

Abscissa

The x (horizontal)-axis of a graph.

Absolute Rate Difference

Absolute rate difference is the difference, in a comparative study, between the event rate in the treatment arm and the event rate in the control arm. Survival with adjuvant chemotherapy for breast cancer is 46.6% at 10 years; the corresponding figure for controls is 39.8% (data from EBCTG1 breast overview):

- Absolute rate difference = $46.6 - 39.8\%$
= 6.8%.
- **Relative risk** (p. 264) reduction is $6.8/39.8\% = 17\%$.
- **Number needed to treat** (p. 216) is $1/0.068 = 15$.

Absolute Risk

Absolute risk simply indicates for an individual or group the probability of a specified event (usually adverse) occurring within a specified time interval. It is related to the concepts of relative risk and absolute rate difference. See also **Relative Risk** (p. 264), **Absolute Rate Difference** (above).

Absorbed Dose

The energy deposited per unit mass of material by ionising radiation is the absorbed dose. The unit is the Gray (Gy), where $1\text{ Gy} = 1\text{ joule kg}^{-1}$ (J kg^{-1}). An older measure, the rad (radiation absorbed dose, 100 ergs g^{-1}) is equivalent to 1/100 of a Gray, i.e. $1\text{ Gy} = 100\text{ rad}$, $1\text{ rad} = 1\text{ cGy}$ (centigray). Defined in this way, Gy is independent of the material irradiated or the type of radiation. Note, however, that the biological effect of any given dose of radiation may well depend on these two factors (see also **Relative Biological Effectiveness** (p. 264), **Quality Factor** (p. 253)). It is

sometimes difficult, particularly when dealing with indirectly ionising radiation, to measure dose directly — in these circumstances it is often useful to use **kerma** (p. 170) as the measure of radiation quantity.

Absorption Rate Constant

Absorption rate constant is a term used in pharmacology to describe the kinetics of drug absorption. It is defined as:

$$\frac{\text{rate of drug absorption}}{\text{amount of drug remaining to be absorbed}}.$$

Accelerated Fractionation

This term is only loosely definable. It implies that, keeping total dose and dose per fraction constant, a course of **fractionated radiotherapy** (p. 131) is given in an overall time which is less than standard. The problem is that there is no agreement on what constitutes a ‘standard’ time. In some departments, 6 weeks is standard, in others it is 3–4 weeks. A useful operational definition would be to define as accelerated any radical treatment given in <3 weeks. The problem here is that a department used to a 6–7-week schedule would define as accelerated a treatment given over 5 weeks; this ‘accelerated’ treatment would still take longer than the 4-week schedules used in many departments. All things are relative, accelerated fractionation is no exception.

Pure acceleration, by the conventional definition, would involve giving 60 Gy in 30 fractions in 3 weeks: this is not tolerated because the rate of dose-accumulation exceeds the tolerance of the acutely responding tissues. In practice, a combination of acceleration and **hyperfractionation** (p. 156) is used, e.g. 70 Gy at $2\text{ Gy fraction}^{-1}\text{ day}^{-1}$ in 7 weeks might be comparable with 72 Gy at 1.6 Gy (t.i.d.) in 5 weeks.

The biological rationale behind accelerated fractionation is that, by keeping the overall treatment time as short as possible, it will minimise the opportunities for clonogenic tumour cells to repopulate during treatment.

Accelerated Repopulation

The term ‘accelerated repopulation’ was introduced into radiobiology to describe an apparent increase in the rate of cellular proliferation in response to treatment with a **cytotoxic** (p. 84) agent such as radiotherapy. In squamous carcinomas of the head and neck, for example, the doubling time before treatment may be ~40–60 days: by the end of a course of radiotherapy the doubling time may be as short as 5–8 days. Although initially described in tumours, the phenomenon can also apply to normal tissues. There are several mechanisms whereby the proliferative rate of a population of cells might increase in response to an external stimulus such as radiation: the **growth fraction** (p. 144) could increase; the **cell loss factor** could be reduced; the duration of the **cell cycle** (p. 52) could be shortened. The clonogen doubling time will, with accelerated repopulation, approach the minimum **potential doubling time** (T_{pot}) (p. 241) for that particular population of cells: whether there is more to accelerated repopulation than simply, by reducing cell loss to zero, an unmasking of the latent T_{pot} , is debatable.

