Chapter 20: Principles of radiotherapy in head and neck cancer

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Radium was discovered in 1898 by Marie and Pierre Curie. Within a few years of its discovery, radium was being used in the treatment of cancer, initially by surface application and subsequently by insertion of sealed containers into tumours. In addition, radon gas sealed in a gold capillary tube was implanted into accessible tumours with, what were at the time, amazing results. Even before the Curies’ discovery, Wilhelm Röntgen had begun his investigation into the luminescence produced by cathode rays, and in 1895 had discovered a phenomenon which, in view of its uncertain nature, he called X radiation.

During the next 30 years, considerable advances were made in understanding both the production of X-rays and the importance of radioactive substances in the treatment of malignant tumours. Associated with the increasing knowledge of the nature and production of electricity was the development of methods of generating high voltages. This knowledge was used to create a high potential difference (voltage) across an evacuated tube in which electrodes were sealed, permitting the production of X-rays of varying energy. The availability of larger amounts of radium led to the first teletherapy units. In such units, the increased distance of the isotope from the tumour produced a higher absorbed dose at a depth within the patient. The early teletherapy radium units were known as radium bombs.

Subsequent progress was slow until World War II (1939-45), when considerable resources were put into research. This investment led directly to the development of the early machines which still exist today, for example linear accelerators, and other means of producing high energy radiation and particles. Simultaneously, the increase in availability of numerous new radioactive isotopes, as a byproduct of atomic weapons’ manufacture, led to new techniques being developed in both the diagnosis and treatment of cancer. In the last 40 years, there have been a great many advances in all treatment modalities. The main reason for this has been the maintenance of centres of excellence, from which have emanated the results of a wealth of research and development, coupled with the provision of advanced equipment to regional cancer treatment centres and the specialization of medical staff in all forms of cancer therapy. In the field of head and neck malignancy, the scope of treatment methods and the varied expertise available, have meant that treatment by an individual in isolation is no longer the norm. Sometimes, the management of a patient is conducted by a team comprising only an otorhinolaryngologist and a radiotherapist also trained in the use of cytotoxic drugs; more often a medical oncologist, a maxillofacial surgeon and a speech therapist complete the range of expertise available in the joint clinic. The concept of the joint clinic has led to an improvement in the treatment of each individual patient. This is reflected by the longer survival period of patients together with a better quality of life.

The best means of establishing such a joint clinic is to come to an agreement with the specialists involved in the many hospitals served by one cancer treatment centre, as to who will provide which particular expertise and hence become part of the cancer treatment team. This will allow others, for example in the field of otolaryngology, to specialize in otological problems and to establish the same sort of collaboration with other colleagues. Only in this way is it possible for the degree of excellence which should be available to be achieved and
for each member of the team to come to know the potential of the other members special
skills.

**Radiotherapy - a scientific or clinical speciality?**

All radiotherapists would admit that a sound knowledge of the basics of physics of
radiation is essential. Similarly, a surgeon would agree that a detailed knowledge of the
different surgical instruments available to him was equally important.

The essential requirements of a radiotherapist and oncologist are a good general
training in medicine and, above all, to be a good clinician. Radiotherapy is without doubt a
clinical speciality where a scientific knowledge of physics and, probably more important, the
biology of tumours and their behaviour, is essential.

**The nature of radiation**

**Electromagnetic radiation**

All electromagnetic radiations have the same characteristics and differ only in energy.
X-rays and gamma rays of the same energy have precisely the same properties and vary only
in the manner by which they are produced. X-rays are produced by the bombardment of a
target by electrons, while gamma rays are produced by the nucleus of radioactive atoms.
There are many other well-known forms of electromagnetic radiation which have the same
properties but behave differently because of their wavelength. Working up the spectrum of
electromagnetic radiation, the longest wavelengths are long wave radio, then short wave radio,
infrared, visible light, ultraviolet and so up to x-rays and gamma rays, the spectrum spreading
from $10^4$ Hz to $10^{20}$ Hz (1 Hz = 1 cycle per second).

Electromagnetic radiation may be thought of as packets of energy which are called
photons.

**Elementary particles**

Radiation emitted from radioactive sources may consist of electromagnetic irradiation
(gamma rays) or particles, or of both. Atoms are made up of elementary particles, of which
only a few are used clinically. the particles which make up the nucleus are protons, which
carry a positive electrical charge, and neutrons, which carry no charge. Electrons carry a
negative electrical charge equal to the positive charge on the proton, and are found travelling
in orbits around the nucleus. A positron is identical to an electron but has a positive rather
than a negative charge.

