after their period.

Screening and Diagnosis

Breast cancer can be cured but the chances are much greater if it is detected early and the tumour is small. Ireland has one of the highest rates of death from breast cancer in the world. It is 15% above the EU average. Currently, women in Ireland between the ages of 50 and 64 can get a free X-ray *mammogram* every two

years. Effective *screening* can reduce breast cancer *mortality* by a 20%.

When cancer is suspected, a *biopsy* is carried out. The doctor uses a needle to take a small piece of *tissue* from the lump in the breast after numbing it using a local *anaesthetic*. Samples may also be taken from lymph nodes under the arm.

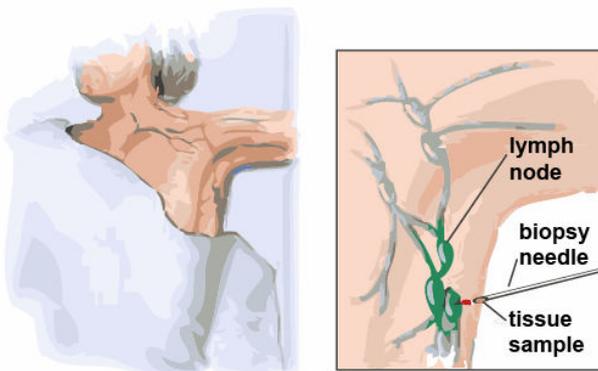
Based on the results of these tests, the appropriate treatment is selected.

Treatment

Following the diagnosis, the patient is given the time, information and support to enable him/her to participate in a fully informed decision about treatment. The options include the following:

Surgery

The trend is to carry out a lumpectomy where just the tumour is removed with some surrounding breast tissue and the breast is conserved, if this is possible. If the tumour is large, then a *mastectomy* may be advised where the whole breast is removed. Breast reconstruction can be carried out in the same operation using muscles from the back, although not all women choose this and artificial alternatives are available. Surgery is often followed by *radiotherapy*.



Radiotherapy

Cells undergoing mitosis are more easily damaged by radiation than cells in interphase. Since cancer cells are rapidly dividing, they can be easily killed by high-energy radiation such as *X-rays*, *gamma rays* or *proton beams*. By moving the radiation source around the cancerous tissue, damage to other cells is minimised. Treatment itself takes only a few minutes each day and is usually continued for several weeks.

Hormone Therapy

Some breast cancer cells carry *hormone* receptors on their surface. These are proteins in the *phospholipid bilayer* of the *cell*

membrane. When the hormone attaches to the receptor on the cell surface, the cell is stimulated to grow and reproduce.

If the cancer cells have a large number of these receptors, then stopping the production of the hormone or blocking it from attaching to the receptor, can inhibit cancer growth.

Chemotherapy

This is the use of drugs to kill cancer cells. The drugs are usually given by means of an intravenous injection over a few hours followed by a period of recovery of three weeks before the next session. A course of chemotherapy usually lasts 4-6 months. Most of the drugs interfere with the replication of the chromosomes or DNA in the cell cycle. Some work by preventing the two strands of DNA from 'unzipping' - a process that preceded replication. They are very effective in killing cancer cells, are dividing rapidly. However, they also kill normal cells that are dividing, causing side effects.

In Conclusion

Breast cancer is one of Ireland's biggest modern health challenges. However, the tide is turning. Breast cancer should not be feared. It will not happen to most people, and, if it does happen, there are lots of treatment options available. Knowledge is expanding and many promising new drugs are showing excellent results. There are now many breast cancer survivors.

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The Waterford site is an Inhalation Manufacturing site with a co-located extensive Research & Development facility and is the Teva Centre of Excellence for respiratory products.

