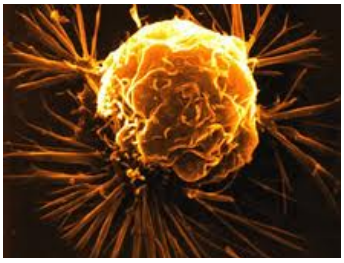
CANCER –

DEFINITIONS, DIAGNOSIS, STAGING, DEATH AND SURVIVAL

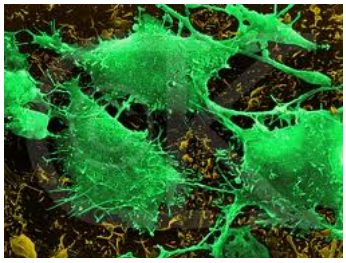
Rod MacLeod

What is cancer?

- Cancer is a term used for diseases in which abnormal cells divide without control and are able to invade other tissues. Cancer cells can spread to other parts of the body through the blood and lymph systems.
- Cancer is not just one disease but many diseases. There are more than 100 different types of cancer. Most cancers are named for the organ or type of cell in which they start

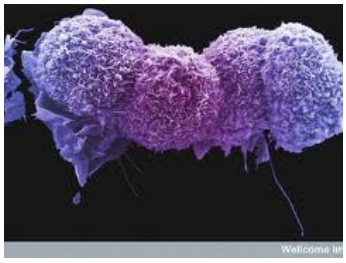


Breast cancer cell



Brain cancer cell

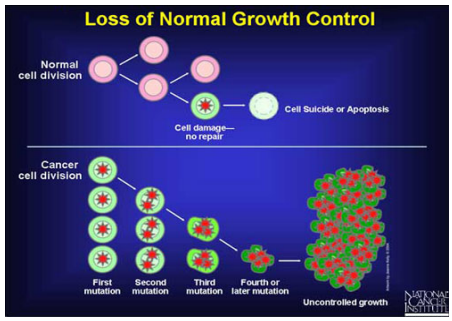
Prostate cancer cells



Lung cancer cells

Cancer types

- **Carcinoma** - cancer that begins in the skin or in tissues that line or cover internal organs.
- **Sarcoma** - cancer that begins in bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.
- **Leukaemia** - cancer that starts in blood-forming tissue such as the bone marrow and causes large numbers of abnormal blood cells to be produced and enter the blood.
- **Lymphoma and myeloma** - cancers that begin in the cells of the immune system
- **Central nervous system cancers** - cancers that begin in the tissues of the brain and spinal cord



Not all tumours are cancerous; tumours can be benign or malignant.

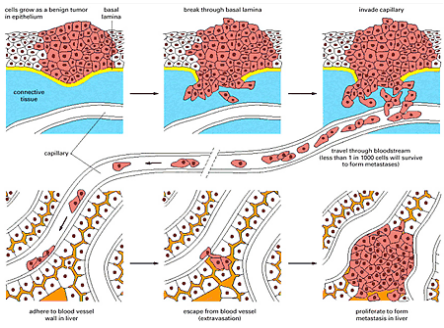
- **Benign tumours** aren't cancerous. They can often be removed, and, in most cases, they do not come back. Cells in benign tumours do not spread to other parts of the body.
- **Malignant tumours** are cancerous. Cells in these tumours can invade nearby tissues and spread to other parts of the body. The spread of cancer from one part of the body to another is called metastasis.

Metastasis

Cancer cell metastasis usually involves the following steps:

- **Local invasion**: Cancer cells invade nearby normal tissue.
- **Intravasation**: Cancer cells invade and move through the walls of nearby lymph vessels or blood vessels.
- **Circulation**: Cancer cells move through the lymphatic system and the bloodstream to other parts of the body.

- **Arrest and extravasation**: Cancer cells arrest, or stop moving, in small blood vessels called capillaries at a distant location. They then invade the walls of the capillaries and migrate into the surrounding tissue.
- **Proliferation**: Cancer cells multiply at the distant location to form micrometastases.
- **Angiogenesis**: Micrometastases stimulate the growth of new blood vessels to obtain a blood supply. A blood supply is needed for continued tumour growth.