In clinical radiotherapeutic practice, electromagnetic radiation, electrons and neutrons
are used.

**Clinical radiotherapy**

The radiotherapist has a considerable wealth of radiotherapeutic modalities available
for use. The most commonly used form of radiation in clinical practice is high energy photons
(electromagnetic radiation), usually produced by linear accelerators but also by the gamma radiation produced by the isotope of cobalt ($^{60}\text{Co}$). One of the advantages of the linear accelerator over cobalt is the former's high output, which results in short treatment times. Cobalt sources decay slowly and have to be changed every 3-5 years, their output becoming less every day, unlike the beam from a linear accelerator which has a constant output.

The older X-ray machines of low energy still have a place in radiotherapy and are used for the treatment of more superficial lesions. This equipment produces X-rays of up to 300,000 volts (300 kV).

The first of the high energy X-ray generators was the Van der Graaf machine. This machine was introduced into clinical practice producing X-rays at an energy of 1.2 million volts (MV), and it was the first equipment to produce megavoltage X-rays, that is over 1 million volts. As the penetration of X-rays depends on their energy, this was a considerable step forward. One advantage of the high energy photon beams of radiation mentioned is the high output of radiation. Of greater importance is the manner in which radiation is absorbed by tissue at different energies. The low energies used to produce diagnostic radiographs make use of photons in the 60-150 kV range. The use for diagnostic purposes of X-rays falling in this range, depending on the method of absorption of the X-rays, is related to the atomic number of the material being irradiated. Because of the considerable variation in the atomic number of body structures, for example in the head and neck, there are considerable differences in methods of absorption by the various structures, and a simple radiograph reveals all the important features, such as bone and different soft tissues, as shades of grey. However, if the same energy of radiation were to be used in the treatment of tumours of the head and neck, great care would be needed as there would be a differential absorption of the radiation, resulting in very high absorbed doses in bone compared with the much lower dose in soft tissue. This variation can approach a ratio of 8:1, bone:soft tissue, and may lead to problems such as bone necrosis. The differential absorption is clearly visible on an ordinary radiograph where the soft tissues show up as black and the bones as white. The white areas show least transmission of X-rays on account of the high absorption, and the black areas demonstrate the high transmission and low absorption. The use of megavoltage radiation overcomes this problem, as all tissues will absorb the same amount of radiation. The absorption of electromagnetic radiation is exponential. For unit depth within the patient or in a water phantom, the same percentage of radiation is absorbed. For example, if in the first centimetre of tissue, 50% of the beam is absorbed, then in the second centimetre, 50% of the remaining 50% will absorbed, leaving 25% of the original applied amount of radiation and so on. With the increase in energy of the beam, the dose absorbed at a depth will become higher and the greater will be the potential for the treatment of deep-seated tumours.

Electrons have an absorption in tissue which is finite and directly related to their energy. As absorption is not exponential and falls off very much more quickly, this type of therapy is of particular advantage in the treatment of superficial lesions or where a block of tissue is to be treated to a finite depth, for example in the neck following block dissection where the underlying pharynx can be spared. As a working rule, the depth to the 80% isodose is approximately one-third of the energy of the beam expressed in million-electron volts (MeV).
The edge of a beam of irradiation is known as the penumbra, and is mainly related to the size of the source of the radiation. This may be a focal spot on a target of a linear accelerator or a piece of radioactive material such as a $^{60}$Co source in a teletherapy machine. The penumbra of the beam produced by a linear accelerator is superior to that produced by other forms of equipment as there is a point source of X-rays, and the scatter of the X-rays within the patient is in a forward direction. The advantage of this property is considerable, especially in the head and neck where it is imperative to administer very accurately a dose of radiation to the tumour volume. This is particularly important, for example, when treating structures around the eye.

Another advantage of megavoltage beams is the skin sparing effect. Beams of radiation with an energy of up to 1 MV always produce the maximum dose on the surface. Unless clever use of multiple beams is employed, with orthovoltage irradiation so that the tumour dose is always very much higher than the skin dose, there will certainly be a very brisk reaction with moist desquamation of the skin. This occurrence tended to give the radiotherapist of the past a reputation for burning the skin. Modern megavoltage beams produce the maximum dose at an approximate depth of, for example, 1.0 cm with 4 MV X-rays, 2.0 cm with 8 MV X-rays and 7.0 cm with 35 MV X-rays. The last example shows the considerable skin sparing which results from an increase in the energy of the beam. Careful choice of energy may be used to advantage. Many radiotherapists do not favour multi-energy, multifunction accelerators, and it is essential to choose equipment which best suits the practice of the department.