Another controversy concerns the timing of any accelerated repopulation: does it start with the first radiation treatment or is there an initial lag period (‘hockey stick’ relationship) before it begins. The lag has been estimated at ~20 days.

The practical consequence of accelerated repopulation is that overall treatment times should be kept as short as possible. If a lag period of 20 days exists then some schedules

such as **CHART** (p. 62) may avoid the problem altogether since the treatment will have finished before accelerated repopulation has been established. With more protracted treatments, over ≥ 4 weeks, accelerated repopulation means that each extra day of treatment corresponds to a loss of effective dose of ~0.4–0.7 Gy. Unanticipated breaks in treatment will result in a loss of tumour control unless some compensatory strategy is used. Such strategies include treating twice a day on days subsequent to missed treatment, thus keeping overall treatment time the same; treating during weekends, again to keep overall time constant; and adding extra fractions at the end of treatment to compensate for missed days, the extra dose required being calculated by formulas based on the BED equation.

Accreditation

With the development of clinical standards and other benchmarks of performance, the process of accreditation is becoming increasingly important. Accreditation may be defined as a process based on a system of external **peer review** (p. 229) using written standards designed to assess the quality of an activity, service or organisation. It is an excellent concept.

Accreditation, as a process rather than as a concept, suffers from all the disadvantages and pitfalls associated with peer review. It has other additional problems associated with it. It could, potentially, be used as an instrument of fiscal control. It could be hijacked by special-interest groups and be used to push through changes that suit a minority, rather than the majority. Minorities are sometimes, but not invariably, right. A set of values imposed by a minority can never, by definition, be democratic. There is no doubt that accreditation has the potential to raise the standards of those organisations or systems that perform poorly; it also has the

potential to reduce excellence to a lowest common denominator. Accreditation relies heavily on assessment of process, rather than outcome. The underlying assumption is that better process will produce better outcome.

Accrual

Accrual is a jargon term used to describe the recruitment of patients to a clinical study. The accrual rate that can reasonably be anticipated is a critical component of study design. Not all patients attending will be eligible for the study, not all eligible patients will enter the study and not all entered patients will complete the study: some horses are unfit for entry into the Grand National, some will not line up at the starting tape and some fall at the fences.

Problems of accrual and attrition have to be anticipated when the study is designed. The ultimate statistical power of the study will depend on the event rate in evaluable patients. There is no point in embarking on a study that is never going to accrue a sufficient number of patients. The issues of sample size, **power** (p. 241) and statistical **significance** were successfully addressed by Jacob Bernoulli over 250 years ago, and yet an appreciable number of published studies on comparisons of treatment continue to accrue so few patients that they would be unable to prove anything: this is the problem of the Type II statistical error.

Accuracy

Accuracy reflects the extent to which a statement or measurement corresponds to the truth: it is possible to be accurate without being precise. It is accurate to say that John Lennon was nearly 6 feet tall; it is, however, less precise than stating that his height was 5 feet 10 inches.

The accuracy of a measurement has to do with how closely it corresponds to the true

state of affairs. It can be distinguished from **precision** (p. 243) since precision is no guarantee of accuracy. The value 3.05 would be an imprecise estimate of π , but it is more accurate than an estimate of 5.100087253. This latter estimate is more precise, containing detail down to the ninth decimal place: it is, unfortunately, more inaccurate. An accurate, but imprecise, measurement is usually preferable to a precise, but inaccurate, one. The ideal measurement is, of course, both accurate and precise.

Acquiescence Response Set

The term used to describe the tendency of subjects to agree with whatever is put to them. This is a problem in, for example, questionnaire studies of **quality of life** (p. 253) and it is certainly a problem on ward rounds: ‘we’re feeling much better today, aren’t we Mrs Smith?’, to which the only reply is, ‘there’s something happening here and you don’t know what it is — do you Dr Jones?’