Common sites of metastases

Cancer type	Site of metastases
Breast	Lung, liver, bone
Colon	Liver, peritoneum, bone
Kidney	Lung, liver, bone
Lung	Adrenal, liver, lung
Melanoma	Lung, skin/muscle, liver
Prostate	Bone, lung, liver
Stomach	Liver, peritoneum, lung

- Metastatic cancer may be treated with
  - systemic therapy (chemotherapy, hormonal therapy),
  - local therapy (surgery, radiation therapy) or
  - a combination of these treatments.

- The choice of treatment generally depends on
  - the type of primary cancer,
  - the size,
  - location, and number of metastases,
  - the patient's age and general health and
  - the types of treatment the patient has had in the past

Staging

- Staging describes the severity of a person's cancer based on the extent of the original (primary) tumour and whether or not cancer has spread in the body. Staging is important for several reasons:
  - Staging helps in planning appropriate treatment.
  - The stage can be used to estimate the person's prognosis.
  - Knowing the stage is important in identifying clinical trials that may be suitable for a particular patient.
  - Staging helps health care providers and researchers exchange information about patients; it also gives them a common terminology for evaluating the results of clinical trials and comparing the results of different trials.

Elements of staging

- Site of the primary tumour
- Tumour size and number of tumours
- Lymph node involvement (spread of cancer into lymph nodes)
- Cell type and tumour grade (how closely the cancer cells resemble normal tissue cells)
- The presence or absence of metastasis

TNM system

...is based on the extent of the tumour **(T)**, the extent of spread to the lymph nodes **(N)**, and the presence of distant metastasis **(M)**. A number is added to each letter to indicate the size or extent of the primary tumour and the extent of cancer spread.

Primary Tumour (T)

- TX Primary tumour cannot be evaluated
- T0 No evidence of primary tumour
- Tis Carcinoma in situ (CIS; abnormal cells are present but have not spread to neighbouring tissue; may become cancer and is sometimes called pre-invasive cancer)
- T1, T2, T3, T4 Size and/or extent of the primary tumour

TNM

Regional Lymph Nodes (N)

- NX Regional lymph nodes cannot be evaluated
- N0 No regional lymph node involvement
- N1, N2, N3 Involvement of regional lymph nodes (number of lymph nodes and/or extent of spread)

TNM

Distant Metastasis (M)

- MX Distant metastasis cannot be evaluated
- M0 No distant metastasis
- M1 Distant metastasis is present

Staging

Stage	Definition
Stage 0	Carcinoma in situ
Stage I, Stage II, and Stage III	Higher numbers indicate more extensive disease: Larger tumour size and/or spread of the cancer beyond the organ in which it first developed to nearby lymph nodes and/or organs adjacent to the location of the primary tumour.
Stage IV	The cancer has spread to another organ(s).

Many cancer registries, such as NCI's Surveillance, Epidemiology, and End Results Program (SEER), use summary staging. This system is used for all types of cancer. It groups cancer cases into five main categories:

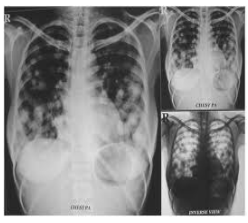
- **In situ**: Abnormal cells are present only in the layer of cells in which they developed
- **Localized**: Cancer is limited to the organ in which it began, without evidence of spread
- **Regional**: Cancer has spread beyond the primary site to nearby lymph nodes or organs and tissues
- **Distant**: Cancer has spread from the primary site to distant organs or distant lymph nodes
- **Unknown**: There is not enough information to determine the stage

Tests for staging

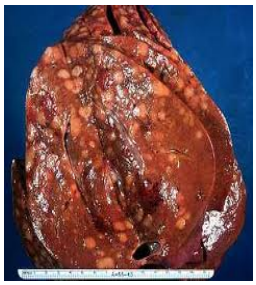
Physical examination – doctor examines the body by looking, feeling, and listening for anything unusual. The physical exam may show the location and size of the tumour(s) and the spread of the cancer to the lymph nodes and/or to other organs

Laboratory tests are studies of blood, urine, other fluids, and tissues taken from the body. For example, tests for liver function and tumour markers

Imaging studies - important tools in determining stage. Procedures such as x-rays, computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, and positron emission tomography (PET) scans.