In the figure, all of the curves are drawn to the same scale and demonstrate the dose distribution in a water phantom (tissue equivalent) of: (1) 8 MV X-rays at 100 cm source skin distance; (2) cobalt-60 teletherapy beam at 80 cm source skin distance; and (3) a betatron beam at 11 MeV. All field sizes are for a 10 x 10 cm field. These illustrate the points made relating to the nature of the penumbra, the absorption, and the depth of the maximum dose. The electron beam shows the different type of absorption and the rapid fall-off of the beam.

Other examples of external beam therapy are illustrated in the figures, which relate to treatment at sites in the head and neck. This figure illustrates a distribution using three fields of radiation, two lateral 30° wedges and an open anterior field. This figure demonstrates a plan produced using two 45° wedges with the beams angled in such a way as to avoid the spinal cord and the opposite eye. All are drawn to the same scale.

**Brachytherapy**

The single, most important, landmark in brachytherapy was the standardization of the rules of radium implantation by Paterson (1934) and Parker (1934); the principles set out in their work are still used today. Between 1950 and the latter part of the 1960s there was a general decline in interest in brachytherapy, owing to the introduction of new advanced megavoltage equipment for external beam therapy. The renewal of interest has been aided by three main events: first, the availability of afterloading, which permits longer periods of time for the insertion of non-radioactive carriers into and around an tumour, into which a radioactive source is subsequently placed; secondly, the development of newer and safer radionuclides; and, thirdly, the availability of computerized dosimetry.
The principles of afterloading is very simple and consists of the introduction of hollow applications; these may be either needles or plastic tubes. With the aid of computer planning, an ideal implant may be computed prior to surgery with unlimited time available to insert the non-radioactive applicators. By using this technique there need be no fear on the part of the operator of excessive exposure to radiation. Once the applicators have been inserted, non-active sources may be introduced into the applicators to localize them within the patient; further dosimetric studies are then carried out. When the operator is satisfied with the distribution, the radioactive sources may be loaded. The loading and unloading of radioactive sources is often carried out by hand; however, more sophisticated methods are available, in particular where large amounts of radioactivity are used when the applicators may be loaded mechanically from a safe containing sources of varying intensity. This technique is particularly applicable in gynaecological intracavitary applications. Its use means that not only the operator, but also the nursing staff are protected, as the sources can be removed before nursing procedures are carried out. Once the patient has been left by the nurse, the sources are automatically reintroduced. Two types of afterloading technique have been used: in the past, high dose rate systems were used which gave the required dose in 20-30 minutes; more recently, the older and more tired, long-exposure techniques have been mimicked using low activity isotopes which are left in situ for up to a week.

A number of artificial radionuclides have become available, some of which have physical characteristics which may be preferable to radium or radon. These include caesium-137, iridium-192, iodine-125 and gold-198. The energy of photons emitted from radium and radon can be as high as 2000 kV, whereas that of caesium is 660 kV, that of iridium 350 kV and that of iodine-125 only 28 kV. It is preferable, when the sources of radiation are situated in the tumour, to use low energy photon energies which penetrate short distances into tissue, thus ensuring that relatively little radiation affects the surrounding normal tissue. The patient benefits from a better dose distribution, while nursing and medical personnel are protected, both by the smaller amount of radiation emitted and by the more effective protective shields.

