



### Incidence and Death rates from Cancer

There were 2,845,560 cases of cancer diagnosed in the UK in 2004 and four sites: breast (18%), lung (13%), bowel or colorectal (13%) and prostate (12%) account for over half of all new cases. The number of deaths from cancer, 153,497 in the UK in 2005, was surpassed in frequency only by deaths from heart and blood vessel disease. Cancer is more common now than it used to be because people live longer and cancer becomes more frequent with increasing age. However, the standardised mortality rates (SMR, expressed as cases per 100,000 population) for all cancers fell by over 17% over the 30 years from 1975 to 2005 from 218 to 180 per 100,000 population despite an increase in incidence from just under 300 to over 350 per 100,000.

The commonest cancer in men is prostate (24%), followed by lung (16%), and colorectum (14%), out of a total of 143,126 male cancers in the UK in 2004. The outlook is however very variable between cancer types. Whereas the outlook for lung cancer is generally poor many older men may harbour prostatic cancer which never causes any problems. In women the commonest cancers are those of the breast (31%) and lung (11%) and then, as in men, the large intestine and rectum (12%) of a total of 141,434 cases.

The frequency of different cancers and the SMR has changed over the years in different ways for different tumours. The incidence of lung cancer initially increased rapidly over the last fifty years in both sexes. This was due to the increase in cigarette smoking but as this has declined in men so has the number of lung cancers reflecting this. The SMR has halved over 30 years (107 per 100,000 deaths in 1971 and 53 in 2005). In women there has been no such fall in smoking habits and the incidence of lung cancer has continued to rise until very recently. The SMR increased from 18 to 30 (a 66% increase) in the late 1980s and has not changed since then reflecting the increase in smoking amongst younger women which has not been offset by a decrease in mortality in those over 60. The SMR for female breast cancer fell by 18% between 1996 and 2005 reflecting both earlier diagnosis and more effective treatment. The cause of breast cancer is not known although various risk factors lead to a greater susceptibility such as increasing age, early onset of menstruation, obesity, a first degree relative with the disease and possibly abnormal exposure to female hormones. Oral contraceptives are not associated with an increase and there is no widely accepted evidence that HRT is either. Hormones must however have a major role as removal of the ovaries reduces the risk significantly although the precise way in which this works is not known.

In men the age standardised mortality rate for prostate cancer has fallen from 30 in the early 1990s to 25 (16%) and the majority of deaths are in those over 70 years of age. Mortality rates for cancers of the colorectum have fallen in both men and women over the last ten years but are substantially higher in women. Cancer of the stomach has notably declined but at the same time cancer of the gullet (oesophagus) appears to have increased in frequency. A reduction in stomach cancer is thought to be associated with a reduction in exposure to dietary cancer inducing agents (carcinogens) and better food preservation and dietary habits. The rise in oesophageal cancer has, for some reason, run in parallel with a reduction in gastric ulcers following the recognition of the importance of drugs to reduce excessive acid secretion in the stomach and the eradication of helicobacter pylori, a bacterium which plays an important role in the development of ulcers. Again, the precise connection between these events is obscure. The age standardised incidence for melanoma of the skin has risen rapidly since the 1980s from around 5 to nearly 14 in women and from just over 2 to nearly 12 in men per 100,000 population attributable to excessive sun exposure and the use of sun beds.

### The mechanism of development of cancer

The fundamental underlying abnormality in all cancers is damage to the genetic material of the cell, the DNA which codes for the large number of molecules which cells produce. These include a wide variety of regulatory molecules which control cell division and growth in the

normal cell by complex inter-acting sequences of chemical reactions so that any normal cell loss e.g. shedding of skin or intestinal epithelial cells or natural cell death is accurately compensated for by cell multiplication. In cancer, this delicate balance between factors which tend to promote cell growth and those that inhibit it, is lost and cell division runs amuck. The genes which are important in controlling normal cell growth become altered by a variety of factors and are transformed into oncogenes. These cause the production of oncoproteins, which are associated with a lack of response to normal growth inhibitory signals, abnormal growth factors and abnormal growth factor receptors on the cell surface. This perpetuates the production of successive generations of cancer cells. The properties of the background non-malignant tissue in which the tumour is growing are also important and the body's natural immune system plays a role weeding out abnormal cells.