Acquired Immunodeficiency Syndrome (AIDS)

This emotive term defines a time-point within the natural history of infection with the **human immunodeficiency virus (HIV)** (p. 151). As with any externally defined event in the natural history of disease, it is a somewhat arbitrary imposition, but one which has pragmatic usefulness in defining a certain degree of immunosuppression. The criteria for defining the existence of AIDS in an individual who tests positive for HIV infection have evolved since the first descriptions of the clinical syndrome in the early 1980s. At that time, it was the coincidence of immunosuppression with *Pneumocystis carinii* pneumonia and Kaposi’s sarcoma that led, in 1984, to the identification of HIV infection. The current definition (Centers for Disease Control, 1993) regards any of the following as

AIDS-defining diagnoses in an individual known to be HIV positive:

- Severe immunosuppression: as defined by a CD4⁺ T-lymphocyte count of <200 cells μl^{-1} or a CD4⁺ level <14%.
- Candidiasis of bronchi, trachea or lungs.
- Candidiasis, oesophageal.
- **Cervical cancer, invasive.**
- Coccidioidomycosis, disseminated or extrapulmonary.
- Cryptococcosis, extrapulmonary.
- Cryptosporidiosis, chronic intestinal (>1 month).
- Cytomegalovirus disease (other than liver, spleen or nodes).
- Cytomegalovirus retinitis (with loss of vision).
- Encephalopathy, HIV-related.
- Herpes simplex: chronic ulcer(s) (>1 month); or bronchitis, pneumonitis or oesophagitis.
- Histoplasmosis, disseminated or extrapulmonary.
- Isosporiasis, chronic intestinal (>1 month).
- **Kaposi's sarcoma.**
- **Lymphoma, Burkitt's** (or equivalent term).
- **Lymphoma, immunoblastic** (or equivalent term).
- **Lymphoma, primary, of brain.**
- *Mycobacterium avium* complex or *M. kansasii*, disseminated or extrapulmonary.
- *Mycobacterium tuberculosis*, any site (pulmonary or extrapulmonary).
- *Mycobacterium*, other species or unidentified species, disseminated or extrapulmonary.
- *Pneumocystis carinii* pneumonia.

- Pneumonia, recurrent.
- Progressive multifocal leukoencephalopathy.
- *Salmonella* septicaemia, recurrent.
- Toxoplasmosis of brain.
- Wasting syndrome due to HIV.

The tumours associated with the diagnosis of AIDS are highlighted. The importance of malignant disease in AIDS should not be underestimated, nor should the global importance of HIV infection in the context of patients with cancer be ignored. In sub-Saharan Africa up to 30% of patients newly diagnosed with cervical cancer are HIV-positive.

The AIDS epidemic has another, equally important, impact on oncology. It can serve as an example of how research can offer at least partial solutions to clinical problems. The pace of research into HIV–AIDS has far outstripped anything that has occurred in cancer research and this has been reflected in the ability to devise and test clinically useful therapies. The lessons that can be learned include:

- Identification of specific molecular targets (**reverse transcriptase (p. 272)**, protease) and development of specific therapies that act on these targets.
- Research driven by a specific focus, as opposed to diffuse curiosity.
- Ability to take potential therapies rapidly from the laboratory to the clinic — streamlined bureaucracy and licensing procedures.
- Ability to carry out rapidly randomised trials that ask, and answer, specific questions.
- The importance of consumerism and advocacy: vocal demands by pressure groups result in action by government and other funding bodies.
- Partnership between the pharmaceutical industry and research agencies.