In addition to the advantages of radioactive sources used for implants, there are three distinct advantages over external beam therapy: the dose distribution is superior, the tumour dose is high while the dose to the surrounding tissue is low, and the dose rate effect is beneficial. The first two advantages can be easily understood whereas the latter may not be so apparent. With an implant, the actual dose rate is considerably lower than with external beam therapy, and the total dose is delivered in a much shorter time; the same total dose may be given in 6 days rather than in 6 weeks. It is recognized that the same dose of radiation delivered in a shorter overall time is more efficient than when given over a longer period (Bedford and Mitchell, 1973). Therefore, it is reasonable to expect a greater destruction of the tumour by delivering the total tumour dose in 1 week rather than in 6 weeks. This would be a disadvantage if normal tissues were subject to the same enhanced radiation damage but with an implant, as was described previously, the dose to the surrounding normal tissue is considerably less and consequently more capable of being tolerated. It has been shown that the oxygen enhancement ratio decreases as the dose rate decreases. Normal tissues are well oxygenated, thus the decrease in dose rate would not make them more susceptible to radiation damage. Malignant tissue, on the other hand, contains a significant number of hypoxic cells which might be more efficiently killed by radiation at the lower dose rate.
Implants of all types are more commonly used in the treatment of small lesions in the oral cavity and pharynx. The method of implantation of radium and caesium varies: the isotope is implanted by being encapsulated in a needle, iridium is implanted in the form of wire, and iodine-125 and gold-198 are implanted as seeds and grains, respectively. The latter remain in place permanently once implanted. Iridium is normally used either as a preshaped 'hairpin' using an introducer, or as a single wire with a looped end for fixation, or in a polyethylene tube by means of the afterloading technique. Seeds or grains require the use of special equipment for insertion.

Radium moulds are now of historical interest only; however, the technique using the less penetrating isotopes is still employed in very selected cases. This technique still applies in the case of carcinoma of the maxillary antrum when there is residual or recurrent disease following surgery. The obturator is marked at the site of persistent disease and a treatment planned with the aid of the planning computer. The radioactive source, or sources, is then placed in the obturator to produce the dose distribution desired. The obturator is worn for the requisite time and a very localized volume in the patient treated.

Where an implant is possible and appropriate, it remains the treatment of choice, surpassing the distribution of external beam therapy and producing better long-term control of tumour.

Factors affecting the efficacy of radiotherapy

The effect of radiotherapy on tumours is dependent on a number of factors, only some of which are at present understood. The immediate effect of radiation on malignant tumours is relatively well understood but of greater significance are the long-term effect and cure rate. The factors affecting the cure of patients with malignant tumours are of considerable importance. Tumours that respond well and disappear with the initial treatment clearly stand a much better chance of being cured than those which appear to be relatively little affected by the initial treatment, but this is by no means the most important factor.

The histology of the tumour may affect its response to radiation therapy and, indeed, its curability. Tumours arising in lymphoid tissue are usually very sensitive to radiation and respond quickly. The chance of curing them is extremely high. Tumours of embryonal origin and those which are anaplastic are also sensitive to irradiation; however, while being initially sensitive and responding well, they may recur at an early stage. Squamous cell tumours and a few adenocarcinomata are sensitive, although they respond slowly after treatment, provided that a sufficiently high dose can be administered and, if possible, in a relatively small volume, for example with an implant. Some slow-growing tumours, however, respond equally slowly and may take many months to disappear completely. This may give cause for anxiety on the part of both patient and clinician in the period immediately after treatment.

Sarcomata arising in soft tissue or in bone are of low sensitivity, with the result that very low cure rates are achieved when treated with radiation. Nevertheless, this form of therapy may be of considerable value when attempting to achieve palliation in patients with widespread or locally advanced disease.
While, in theory, an attempt is being made to destroy all malignant cells in order to achieve a cure, it is unlikely, in practice - even in the case of those tumours in which a cure is achieved - that all cells will have been killed. The tumours most likely to be cured with radiation are obviously the small lesions where high doses can be achieved without the neighbouring structures being affected to an unacceptable degree. Experimental work has shown that in small tumours of as little as 1 cm or less in diameter there may be areas of anoxia. Large tumours definitively contain areas of hypoxia, anoxia and, in some instances, central necrosis, although transplantable and viable cells remain within the necrotic area. Gray et al (1953) demonstrated that hypoxia protects tumour cells from the effects of radiation and is therefore of paramount importance in cases where radiotherapy has failed to achieve a cure. In recognition of the pioneering work of Gray, the new SI unit of absorbed dose of radiation has been named after him; one gray (Gy) is equivalent to 100 of the former unit, the rad.