The daughter cells also have abnormal properties such as being able to invade tissues around the organ (local spread) and to penetrate blood and lymphatic vessels (enabling distant spread). These cells are also able to stimulate growth of their own blood supply and often seem to be able to escape from the body's immune surveillance system and to resist the normal process of programmed cell death (apoptosis) which is a normal physiological mechanism for keeping cell populations in balance. Finally, it is well recognised that general emotional well being may have a profound influence on the behaviour of cancers in some individuals.

Cancer most commonly arises in epithelium where cell turnover is high – where cells line the surfaces of body tubes and cavities. In general, the more abnormalities in the cell DNA, the more aggressive the tumour is and the appearances of the tumour cells under the microscope resemble their normal counterparts less and less. These tumours are called poorly differentiated as opposed to well differentiated tumours with a better prospect of cure and a longer natural history.

### The causes of DNA damage:

#### Environment

The factors causing DNA damage are known in some cases. Environmental factors such as smoking are extremely important, not only as a major cause of lung cancer, but also as a very important factor in numerous other cancers such as those of the bladder and larynx in these instances probably acting in concert with other factors which are as yet undefined. If nobody smoked, there would be a huge reduction in cancers of very many types. It is well known that radiation causes cancer as seen in the increase of leukaemias and other cancers amongst survivors of the atomic bombs and following radiation leaks. Following the Chernobyl disaster there has been a huge increase in thyroid cancer which previously was quite uncommon. Mesothelioma which is a cancer arising in the membrane lining the chest and abdominal cavity as well as covering the surface of the lung and intestine is directly caused by exposure to certain types of asbestos. These tumours develop many years after exposure, sometimes only to small amounts of the substance and currently in the UK there is an epidemic of this type of tumour following exposure in the 1950s and 60s.

#### Infection

Viruses may integrate their genetic material into cells and are a common cause of cancer in animals but their role in man is only well established in a few cases such as cancer of the neck of the womb (cervix), the culprit being some forms of wart or human "papilloma" virus. Vaccines have been developed against these strains and should protect against the disease. There is evidence that bacteria may have an important role in the development of cancers of the lymphoid cells of the immune system (lymphoma) in both the stomach and the skin. Viruses causing inflammation of the liver (hepatitis) may eventually lead to liver cancer.

#### Heredity

The underlying susceptibility of different people to the development of cancers of different types also varies in exactly the same way as the tendency to develop chronic diseases such as diabetes or heart disease. This is directly related to the genes that they carry. Gradually the genetic profiles making individuals susceptible are being worked out but it is rare for single individual genes alone to be responsible. Some cancers appear to run in families. Carriage of particular genes (BRAC 1 and 2) accounts for susceptibility to the development of

breast cancer in many members of some families but this is rare compared with the overall frequency of breast cancer. The vast majority of breast cancers do not arise on this basis although these genes may still play a role together with many others in non-familial cases. Another example is carriage of the dominant gene responsible for the development of large numbers of polyps in the large intestine many of which will go on to cancer but this is again very rare compared with the overall frequency of colonic cancer. In some people there is an absence of the ability to repair DNA errors which inevitably occur occasionally when normal cells divide. These errors are eliminated consistently by most people. In some families the failure of this mechanism is associated with the development of many different types of cancer such as cancer of the lining of the body of the uterus (endometrium) and cancers of the large intestine. Having said this, the precise genetic mutations responsible for most familial clusters of cancer are likely to be multiple and complex.

