Cancer - how and why?

Over the years I have written about lots of different cancers. There are, after all, about 200 different types, all characterised by the uncontrollable reproduction of body cells. The cancerous mass which develops can invade locally destroying tissue or some of the cancer cells can spread from one part of the body to another through blood or lymph to produce metastases. But how and why does it happen?

The first thing to understand is why does a healthy body suddenly produce a cancer cell. After all, the body has an estimated thirty-five trillion cells and about thirty-five million of them are replaced every minute. The cells are the building blocks of all the different organs which combine to form the body.

We all start life as a single cell formed by the fusion of an ovum with a sperm.

The single cell divides into two, and then four, and then eight, and then sixteen and so on. Soon there is a ball of cells.

Some of the cells, pre-programmed genetically, will develop into different types of cell to form particular structures or shapes, this process, differentiation, causes the infant to form and, in the case of the human child, the structures which form the body are complete after thirteen weeks of gestation. Thereafter during the pregnancy, the baby simply grows. After birth, the child grows to be an adult and is a miraculous cell dividing machine.

It is only to be expected that not every cell manufactured through division is normal. Cells contain DNA (deoxyribonucleic acid) formed in long chains (chromosomes) which are composed of millions of genes. The cells become abnormal if their DNA (which contains the whole blueprint for that cell’s structure and function) becomes abnormal.

The body has an effective immune system able to identify abnormal cells and usually
they are eliminated. It is when the immune system fails us and allows abnormal cells to start to divide uncontrollably that a tumour is formed.

Tumours take one of two forms. They may be **benign** (non-cancerous) or they may be **malignant** (cancerous). Clearly it is vital to distinguish between the two. Cancerous (malignant) tumours:

a) spread uncontrollably to surrounding tissue  
b) destroy the surrounding tissue  
c) can spread distantly to cause other tumours

Cancer cells do not behave like normal cells. They cease to be controlled by the body and continue to replicate unabated. They also lose the ability to die (normal cells die after a certain period as a result of pre-programmed death written in to the genetic code). Cancerous lumps are less able to hold together and parts may break off and spread through the blood or lymph vessels to lodge in some other part of the body and start growing again. Tumours that grow distantly are called **metastases**

*Data for the UK, from Cancer Research UK*, provides the following information:

- New cases of cancer (2014)  
  356,860  
- Deaths from cancer (2014)  
  163,444  
- Survival  
  (10 yrs or more, year 2010-11)  
  England and Wales)  
  50%  
- Preventable cases of cancer (UK)  
  42%

**What changes cause normal cells to become cancerous?**

Normal cells behave in a predictable way. They grow, they divide, they die. The process, (mitosis) results in one cell producing two identical daughter cells. The chromosomes are split equally between the cells.

Programmed death is called **apoptosis**. When the process breaks down, abnormal cells may form and cancer develops. Unlike the normal cells, cancer cells do not incorporate programmed death into their cycle and so they grow and divide relentlessly, out of control to form a tumour mass.

Things go wrong when mutations occur (that is the inclusion of one or more abnormalities in the genetic structure). As scientists have discovered more about genes and chromosomes, it has become clear that what appears as simple cell division is influenced by genes that tell the cell when to divide, genes that tell the cell not to divide, genes that tell the cell to self-destruct if something goes wrong and repair genes to tell the cell to repair damaged DNA. Given the rate of cell division it is amazing that the system works as well as it does.

In very basic terms, cancer is the likely consequence when a genetic mutation prevents the self-destruct mechanism from operating and resulting in uncontrolled growth.

**What makes genetic change occur?**

Mutations may occur by chance during cell division. In addition there are a number of agents which can cause genetic material to become damaged. They are called carcinogens and there are a very large number of them. They are found...
domestically and industrially. Examples of physical factors include:

- X-radiation
- Gamma radiation
- Radiation from the sun
- Asbestos
- Tobacco
- Arsenic
- Diesel exhaust fumes

The carcinogens can affect the DNA by splitting off fragments called free radicals, which are positively charged. They attract negatively-charged electrons resulting in damage to other molecules which affects the ability of the cell to operate.

Viruses too may cause genetic mutations. They include:

- Human papillomavirus (cervical cancer)
- Hepatitis B & C (liver cancer)
- Epstein-Barr virus (causes glandular fever but may also cause some cancers)
- HIV and any other virus which weakens the immune system.

It is now known that some genes actually incorporate a predisposition to become cancerous. A child may be born with the mutation which, in later life, will make it more likely that cells will change and become cancerous.

**The initiation and promotion of cancer**

It has long been recognised that, for example, smoking increases the risk of cancer but not everyone that smokes develops a tumour in the lung. It was a source of frustration to me when trying to convince patients to stop smoking, that they would often point to an elderly relative who “smokes forty a day and is fit as a flea at ninety years of age!” Allowing for the exaggerated assessment of general health, nonetheless the smoking hadn’t caused cancer.