Pathology reports may include information about the size of the tumour, the growth of the tumour into other tissues and organs, the type of cancer cells, and the grade of the tumour.

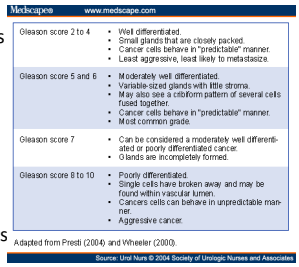


Grading

Grade	
GX	Unable to assess
G1	Well differentiated (low grade)
G2	Moderately differentiated
G3	Poorly differentiated (high grade)
G4	Undifferentiated

Other grades include

- The Gleason system uses scores ranging from Grade 2 to Grade 10. Lower Gleason scores describe well-differentiated, less aggressive tumours. Higher scores describe poorly differentiated, more aggressive tumours



Tumour markers

A substance that may be found in tumour tissue or released from a tumour into the blood or other body fluids. A high level may mean that a certain type of cancer is in the body. Examples of tumour markers include CA 125 (in ovarian cancer), CA 15-3 (in breast cancer), CEA (in ovarian, lung, breast, pancreas, and gastrointestinal tract cancers), and PSA (in prostate cancer).

Genetic markers

- *BRCA1* and *BRCA2* are human genes that belong to a class of genes known as tumour suppressors. Mutation of these genes has been linked to hereditary breast and ovarian cancer.
- A woman's risk of developing breast and/or ovarian cancer is greatly increased if she inherits a deleterious (harmful) *BRCA1* or *BRCA2* mutation. Men with these mutations also have an increased risk of breast cancer. Both men and women who have harmful *BRCA1* or *BRCA2* mutations may be at increased risk of other cancers.
- Genetic tests are available to check for *BRCA1* and *BRCA2* mutations. Genetic counselling is recommended before and after the tests.
- If a harmful *BRCA1* or *BRCA2* mutation is found, several options are available to help a person manage their cancer risk

- According to estimates of lifetime risk, about 12% of women (120 out of 1,000) in the general population will develop breast cancer sometime during their lives compared with about 60% women (600 out of 1,000) who have inherited a harmful mutation in *BRCA1* or *BRCA2* (i.e. 5 times more likely to develop breast cancer than a woman who does not have such a mutation).
- Lifetime risk estimates for ovarian cancer among women in the general population indicate that 1.4 % (14 out of 1,000) will be diagnosed with ovarian cancer compared with 15 to 40% women (150–400 out of 1,000) who have a harmful *BRCA1* or *BRCA2* mutation

- CA-125 may be found in high amounts in the blood of patients with certain types of cancer, including ovarian cancer. CA-125 levels may also help monitor how well cancer treatments are working or if cancer has come back.

PART TWO

CANCER –

DEFINITIONS, DIAGNOSIS, STAGING, DEATH AND SURVIVAL

Prof Rod MacLeod

Incidence

How many people are diagnosed with cancer?

- 108,368 new cases of cancer were diagnosed in Australia in 2007 (excluding basal and squamous cell carcinomas of the skin).
- 57% of the newly diagnosed cancer cases in 2007 were in males.

What is the risk of being diagnosed with cancer?

- before the age of 75 years is 1 in 3 for males and 1 in 4 for females.
- before age 85 years is higher, at 1 in 2 for males and 1 in 3 for females.