### Behaviour of cancer

Different types of cancer behave in different ways. Some are dominated by local spread for instance, a very common skin cancer called basal cell carcinoma or rodent ulcer. Others may stay confined to a small micro-anatomical area for a long time before invading, for instance in the epithelium in which they originate, before invading into the surrounding supporting structures. An example of this is carcinoma in situ of the neck of the womb revealed by a cervical smear test or carcinoma in situ arising in breast ducts identified on a screening mammogram. Yet other cancers may be locally invasive from the start such as well differentiated breast or prostatic cancer but not spread (metastasise) for a very long time. Even if spread has occurred through the lymphatic vessels with tumour cells lodged in local lymph glands they may never spread beyond this stage, a good example being one of the forms of thyroid cancer. Chronic lymphatic leukaemia may be symptomless for many years. In these cases local treatment or even none at all in the case of chronic lymphatic leukaemia or some forms of prostate cancer is all that is needed. These patients are regularly monitored so that more intense treatment can be instituted if things change. In this situation the only major problem to the sufferer may be the thought of having the disease and fear because of the uncertainty about the future. There will inevitably be some disappointments even within the usually well behaved groups of cancers in the same way that amongst some very aggressive cancers there are occasional unexpected complete cures. This is why the statistics for cancer are usually recorded as a percentage survival over five or ten years or longer. This gives an average statistical estimate of outlook which of course does not necessarily apply to a particular individual. Even amongst lung cancer where say, 93% of people die within 5 years, amongst 5000 cases 350 people will survive for this length of time.

Whereas the survival rates for breast cancer have shown much improvement over the last 30 years (increasing from 52% to 81% at five years and from 41% to 73% at ten years) those for lung have remained constant at 4 to 5% at ten years although there has been some improvement at the 5 year level. Survival rates from colorectal cancers have almost doubled at both 5 and ten years from around 25% to around 50%.

### Diagnosis

Over recent years there has been a marked improvement in disease-free intervals in terms of years from diagnosis for very many cancers as well as in overall survival and cure rates. One of the changes contributing to this is that the data on the precise site and extent of the cancer in the organ where it has arisen, its degree of resemblance or otherwise to normal cells (differentiation) and whether or not it has spread locally (staging) is now recorded in a standard way so that treatment can be tailored more appropriately. This is possible because of the changes in techniques in diagnostic radiology (MRI and CT scanning) and improvements in the way cancers are analysed and classified under the microscope. A further innovation has been the introduction of the Multidisciplinary Team approach throughout the NHS in which all cases of cancer are discussed on a regular basis at a forum comprising surgeons, oncologists, palliative care physicians, radiologists and histopathologists together with senior specialist nurses in cancer care so that optimum treatment is tailored specifically for each patient following peer review of the diagnosis and discussion of treatment options. Increasingly patients are directly and actively involved in these discussions.

## Treatment

The other major factor associated with improved survival rates is improvement in treatment. Many more cancers can now be significantly modified by modern treatments often given in combination – surgery, radiotherapy, and chemotherapy. This means that whilst not necessarily cured in the long term, patients may have long periods of disease-free health before the tumour relapses.

With regard to treatment in the earlier stages of the disease, huge progress is being made. Firstly, it has been realised that much less radical surgery is just as effective as more extensive removal of normal tissue around the tumour. For instance, removal of the complete breast (mastectomy) is now a rare event unless the tumour is very big or the case is one of recurrence. The same applies to removal of melanomas of the skin (cancer of the pigment producing cells) so that disfiguring scars are not produced. Secondly, surgical techniques are more sophisticated; even internal cancers can be removed successfully using “key-hole” surgery and these techniques are being widely introduced for bowel, prostate and kidney cancer amongst others. This means that there is far less post-operative pain, and patients are mobile by the next or subsequent day following the operation. They are discharged home earlier and suffer fewer complications. It has also been realised that treatment of tumours with drugs or radiotherapy before surgery to kill a lot of the cancer cells improves success rates. In some uncommon tumours of children (soft tissue tumours – sarcomas and kidney tumours) for example, cancers that were previously usually fatal are now frequently cured. Similar significant improvements are also being seen in common adult tumours such as colon and bladder cancer. There have been major developments in the way that radiotherapy is delivered with more sophisticated machines (linear accelerators). This leads to increasing cure rates whilst side effects are reduced. New techniques such as conformal therapy mean that tumours can be targeted accurately and normal tissues spared from radiation.