It is now realised that, for lung cancer to develop, there needs to be an initiator and a promoter. The initiator is genetic and gives the individual the predisposition to develop cancer.

The carcinogens in tobacco smoke provide the promoter, the agent that ‘switches on’ the genetic change so that the cancer develops. The mechanism by which this actually happens is far from fully understood.

Therefore, someone without the genetic predisposition can smoke and not develop cancer whilst someone with the predisposition is at very much higher risk of cancer even with moderate smoking.

Roy Castle, a non-smoker, famously developed lung cancer, believed to be due to passively inhaling cigarette smoke in theatres and clubs where he played.

Cancers can occur in almost any tissue and almost any location.

They can broadly be classified into one of five groups.

- **Carcinomas** These are tumours that develop from those cells that form the covering of the body or which line the internal parts of the body which make contact with the outside; skin, mouth, lung, bowel
- **Sarcomas** Usually aggressive, these tumours occur in muscle, bone, cartilage and connective tissues
- **Adenomas** These are glandular tumours that may occur in any glandular tissue, either specific such as the adrenal or the thyroid, or in the glands in organs such as the gut.
- **Lymphomas** occur in lymphatic tissues
- **Leukaemias** are associated with the blood
Assessing the prognosis and treatability of a cancer

Clearly it is important to diagnose a cancer as quickly as possible. The earlier the diagnosis is made, the more likely the chances of treating it successfully. There are processes that assist in confirming the nature, the degree of aggressiveness and the degree of spread.

1. **Biopsy**: A process for obtaining a sample of the tumour for examination under a microscope. This may be done by excising (cutting out) a sample of the tissue or drawing it up through a wide-bore needle. The sample is then prepared for viewing. This enables the microscopist:
   a. To confirm the diagnosis of cancer
   b. To assess how invasive the cancer might be. In general the more the cancer cells resemble the normal cells from which they mutated, the less aggressive they are. A tumour where the cells look very like the tissue from which it comes is called **well-differentiated**. If it lacks features of the tissue, it is called **poorly-differentiated** or **anaplastic**.
   c. To provide information that the cancer clinician (**oncologist**) requires to treat the patient.

2. **Blood and body fluid investigations**. A variety of blood and other tests may be carried out to identify changes in levels of particular cancers. Increase in certain enzymes or hormones may give a clue to the origin or degree of involvement of structures such as the liver, bone or the prostate.

3. **Scanning**. Once the tumour has spread from its original (primary) site and metastases exist elsewhere in the body, treatment may be more difficult and the prognosis may be less favourable. **Ultrasound**, **CT**, **MRI** and other types of scan are used to find any evidence of spread.

Once these and other tests have been completed, it is possible to establish the nature and degree of spread of the tumour. A system called **TNM** may be used to categorise the tumour.

- **T (1-4)** the size and direct spread of the tumour
- **N (0-3)** the degree of involvement of lymph nodes
- **M (0-1)** whether there is distant spread

Of course there is huge amounts of research in progress and, within a relatively short period, there will undoubtedly be more accurate, quicker and less intrusive ways of identifying and categorising tumours.

Research achievements are developing very rapidly. Major progress has accelerated in the last twenty-five years.

The Ancient Egyptians knew about cancer and evidence has been found in Mummies, bones and in Egyptian manuscripts.

**Hippocrates** used the term carcinoma to describe ulcer-like tumours and **Celsus** translated the Greek word into **cancer** to describe the crab-like way in which tumours spread through tissues. Galen in about 180 AD first used the word **oncos** to describe the swelling from which the word **oncologist** (cancer specialist) comes.

The Roman theory of the four humours, with an excess of **black bile** leading to cancer, was a popular concept for over a millennium.

In the fifteenth to seventeenth centuries noted anatomists and physicians of the time began to recognise the more sinister characteristics of cancers.
John Hunter in the later years of the eighteen century reported that cancers could be cured by removal.

In the nineteenth century, the discovery of the microscope and the pioneering work of Virchow, along with developments in post-mortem analysis, led to the first realisation that cancer cells were different and spread was a key component of the disease.

It was not until the early twentieth century that researchers started to make inroads into the cause and development of cancer.

*Minimising the ‘why’*

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Many cancers are beyond our control to prevent because they occur by chance or by agents as yet unidentified. However, there are things that can be done to reduce the risk.

1. STOP SMOKING
2. Drink alcohol in moderation
3. Exercise regularly
4. Eat healthily. There are some foods where there is some evidence, but perhaps not conclusive, that particular foods may increase the risk of cancer. Processed meats are an example. Perhaps the best advice is to eat a wide range of foods in moderation rather than consuming large quantities of meat or fried foods, for example.

Next time, we shall look at the symptoms with which cancer might present, the problems of diagnosis and the treatments available.