Cancer research suffers from the disadvantage, compared with research into HIV–AIDS, that it has been around a while, a period long enough for disillusion and cynicism to have set in, and long enough for vested interests and orthodox dogmas to dictate what is, and what is not, studied. There was no rulebook for HIV–AIDS whereas cancer research has been governed over the years by a reluctance to depart from set principles — even though those principles have not proved particularly successful in delivering effective therapies. The argument has always been that of the First World War generals, ‘one final push’, a plea for yet more resource. There has been a conspicuous reluctance to question whether the assumptions made are, in fact, valid. Are the screening programmes for new drugs effective or are clinically useful drugs eliminated because they fail in a rodent model? A treatment that does not produce **complete responses** (p. 70) is defined as ineffective, even though it may be clinically useful in terms of providing a patient with a period of clinical stability. Novel mechanisms of action, e.g. inhibition of angiogenesis, will require clinical assessments that have not yet been devised: an **angiogenesis** (p. 14) inhibitor is unlikely to produce a complete response, but it might lower the incidence and slow the growth of metastases. Experience with HIV–AIDS should help re-educate oncologists in how to think rationally from basic principles rather than simply repeating the mistakes of the past.

Activity

The activity of a sample of a radioactive isotope is defined as the rate of decay:

$$\Delta N/\Delta t,$$

where ΔN is the change in the number of radioactive atoms and Δt is the time interval. Its unit is the **becquerel** (Bq) (p. 26), where

$$1\text{ Bq} = 1\text{ disintegration s}^{-1}.$$

It appears in the definition of the **transformation constant** (p. 313), and by extension, in the **half-life** (p. 147) equation.

Actuarial

An actuarial method combines estimates of probability into a tabular structure. These methods originate in accounting and in the calculation of insurance premiums, but their main role in oncology is in survival analysis. The essential feature of the method is that where a data set is incomplete and not all patients have been followed up until death (i.e. the data are censored), the information we have can be used to predict the future pattern of the **mortality rate** (p. 207) in the whole group. The most commonly used actuarial method for survival analysis is the **Kaplan–Meier Method** (p. 170). Where survival times are only known approximately then the **lifetable** (p. 179) method can be used.

Actuarial Assumption

Actuarial assumption is an assumption used in the construction of a **lifetable** (p. 179) — it is assumed that the distribution of censoring is uniform during a given time interval. For example, if 30 patients enter a 6-month interval and at the end of the period 20 patients are known to have survived and six are known to have died, then there are four censored survival times. We can, using the actuarial assumption, calculate the average number of patients at risk during the interval as:

$$30 - (4/2) = 28.$$

Actuarial Methods in Calculating Complication Rates

Only those patients who survive long enough are candidates for late complications of treatment. Crude estimates of complication rates may underestimate the incidence of late

complications associated with a particular regimen or technique: patients who have already died from cancer cannot be assessed for treatment-related complications. Actuarial methods offer only a partial solution to this difficulty. If the last survivor develops a complication then this will exaggerate any complication rate calculated actuarially. Figure 1 shows an actuarial plot from a series of patients in which the crude complication rate is 29% (6/21).

The complication-free survival would be calculated actuarially as 50% (not 71%, i.e. $100 - 29\%$). The use of the **crude rate** (p. 81) would have led to underestimation of the likely complication rate.

Figure 2 has data for a study in which the last surviving patient suffers a complication — the crude complication rate is still 6/21 (29%).

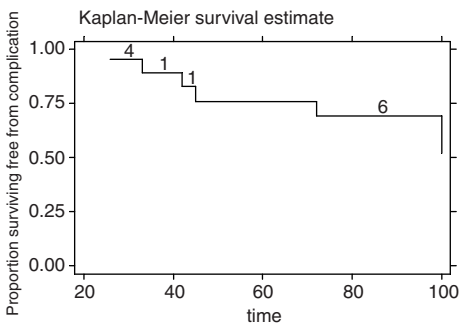


Figure 1.

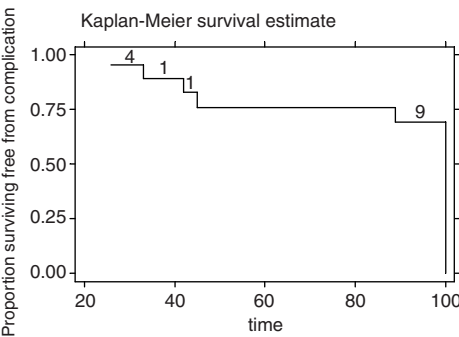


Figure 2.