Many new drugs which are very effective are now routinely used. Some of these are similar to the well established chemotherapy drugs which interfere with cancer cell growth through their effect on DNA. But others work by affecting the hormonal environment making it more difficult for cancer cells to grow. This approach is very effective in breast cancer with the use of drugs such as Tamoxifen and Letrozole or Exemestane. In prostate cancer, agents interfering with the effect of male hormones, hold the tumour in check. Newer drugs are tailor made molecules which block receptors on cells which are important in the complex chain of reactions leading to cell growth. An example is Herceptin which blocks a growth factor receptor on breast cancer cells. Yet other drugs are like antibodies which home in on antigens on the cell surfaces again interfering with cell growth such as Rituximab a drug used in lymphoma treatment.

In contrast to the success of these treatments, no properly-conducted trials have shown 'alternative' or 'complementary' therapies to have any effect on tumour size or progression. Cancers can sometimes shrink without medical intervention, and oncology departments have reported cases where proven cancers have disappeared without treatment, but such spontaneous remission is extremely rare."

Given the failure of alternative or complementary interventions to demonstrate improvements in mortality, and the serious risks to patients who do not seek proper medical treatment, no therapy should be offered by non medically-qualified personnel which claims or implies that it can modify the disease.

Some cancer patients report unsatisfactory contacts with health professionals, with insufficient time spent on explaining issues and talking through strategies and prognosis. This is perhaps unsurprising given the pressure on oncology departments, but is one area where properly qualified clinicians might learn from private 'alternative' practitioners

The fear of cancer seems to be much greater than the fear of other chronic diseases but most cancers behave in a very similar way. A person may suffer a heart attack, be well for many years and then have another, go into heart failure or suffer a stroke – all these events being due to the same underlying disease process – a narrowing of the arteries supplying blood to different organs. A person with rheumatoid arthritis may suffer acute episodes of pain and immobility and then improve only to relapse later. Gradually the affected joints become more and more damaged. In the same way many cancers are treated successfully initially but may return at the same site years later. Even then, further treatment is often successful. The

disease may spread to local lymph glands and still be cured. When it spreads widely, chemotherapy is often helpful in prolonging life. Another reason for the dread that cancer provokes is because people associate it with severe pain and a very unpleasant way of dying. There have been huge strides made in the management of severe pain and with radiotherapy and/or modern drugs often used in combination and carefully related to the patient's needs, and nowadays there is no reason why anyone should suffer unnecessarily. This treatment is often carried out in specialised centres such as hospices where the doctors, nurses and all the other health workers are especially trained in palliative care. These professionals are expert in dealing with the other symptoms of weakness, poor appetite, nausea or just generally feeling unwell. They are trained to provide psychological, physical and practical support. They behave naturally, are cheerful and friendly and it is often surprising how helpful this is even if the patient is terminally ill.

There are also numerous charitable organisations other than those which are hospital and general practice based providing a wide variety of services, information and advice for cancer patients, relatives and carers. The foremost cancer charity in the UK, Cancer Research provides a wide range of awareness leaflets, a clinical trials database for the public, and comprehensive statistics as well as funding research into all aspects of the disease including educational and psychological support. Cancerbackup provides information, advice, leaflets on treatment and living with cancer as well as 8 walk-in centres based in hospitals in the UK. Macmillan Cancer Support provides practical, medical, nursing and emotional support. Many oncology departments and surgical cancer services have direct links with Macmillan nurses who can provide important continuity of care between the specialised hospital departments and the community. Marie Curie Cancer Care also provides free nursing care to patients in their own homes and funds research programmes. There are also some organisations dedicated to cancers of specific sites such as Breast Cancer Care, and Breakthrough Breast Cancer and details of those dealing with other sites are easily accessed through the organisations listed above.