Attempts have been made to overcome the problems relating to the presence of hypoxic cells within tumours. The first attempt to influence hypoxic cells was made by Churchill-Davidson, Sanger and Thomlinson (1957) with the use of hyperbaric oxygen. The results of the British trials of hyperbaric oxygen used in conjunction with radiotherapy were coordinated by the Medical Research Council and published in 1977 and 1978 (Henk, Kunkler and Smith, 1977; Dische, 1978; Watson et al, 1978). These trials demonstrated a highly significant initial increase in tumour control in patients with carcinoma of both the cervix and uterus, and in those with carcinoma of the larynx. However, disappointing long-term responses were observed at 5 years. The methods used were not without criticism and were difficult to use. It is important to remember that not only are the hypoxic cells supplied with more oxygen but that the tissues with a good blood supply also receive higher concentrations of oxygen under hyperbaric conditions, which may lead to necrosis.

Neutrons or heavily charged particles are densely ionizing and damage cells more effectively than photons. Furthermore, their effect is relatively independent of the presence of oxygen. In tissue culture, Gray showed an enhancement of 2.5-3.0 for X-rays whereas, with neutrons, an enhancement of approximately 1.5-1.8 was seen, indicating an effective increase of 50-80% in dose to hypoxic cells only. It has also been suggested that as cells may be more sensitive to X-rays at different phases of the cell cycle, but that such variations are much smaller with neutrons, there may be fewer surviving cells able to regrow in any such resistant phase if neutron therapy is used. The therapeutic ratio using neutrons is close to one, and necrosis of both normal and tumour tissue is not infrequently observed.

The ideal method of dealing with anoxic or hypoxic cells within a tumour would be that of inducing all the cells, whether normal or hypoxic, to be equally sensitive. Chemical compounds have been developed which have the action of sensitizing hypoxic cells. These compounds reach the hypoxic cells which are inaccessible to oxygen, and they do not sensitize the normal or well-oxygenated cells (Adams, 1972, 1977; Adams et al, 1976; Fowler, Adams and Denekamp, 1976; Fowler and Denekamp, 1979). The concentration required to produce full sensitivity, using the present sensitizers, is unsatisfactory because of the side-effects, in particular neurotoxicity.

Other methods of affecting the sensitivity of tumours to radiotherapy, with no direct relation to the oxygen effect, are under trial. The most interesting of these to date has been the use of hyperthermia. It was initially suggested that whole-body hyperthermia be
undertaken, and this was subsequently carried out in patients with disseminated disease who were otherwise fit and, in most cases, young. The combination of hyperthermia and radiation is extremely difficult under such conditions, and the best hope for hyperthermia is unlikely to be the whole-body approach. Whole-body hyperthermia may be of value in association with chemotherapy. Temperatures in the range of 42-45°C have been achieved for 15 minutes to one hour (Field and Bleehen, 1979). Success using heat alone has been claimed by Hahn et al (1979) in tumours recurring after full doses of radiotherapy. Whole-body hyperthermia is easily achieved but the methods are cumbersome and the patient often requires a general anaesthetic; no temperature difference is achieved between tumour and normal tissues. Isolated perfusion has been used for many years, often associated with cytotoxic chemotherapy, but this is limited to an easily perfusable site such as a limb. Ultrasonic heating of a limited volume, which may be used with radiation therapy, is more convenient and relatively cheap (Marmor et al, 1979; Marmor and Hahn, 1980). The field of hyperthermia is an interesting and rapidly developing form of potential cancer treatment.

**The planning of radiotherapy**

As will be apparent from the section dealing with the factors which influence the outcome of radiotherapy, it is essential first to be aware of the nature of the disease and to establish whether other modalities of treatment are to be employed, for example postradiotherapy surgery, or whether surgery and/or chemotherapy have been employed. It is also important to determine from the outset whether the treatment is to be radical or palliative.

The radiotherapist must be aware of the patterns of local and lymphatic spread for each tumour type, thus enabling the design of radiation techniques, which will eradicate the tumour but preserve the normal tissue within the radiation field, to be prepared in advance. ideally, the field should encompass the primary tumour together with its local spread, and prevent regrowth at the edges of the treatment volume.

The smaller the volume to be treated the better, because if the volume to be treated is small, it is possible to administer a high and hopefully curative dose of radiation. Small volumes may well be treated with interstitial radiotherapy which permits very high doses, but with such a rapid reduction of radiation around the treatment volume that the necessary sparing of the surrounding tissues is achieved.

Clinical examination, including examination under anaesthetic at the time of biopsy, routine radiology, computerized tomography (CT) and magnetic resonance (MR) give the type of information which is required, particularly in the planning of large volumes. This information must be used in conjunction with knowledge of the behaviour of the type of tumour to be treated.