The complication-free survival would be calculated actuarially as 0%. There is no easy solution to the problem of trying to use **censored data** (p. 60) to estimate the probability of events occurring later in follow-up: the important thing is to be aware of the pitfalls associated both with crude rates and with actuarial calculations.

Actuarial Lifetable

An actuarial lifetable is used to analyse time-dependent data, such as survival after treatment, when the exact dates of events are not known. Events may occur between follow-up visits: at the earlier visit they are recorded as absent but are recorded as present at the next visit. The precise date of onset cannot, however, be determined. The actuarial method simply defines the time of onset as the midpoint of the interval used to construct the table. A similar assumption (the actuarial assumption) is made concerning the timing of censored observations. Intervals commonly used for lifetables based on clinical studies are 3 months to 1 year.

Acute (Early) Side-Effects of Cancer Treatment

The side-effects of cancer treatment can, for convenience, be divided into early and late: in the jargon, acute and late morbidity. Acute effects are those that occur at and around the time of treatment. **Late effects** (p. 174) are those that arise at least 3 months after the completion of treatment. The distinction is not always clear cut — early effects may fail to resolve and lead directly to late effects, so-called **consequential late effects** (p. 73).

The acute effects mainly affect those normal tissues that divide rapidly: the skin and its appendages (such as the hair follicles), the

lining of the gastrointestinal tract, the bone marrow and the germinal cells of the **testis** (p. 306). Radiation will affect only those normal tissues within the irradiated area (patients who have radiotherapy to the chest do not go bald as a result of radiotherapy). Chemotherapy can potentially affect all rapidly dividing normal tissues, though the precise spectrum of toxicity varies from drug to drug.

Normal tissue	Symptoms and signs of cytotoxic damage
Oral mucosa	sore mouth, mucositis, pain on swallowing
Oesophageal lining	pain and difficulty on swallowing
Laryngeal lining	stridor, hoarse voice
Lining of stomach and small bowel	nausea, vomiting, diarrhoea
Lining of large bowel	diarrhoea, mucus discharge, bleeding, tenesmus, itch
Lining of bladder	frequency, dysuria, cystitis
Skin	itch, burning sensation, erythema, desquamation, hair loss
Germinal epithelium of testis	azoospermia, infertility
Bone marrow	leucopenia, thrombocytopenia, anaemia

Repair of acute damage to dividing tissues is an energy-dependent process. This may, in part, explain why fatigue is such an important, but often unrecognised, acute effect of cancer treatment.

Adaptation Response

Adaptation response is the process where cells, which appear to be in stable arrest in terms of the **cell cycle** (p. 52), can re-enter the cell cycle and resume growth and division. The process mainly depends upon environmental factors.

Address Labels

Address labels are specific amino acid sequences on newly synthesised proteins that ensure that the protein is directed to the appropriate site within the cell for processing. The **signal recognition particle** (p. 286) is one such destination; another, for which the PACS-1 sequence is the label, is the trans-Golgi network.

Adduct

A complex that forms when a chemical, such as a drug, binds to a biological molecule, such as DNA or protein. The formation of adducts between drugs and DNA is one of the mechanisms of action of **cytotoxic drugs** (p. 84).

ADEPT (Antibody-Directed Enzyme Prodrug Therapy) = ADC (Antibody-Directed Catalysis)

An enzyme-linked antibody is directed against an antigen that is tumour-specific. The enzyme is then used to convert an inactive precursor (**prodrug**) (p. 246) to an active cytotoxic agent. Since this activation will only occur where there is enzyme, and since, thanks to the antibody, there is only enzyme where there is tumour, the approach offers a means of improving the **selective toxicity** (p. 282) of cancer therapy. Examples of this approach include:

- MAb BW 431/26 conjugated to alkaline **phosphatase** (p. 233), the antibody binds to CEA, the enzyme activates **etoposide** (p. 119) phosphate (prodrug) and the locally active cytotoxic agent is etoposide.
- MAb 323/A3 (antibody to a membrane glycoprotein found in carcinomas) conjugated to β -glucuronidase, epirubicin

glucuronide is given as prodrug, epirubicin is the active agent.