In New Zealand

Cancer is the leading cause of death in New Zealand accounting for 29.4% of all deaths

- 18,610 new cancer diagnoses and 7,970 cancer deaths in New Zealand
- Every day around 51 people are diagnosed with cancer in New Zealand and there are 22 cancer deaths

In New Zealand

Most common cancers

1. Colorectal 14.6% (2716 cases)
2. Breast (13.3% (2479 cases)
3. Prostate 13.3% (2471 cases)
4. Melanoma 10.8% (2017 cases)
5. Lung 8.9% (1659 cases)

Leading cause of cancer deaths

1. Lung 18.2% (1451)
2. Colorectal 15.3% (1222)
3. Breast 8.2% (652)
4. Prostate 7.1% (564)
5. Pancreas 4.1% (353)

In New Zealand

Females

- 8,963 new diagnoses and 3,786 deaths

Most common cancer diagnoses for females:

1. Breast 27.4% (2,458)
2. Colorectal 15.5% (1,385)
3. Melanoma 9.8% (910)

Leading cause of death for females:

1. Breast 17.1% (647)
2. Colorectal 16.2% (614)
3. Lung 15.5% (587)

In New Zealand

Males

- 9,647 new diagnoses and 4,184 deaths

Most common cancer diagnoses for males:

1. Prostate 25.6% (2,471)
2. Colorectal 13.8% (1,331)
3. Melanoma 11.5% (1,107)

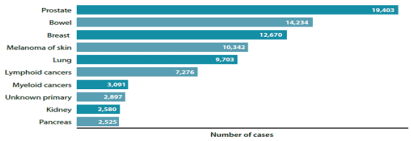
Most common cancer deaths for males:

1. Lung 20.7 (864)
2. Colorectal 14.5% (608)
3. Prostate 13.5% (564)

Which cancers are common in Australia?

In 2007, the most commonly reported cancers were:

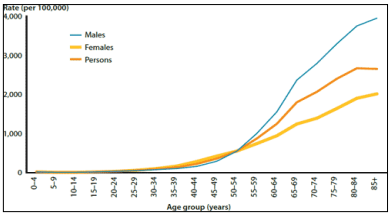
- Prostate cancer (19,403 cases)
- Bowel cancer (14,234 cases)
- Breast cancer (12,670 cases)
- Melanoma of the skin (10,342 cases)
- Lung cancer (9,703 cases).



The 10 most commonly diagnosed cancers, Australia, 2007

Do cancer rates differ with age?

In 2007, the likelihood of being diagnosed with cancer increased with age in both males and females.

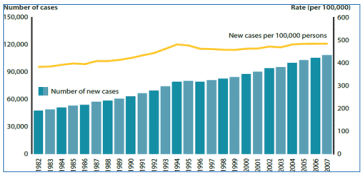


Notes
1.The rates shown are age-specific rates.
2.The data pertain to cancers coded in ICD-10 as C00-C97, D45, D46, D47.1 and D47.3 with the exception of those C44 codes which indicate a basal or squamous cell carcinoma of the skin.
Source: AIHW Australian Cancer Database.
Age-specific incidence rates for all cancers combined, Australia, 2007

How has the occurrence of cancer changed over time?

The number of new cancer cases more than doubled between 1982 and 2007. In 1982, 47,350 new cases of cancer were diagnosed in Australia compared with 108,368 cases in 2007.

- The incidence rate for all cancers combined increased by 27% from 383 cases per 100,000 people in 1982 to 485 cases per 100,000 people in 2007.



Notes
1.The rates were age-standardised to the Australian population as at 30 June 2001.
2.The data pertain to cancers coded in ICD-10 as C00–C97, D45, D46, D47.1 and D47.3 with the exception of those C44 codes which indicate a basal or squamous cell carcinoma of the skin.
Source: AIHW Australian Cancer Database.
Incidence of all cancers combined, Australia, 1982 to 2007

Mortality (Australia)

How many people died from cancer in 2007?

- 39,884 (22,562 males and 17,322 females), this equates to an average of 109 people every day.
- Cancer was the second most common cause of death in 2007, accounting for approximately three of every ten deaths (29%).

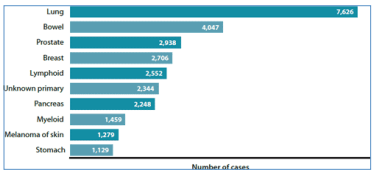
What is the risk of dying from cancer?

- before the age of 75 years is 1 in 8 for males and 1 in 12 for females.
- before the age of 85 years is higher, at 1 in 4 for males and 1 in 6 for females.