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Understanding Breast Cancer

Teaching Notes

Syllabus Reference

The appropriate syllabus references are:

Leaving Certificate Biology

- 2.3.3 The Cell Cycle
- 2.5.4 DNA replication
- 2.5.7 Causes of variation, mutations, genetic engineering
- 3.3.2 Lymphatic system, lymph nodes
- 3.6.2 Use of IVF
- 2.1.3 Cell membrane structure
- 1.1.2 Scientific Method

Learning Outcomes

On completion of this lesson, students should be able to:

- Describe the cell cycle and how it is controlled.
- Outline how the cell cycle varies in different tissues of the body.
- State what an oncogene is and how it affects the cell cycle.
- Distinguish between benign and malignant tumours.
- Understand the significance of the BRCA1 and BRCA2 genes for breast cancer.
- Describe the symptoms of breast cancer and how to carry out a breast check.

- Understand the importance of the Breast Check screening programme.
- Distinguish between various treatment options and how they work: surgery, radiotherapy, hormone therapy, chemotherapy.
- Describe how the drug Tamoxifen and the monoclonal antibody Herceptin work in the treatment of breast cancer.

General Learning Points

The following information can be used to revise the lesson's main learning points and inform discussion.

- One in three people get cancer in the course of their lives.
- About half of all cancers can be avoided by following the Code Against Cancer.
- The cell cycle has two main stages – interphase and mitosis.
- A mutation in a cell cycle control gene or in a gene producing growth factors can cause them to become overactive; they are then called oncogenes, or cancer causing genes.
- A cluster of cancer cells is called a tumour. If they remain together the tumour is said to be benign.
- Early detection and treatment improves recovery rates.

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Understanding Breast Cancer Exercises

Student Activities

Lifestyle and Cancer

Some studies have shown that 70-90% of all cancers are environmental. Lifestyle related factors are the most important and preventable. Tobacco consumption accounts for 50% of all cancers in men. Diet accounts for 20-30% of cancers. Appropriate changes in lifestyle can reduce the mortality from many forms of cancer and heart diseases. The cancers most associated with diet are those of the mouth, throat, stomach, large intestine, and breast cancer.

Studies on migrant populations demonstrated the significance of environmental factors, compared to genetic predisposition. Japanese have the highest rate of stomach cancer and very low rates of colon cancer and breast cancer. Among the Japanese who have migrated to the USA, stomach cancer rates dropped considerably and the rates of colon and breast cancer increased to that of Americans. Further studies suggested high fat or meat consumption as risk factors and a diets rich in fruits and green and yellow vegetables reduced cancer rates.

Alcohol consumption may also be important. Researchers compared the lightest drinkers - two or fewer drinks a week - with people who drank more. They found that one drink per day increases risk of getting breast cancer by 40%, two drinks a day increases risk by 70%.

World Health Organisation data shows that breast cancer is three times more common in Ireland than in Japan. This study suggested the Japanese lifestyle was in some way protective against breast cancer.

- (i) List as many things as you can about the differences in lifestyle in Japan that might be involved.
- (ii) Design an experiment to test one of your ideas. Think carefully about your experimental design to ensure that your results are fair and free from bias.

True/False Questions

- | | | |
|---|---|---|
| a) You can choose to avoid at least 50% of cancers by following the European Code Against Cancer. | T | F |
| b) The cell cycle of cells in the membranes lining the intestines is much longer than for muscle cells. | T | F |
| c) In benign tumours cells break off & spread to other tissues. | T | F |
| d) Oncogenes are genes that cause cancer by interfering with controls of the cell cycle. | T | F |
| e) The unmutated form of the BRCA1 gene protects against cancer by helping to repair DNA. | T | F |
| f) We all have the BRCA1 gene. | T | F |
| g) The monoclonal antibody Herceptin is only useful in treating cancers that have HER2+ receptors on their surface. | T | F |
| h) Most breast cancers are found by Breast Check screening. | T | F |
| i) Dennis Slamon developed Tamoxifen. | T | F |

Check your answers to these questions on www.sta.ie

Examination Questions

Leaving Certificate Biology (HL)

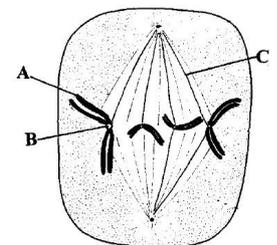
- 2009 14(b) (iv) What is meant by *in vitro* fertilisation?
- 2005 5(e) When the control of the cell cycle is lost cancer may result. Suggest 2 possible causes of cancer.
- 10(a) What is meant by genetic engineering? State two applications of genetic engineering.