### Assessment of new treatments

It is now widely accepted that new treatments must be properly compared with each other and with established treatments before they can be put into general use. This can only be done properly and without bias in controlled trials where different treatments are directly compared in two groups of identical patients. Health Watch strongly supports this approach for both orthodox and unorthodox treatment and helps to monitor situations where inappropriate claims are made for treatments which have not been subjected to this vigorous process. It is also important to identify trials in which claims about the efficacy of a drug have been made on an incorrect basis either because the data have been misinterpreted, there is a bias present, or sometimes, and most unfortunately, because the results have been falsified. The National Clinical Research Network in the UK has increased the number of patients able to enter clinical trials of new treatments to a record high, with more patients than in the U.S. or any other European country. This will lead to further improvements in treatment in the future.

### Screening and prevention

In cancer, as with all diseases, prevention is better than cure. Screening programmes to detect early cancer are well established for cervical and breast cancers in the UK and many authorities agree that they have made a significant impact on survival. Although there is no universal agreement and the evidence is not as clear cut as some would have it, these screening programmes are set to continue. The evidence for the effectiveness of screening for bowel cancer is good and the programme is due to be implemented in the UK. Currently there is insufficient evidence to merit the introduction of a programme for screening for prostatic cancer. Sadly there is widespread agreement that there is no effective method of screening for lung cancer.

So what else can be done to prevent cancer developing? Apart from giving up smoking which would lead to a huge reduction in the numbers of many types of cancer, a sensible attitude to sun exposure would curb the rise in skin cancers, particularly melanoma which has increased recently. We depend on careful research and observation to identify links between cancers and external agents as in the example of asbestos and mesothelioma quoted above. Otherwise a generally healthy life-style with plenty of exercise, a good balanced diet including

vegetables and fruit which contain anti-oxidants, (substances which are important in reducing damage to cells) and avoidance of obesity are very important factors.

### Conclusion

The causes of many cancers are still unknown and may well prove to be multifactorial. It is also unlikely that there will be a single cure. In future, it will be possible to further subdivide cancers of a particular organ or site previously regarded as a homogenous group. Using a combination of techniques it should become feasible to accurately characterise the cancer cells forming a given tumour. This might include their appearances under the microscope (morphology), the abnormal genes, the different growth factor receptors on the cancer cells, the biologically active compounds produced by the malignant cells, and the local tissue environment of the tumour cells as well as the tumour extent. Hopefully this will lead to a much more specific, effective and individually tailored treatment regime for individual cases.

Prepared by Dr Leo Horton and approved by the HealthWatch Executive committee 9/1/2008.

### Useful Contact Details

**Cancer Research UK:** PO Box 123, Lincoln's Inn Fields, London WC2A 3PX Tel: 020 7240 2000, <http://www.cancerresearchuk.org>

**Cancerbackup:** 3, Bath Place, Rivington Street, London EC2A 3JR Tel: 0808 800 1234 <http://www.cancerbackup.org.uk>

**Breast Cancer Care:** 5-13, Great Suffolk Street, London SE1 0NS Tel: 0845 0920 800 <http://www.breastcancercare.org.uk>

**Breakthrough Breast Cancer:** 3<sup>rd</sup> Floor, Weston House, High Holborn, London WC1V 7EX Tel: 0800 100 200, [www.breakthroughbreastcancer.org.uk](http://www.breakthroughbreastcancer.org.uk)

**Marie Curie Cancer Care:** 89, Albert Embankment London, SE1 7TP Tel: 020 7599 7777  
29, Albany Street, Edinburgh, EH1 3QN Tel: 01314 563 700  
Block C Mamhilad House, Mamhilad Park Estate, Pontypool, Torfaen NP4 0HZ Tel: 01495 740 827  
60 Knock Rd., Belfast, BT5 6LQ Tel: 0289 088  
<http://www.mariecurie.org.uk>

**Macmillan Cancer Support:** 89, Albert Embankment London SE1 7UQ Tel: 020 7840 7840 [www.macmillan.org.uk](http://www.macmillan.org.uk)