This approach is also sometimes called antibody-directed catalysis (ADC).

Adhesion Molecules

A group of diverse molecules essential for normal tissue function and that has important roles in cell growth and differentiation, embryological development, and wound repair. There are four main families:

- Integrins.
- Immunoglobulin superfamily, e.g. N-CAM, PECAM-1.
- **Cadherins** (p. 39).
- **Selectins** (p. 281).

The first three interact with proteins. Selectins and lectins are unusual in that they interact not with proteins but with carbohydrate molecules, e.g. on the surface of white blood cells or endothelial cells. Lectins are of plant origin but have found wide application as stimulators of proliferation (mitogens) in the culture of mammalian cells. They are also useful in blood grouping and in the immuno-cytochemistry of carbohydrates.

Disruption of the function of **adhesion molecules** (p. 8) is of critical importance to several aspects of the **malignant process** (p. 185): uncontrolled proliferation, local **invasion** (p. 167) and **metastasis** (p. 198) formation.

Adhesion molecules include **E-cadherin** (p. 111), **fibronectin** (p. 128), the integrins and **desmogleins** (p. 94).

Adjuvant Treatment

Adjuvant treatment is treatment given in addition to definitive treatment in an attempt to lower the risk of relapse. The concept is

based on the following assumptions and observations:

- There has been abundant time during the natural history of a cancer for a malignant cells to spread beyond the clinically demonstrable tumour (micrometastatic disease).
- There may be microscopic local or disseminated disease remaining after apparently successful treatment for cancer.
- No imaging technique currently available can detect single cancer cells.
- Accurate tumour markers are available only for a few rare tumours (e.g. choriocarcinoma).
- Microscopic residual disease is undetectable using currently available technology.
- A single cancer cell persisting after initial treatment is sufficient to cause recurrence.
- Dispersed, small-volume tumours are more sensitive to treatment than bulky tumours.
- Treatment given earlier is more effective than treatment given later: cells are more actively proliferating; drug resistance is less likely.

It is implicit within the concept of adjuvant treatment that there will be three categories of patient:

- Patients who have no residual disease after their initial treatment and for whom adjuvant treatment can confer no benefit.
- Patients who have residual disease but whose disease is refractory to therapy and who are destined to recur in spite of adjuvant treatment.
- Patients who have residual disease and whose disease will be eradicated by adjuvant treatment.

ADME

ADME is an acronym that describes the key processes by which the body handles an administered drug or chemical:

- Absorption.
- Distribution.
- Metabolism.
- Excretion.

Pharmacokinetics (p. 232) is the study of the time-course of these processes. The analogous processes at the cellular level are:

- Uptake.
- Intracellular distribution.
- Biotransformation.
- Efflux.

Adenosine Diphosphoribosyl Transferase (ADPRT)

Adenosine diphosphoribosyl transferase (ADPRT) is an enzyme concerned with repair of **DNA damage** (p. 98). It is bound to **chromatin** (p. 63) and is inhibited by **nicotinamide** (p. 214).

Ageing

The incidence of most forms of cancer rises with age. This is particularly true for cancers of the large bowel and prostate. This suggests that, for some reason, the development of cancer could be regarded as part of the ageing process. There is probably no one simple explanation for this. Many different factors are undoubtedly involved and these could include diminished immune competence leading to relative failure of immune surveillance; increased accumulation of mutations in nuclear DNA over time leading to increased risk of acquiring malignant genotype; age-related changes in

the expression of tumour suppressor genes; mutations in mitochondrial DNA causing increased mitochondrial production of carcinogenic-**free radicals** (p. 132); and increased duration of exposure to environmental carcinogens. The change in the age distribution of the population in the developed world, with an increasing proportion of older persons, has implications for oncology. We can expect to see an increased number of older people with cancer, in both absolute and relative terms.