Leaving Certificate Biology (OL)

- 2008 4(e) A change in the genetic material in an organism is called a
- 2007 11(b) (i) What is meant by tissue culture?
- (v) What type of cell division, mitosis or meiosis, is involved in tissue culture?
- (vi) Give one other application of tissue culture apart from skin grafting.
- 2006 11(c) (i) What is genetic engineering?
- (ii) Give one example of genetic engineering involving an animal and one involving a plant.

Leaving Certificate Biology (HL) 2007, Q. 3

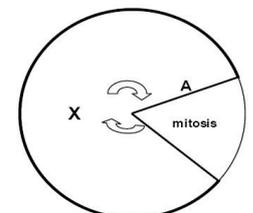
Study the diagram of a stage of mitosis in a diploid cell and then answer the questions below.



- (a) Name A, B and C.
- (b) What stage of mitosis is shown? Give a reason for your answer.
- (c) What is the diploid number of this nucleus which is undergoing mitosis?
- (d) Give a role of structure A.
- (e) Some cells in the human body undergo meiosis. Give one function of meiosis.

Leaving Certificate Biology (HL) 2008, Q. 2

2. The diagram represents the cell cycle.



- (a) What stage of the cycle is represented by X?
- (b) Give the names of the two processes involving DNA, which take place during stage X.
- (c) For convenience of study, mitosis is divided into four stages. List these in order starting at A.
- (d) In which of the stages of mitosis that you have listed in (c) would you expect to see the spindle fibres contracting?
- (e) Explain the term diploid number.
- (f) What term is used to describe a group of disorders of the body in which cells lose the normal regulation of mitosis?

Did You Know?

1. Melissa Ethridge (singer, Grammy Award winner), Kylie Minogue (singer), Edie Falco (Sopranos star), Richard Rountree (Shaft star) and Kate Jackson (Charlie's Angels star) are all breast cancer survivors.
2. You can choose to avoid about 50% of cancers by following the European Code Against Cancer i.e. do not smoke, limit alcohol consumption, eat 5 portions/day of fruit and vegetables, avoid being overweight, avoid sunburn, participate in screening.
3. About 90% of lumps are first found by self examination, so it makes sense for women to examine their breasts regularly. About 80% of lump biopsies are found not to be cancerous.
4. Plants have been the source of some of the most powerful anti-cancer drugs; e.g. taxanes are extracted from the yew tree and prevent the growth and reproduction of cancer cells.
5. A study in Sweden found that breast cancer survivors who took Hormone Replacement Therapy (HRT) to relieve menopausal symptoms had more than three times as many breast cancer recurrences as survivors who did not take HRT.

Biographical Notes

Many scientists are currently contributing to our knowledge of cells and how they work and hence how a disease such as cancer can be prevented and cured. Just two of these are included here.

Dr Arthur Walpole saw that a drug, *Tamoxifen*, originally developed as a 'morning after' pill had potential in treating breast cancers that are ER+, i.e. whose cells carry receptors for oestrogen, which stimulates their growth and reproduction. Tamoxifen competes with oestrogen to bind to the oestrogen receptors and slows the cell cycle.

Dr. Dennis Slamon was involved in developing *Herceptin* which has proved very effective in the treatment of the cancers in which the cells have many HER2+ receptors on their surface and are typically very fast growing. Herceptin is a monoclonal antibody. Antibodies are proteins that are produced by a type of white blood cell in response to an infection. A film of this work, 'Living Proof' was released in 2008.

Revise the Terms

Can you recall the meaning of the following terms? Reviewing terminology is a powerful aid to recall and retention.

Anaesthetic, benign tumour, biopsy, cell membrane, chromosomes, control gene, diagnosis, gamma rays, growth factor, hormone, interphase, malignant tumour, mammogram, mastectomy, mitosis, mortality, mutation, oncogene, phospholipid bilayer, proton beams, radiotherapy, receptor, screening, tissue, tumour, X-rays.

Check the Glossary of Terms for this lesson at www.sta.ie