While the use of high technology is becoming more commonplace, it is important not to place unjustified faith in its use. At present, there is still much to be learnt about the use and abuse of high technology, and there is still no substitute for good clinical judgement and, more importantly, for experience.

When planning treatment in such detail, it is desirable, in the case of tumours of the head and neck, to be able accurately to reproduce treatment plans in the patient at each
fraction. A method of comfortably maintaining the position of the patient at each sitting is imperative. It is the normal practice in centres of excellence to produce 'shells' which fit over the patient very accurately. The process of preparation is as follows. After the treatment volume has been decided, the patient is positioned as comfortably as possible in the treatment position on the equivalent of a treatment couch. A substance based on sodium alginate, but also containing diatomaceous earth, lead silicate and calcium sulphide, is mixed with water to a suitable consistency and applied to the face where most detail is required. Over this, moist plaster of Paris bandages are applied to the area of interest on the head and neck; these may be removed after a short time, following the prior application of a releasing agent. Patients usually do not find this a frightening or difficult experience, especially when carried out by an experienced technician. Once the mask has been removed, a releasing agent is placed inside, and the whole filled with plaster of Paris. This should be carried out without undue delay as the alginate will shrink if allowed to dry. After the positive inner plaster has dried, the outer covering is removed and an accurate case of the patient remains; this is so accurate that even the pores of the skin are clearly visible. When this cast is completely dry, a shell is produced by vacuum forming with heated cellulose acetate butyrate. This is then used for the planning process and during the subsequent treatment.

In recent years, there has been considerable discussion about the size of each dose and the frequency at which each should be given. Fractionation varies from centre to centre, but the dose and the time period over which it has been given is usually compared to the biological equivalent of 60-65 Gy in 6-6.5 weeks. In some centres, where travelling for the patient is very difficult and hospitalization impossible, single fractions may be given for very small lesions, and treatments once a week for 6 weeks are becoming more common; provided that the site is suitable and the biological protocols are carefully followed, consideration can be given to these forms of fractionation. Hyperfractionation with three fractions each day for approximately 11 days has been administered to advanced cases and, in some of these patients, remarkable results have been obtained.

In the head and neck there are structures which are highly sensitive to radiation and which must always be considered when a decision is being made on a particular treatment plan. These structures are the spinal cord, the lens of the eye, the salivary glands and the lacrimal gland. A dose in excess of 40 Gy in 6 weeks may cause transverse myelitis of the spinal cord. Doses in excess of 6 Gy may cause radiation cataract. Higher and less precise doses give rise to salivary gland dysfunction and very rarely to non-functioning of the lacrimal gland with an ensuing dry eye.

**Care of the patient during radiotherapy**

Prior to the commencement of radiotherapy, an assessment of the nutritional state of the patient should be made. When afflicted by tumours of the oral cavity or pharynx, patients may well have difficulty and/or pain on swallowing and their nutritional status may well be impaired. The treatment required will depend on the degree of malnutrition and will vary from simple administration of vitamin supplements to feeding with an extremely fine nasogastric tube. As the tube is so well tolerated and easy to use, patients are able to look after themselves at home, whereby avoiding hospitalization. It is usual to feed the patient a proprietary compound which provides sufficient calorie intake as well as the necessary vitamins etc. Some patients may require simple dietary advice, such as the use of puréed food.
It may also be of value to administer additional iron if the patient is anaemic as a result of poor food intake in the preceding months.

The treatment of tumours of the mouth exercises the skills of the radiotherapist, because it is important to avoid producing a dry mouth. This can be accomplished by very careful planning in the majority of patients. Unnecessary treatment of the major salivary glands should be avoided where possible, without prejudicing the volume of the mouth or neck which requires treatment. Failure to avoid a dry mouth will usually lead to blackening of the teeth and gross caries, resulting in the necessity for removal. Attempts have been made to save the teeth in the most difficult circumstances by the production of protective splints which are worn until the return of some salivary flow has taken place. Some patients find the splints uncomfortable to wear and a number of departments do not have the facilities for their production.

As a result of endarteritis in the blood vessels in the irradiated area, the blood supply of the mandible and the maxilla may be impaired following radiotherapy, and this is a particular problem in the former. The subsequent removal of teeth may be followed by radiation bone necrosis and this must be avoided by preventative methods. In patients with few and poor quality teeth, removal is best carried out before radiotherapy is commenced. In young patients, where the teeth are of good quality and where care is obviously taken of the dentition, it may be possible to save the teeth. In the event of the teeth’s requiring removal following radiotherapy, this is best carried out in a maxillofacial unit, with great care and as gently as possible, creating the least possible trauma, and under antibiotic cover.