Age-Standardised Rate

Age-standardised rate (ASR) is a summary measure of a rate that a population would have if it had a standard age structure. Standardisation is necessary when comparing several populations that differ with respect to age because age has such a powerful influence on the risk of cancer. This is particularly true when cancer incidence in the developed world is compared with the incidence in the developing world. The most frequently used standard population is the World standard population. The calculated incidence or **mortality rate** (p. 207) is then called World Standardised incidence or mortality rate. It is also expressed per 100 000 population.

A-Kinase (Cyclic AMP-Dependent Protein Kinase)

The enzyme through which the intracellular messenger, cyclic AMP, acts to control cellular functions. It transfers phosphate groups from ATP to threonine and serine residues on target proteins. It activates phosphorylase kinase and glycogen **phosphorylase** (p. 234), with important effects on energy metabolism (release of glucose from glycogen). A-kinase also activates genes via the **CREB binding protein** (p. 80).

ALARA

The ALARA concept (As Low As Reasonably Achievable) is used to underpin modern guidelines and regulations concerning radiation protection. The concept involves conceding the principle that some degree of radiation exposure is, for each individual, unavoidable. Background radiation, from rocks and cosmic rays, affects us all. Any exposure as a result of medical or industrial uses of radiation is simply an addition to an inevitable exposure. Against this background it is both unnecessary and impossible to achieve zero exposure. The exercise becomes one of damage limitation: to increase exposure no more than is absolutely necessary. The goal is simply to minimise, using reasonable precautions and procedures, the dose of radiation received by any individual as a result of medical intervention or occupational exposure.

Alkylation, Alkylating Agent

Alkylation is the process where an alkyl group replaces a hydrogen atom in a compound. An alkyl group is simply an alkane that has lost a hydrogen atom. An alkane is an organic molecule consisting of chains, either branched or unbranched, of carbon and hydrogen atoms where all of the bonds between carbon atoms are single bonds.

An alkylating agent is a substance, typically a cytotoxic drug, that replaces the hydrogen in the hydrogen bonds between the complementary DNA base pairs with an alkyl group. This binds the complementary **DNA strands** (p. 101) irreversibly and interferes with cell division by preventing DNA **replication** (p. 267). **Cyclophosphamide** (p. 83), busulphan, melphalan and chlorambucil are typical examples of alkylating agents used in the chemotherapy of malignant disease.

Allelic Heterogeneity

This occurs when a disease may be caused by more than one type of mutation within a specific gene.

All or None Phenomenon

A term used in grading evidence dealing with treatment or prevention of illness. It occurs when before the treatment became available all patients died, but after introducing the treatment some patients survive. Alternatively, it would occur if before introducing the new treatment some patients died, but after its introduction none died. In the NHS R&D classification the all or none phenomenon is categorised as Grade A level 1c.

α/β Ratio

This radiobiological term, derived from the linear–quadratic model of **radiation-induced cell killing** (p. 256), describes the curviness of the shoulder of the cell survival curve. The α component of the ratio, which is directly proportional to dose, indicates single-target single-hit killing and, as such, gives a measure of the intrinsic **radiosensitivity** (p. 260). The β component, which is proportional to $(\text{dose})^2$, gives an indication of the killing due to multiple hits on several targets. The α/β ratio is that dose of radiation at which single- and multiple-hit killing are equal. Units are: α (Gy^{-1}); β (Gy^{-2}); α/β ratio (Gy).

Tumours, and acute radiation effects such as skin erythema and mucositis, have fairly high α/β ratios (typically 10 Gy) compared with those for late radiation effects, such as subcutaneous fibrosis and **radiation myelopathy** (p. 256), (typically 3 Gy): the initial slope of the cell survival curve is curvier for late responding tissues than for tumours and acutely responding tissues. Reducing fraction size will, therefore, selectively tend to spare late responding tissues compared with