Which cancers lead to most deaths?

In 2007, the most common causes of cancer death in Australia were:

Lung cancer (7,626 deaths) Bowel cancer (4,047 deaths)
Prostate cancer (2,938 deaths) Breast cancer (2,706 deaths)
Lymphoid cancers (2,552 deaths).

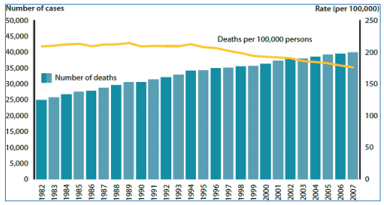


Source: AIHW National Mortality Database.
The 10 most common causes of death from cancer, Australia, 2007

How has mortality changed over time?

The number of deaths from cancer has increased by 60% from 1982 (24,922 deaths) to 2007 (39,884 deaths).

The age-standardised mortality rate for all cancers combined fell by 16% from 209 deaths per 100,000 people in 1982 to 176 deaths per 100,000 people in 2007.



Source: AIHW National Mortality Database.
The 10 most common causes of death from cancer, Australia, 2007

Survival

What is the prospect of survival in Australia?

- For those diagnosed with cancer between 1998 and 2004, the 5-year relative survival for all cancers combined, was 61%.
- Females had a better chance of survival than males, with the 5-year relative survival estimate equalling 64% for females and 58% for males.

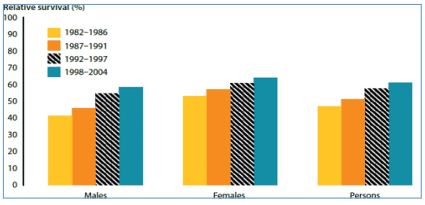
What is the prospect of survival?

Notes
1. The highlighted male/female symbols represent the % of males/females that will be alive 5-years after a diagnosis of cancer.
2. The data pertain to cancers coded in ICD-10 as C00-C97 (except for C44), D45, D46, D47.1 and D47.3.

Source: AIHW, CA & AACR 2008.
Five-year relative survival, all cancers combined, Australia, 1998–2004

How has survival changed over time?

The 5-year relative survival for males increased from 41% in 1982–1986 to 58% in 1998–2004. There was a similar improvement for females over these periods– from 53% to 64%.



Note: The data pertain to cancers coded in ICD-10 as C00-C97 (except for C44), D45, D46, D47.1 and D47.3.
Source: AIHW, CA & AACR 2008.
Five-year relative survival, all cancers combined, Australia, 1982–1986 to 1998–2004

Reference

AIHW, CA (Cancer Australia) & AACR (Australasian Association of Cancer Registries) 2008. *Cancer survival and prevalence in Australia: cancers diagnosed from 1982 to 2004*. Cancer series no. 42. Cat. No. CAN 38. Canberra: AIHW.

Further reading

- Disibio G, French SW. Metastatic patterns of cancer: results from a large autopsy study. *Archives of Pathology & Laboratory Medicine* 2008; 132(6):931–939
- Talmadge JE, Fidler IJ. AACR centennial series: the biology of cancer metastasis: historical perspective. *Cancer Research* 2010; 70(14):5649–5669
- Coghlin C, Murray GI. Current and emerging concepts in tumour metastasis. *Journal of Pathology* 2010; 222(1):1–15

Fact sheets

- National Cancer Institute Fact Sheet 5.9, *Tumor Grade: Questions and Answers* (http://www.cancer.gov/cancertopics/factsheet/detection/tumor-grade)
- National Cancer Institute Fact Sheet 5.18, *Tumor Markers: Questions and Answers* (http://www.cancer.gov/cancertopics/factsheet/detection/tumor-markers)
- National Cancer Institute Fact Sheet 5.27, *Interpreting Laboratory Test Results* (http://www.cancer.gov/cancertopics/factsheet/detection/laboratory-tests)
- National Cancer Institute Fact Sheet 6.20, *Metastatic Cancer: Questions and Answers* (http://www.cancer.gov/cancertopics/factsheet/sites-types/metastatic)
- http://www.cancernz.org.nz