During a radical course of radiotherapy, it is inevitable that patients will develop reactions in both the tumour and, more importantly, in normal tissues. Depending on the type of radiation used, there may or may not be a skin reaction. The skin very commonly reacts to electron beam therapy, although this is less likely to occur with megavoltage therapy. It is essential, therefore, before the commencement of treatment to instruct the patient in the care of the skin. Most important is the avoidance of any irritation of the skin. Such irritants may take very many forms including exposure to the sun (another source of electromagnetic irradiation), washing with soap, and dressings which may be required to prevent discharging wounds and sinuses from further irritating the skin. Adhesive plaster of all types must be banned from the treatment area and ‘netalast’ dressings, a form of stretching, loosely woven material, should be used in preference. The use of a scarf made of silk - a material which is not only soft but also allows free passage of air to the skin, thereby permitting evaporation of any perspiration - should be advised in order both to prevent rough clothes from irritating the area and to protect it from the sun. Male patients should be advised to give up wet shaving during treatment and to shave as gently as possible with an electric razor.

There may be very few indications on the skin of patients during the early part of treatment, but with external beam therapy there will be visible signs on the mucous membrane from a relatively early stage. Initially, some erythema will be visible and this will proceed to a stage where a fibrinous exudate, sometimes called radiation mucositis, becomes apparent. The radiotherapist welcomes this appearance as an indication of a satisfactory reaction to the treatment, but prefers to encounter this on completion of therapy as it is a manifestation that the tissues are approaching the limit of normal tolerance. The patient should, as with the skin, be warned of the kind of trauma which will both advance the onset of mucositis and make
the reaction of the tissues worse. The commonest irritants are alcohol, tobacco and strongly spiced foods, which should all be avoided. As the fibrinous exudate increases there is likely to be an increase in pain associated with it, especially on swallowing. The patient will inevitably become more miserable and is likely to become less well nourished, again as a result of treatment. Many types of proprietary medication have been produced to treat the soreness, but simple aspirin mucilage is as effective as most of these. This may be given 20 minutes before meals, and helps by producing not only a local anaesthetic effect but also the systemic effect of analgesia.

Patients who are treated with an implant, usually in the oral cavity, develop the typical radiation mucositis approximately a week or 10 days after the removal of radium or irridium and this may be treated as above. The reaction commonly lasts for 3-4 weeks.

During radiotherapy and especially in debilitated patients who may well have a degree of immune suppression, whether local or general, infection is a frequent occurrence. The commonest infection of the oral cavity or pharynx is by *Candida* and is even more predominant when antibiotics are required. Treatment should be immediate and, after swabbing for culture, amphotericin lozenges should be prescribed. As these lozenges dissolve only very slowly, one should be kept in the mouth at all times. Culture may reveal resistant forms of *Candida* and the help of the microbiologist is indispensable in these cases.

While these immediate reactions are visible, it is essential not to lose sight of the long-term reactions. The salivary glands are of importance in this respect. Saliva performs several functions, each of which assists in the prevention of dental caries. It dilutes foods, buffers and dilutes acids produced by fermentation, and constantly washes away food particles and organisms from the mouth. In spite of pre-irradiation precautions, a proportion of irradiated patients will sooner or later develop osteoradionecrosis, a condition which is usually accompanied by pain. Sequestration of dead bone may occur, and this process may take months or indeed years. The availability of megavoltage radiation, with its bone-sparing effect, in no way reduces the need for careful pre-treatment dental evaluation.

The use of electron beam therapy has also led to deafness when treating sites which include the external auditory meatus, as there may be funnelling of the electrons down the canal, which can give rise to late reactions of the temporal bone consisting of atrophy of the membranous labyrinth and osteoradionecrosis.

Adults who as children had retinoblastoma treated with radiotherapy have been known to develop osteosarcoma in the bones of the orbit as much as 20-30 years subsequent to treatment.

**Combined radiotherapy and chemotherapy**

The treatment of malignant disease of the head and neck is rarely by means of chemotherapy alone. Over recent years, more attention has been paid to the use of combinations of treatment, most commonly surgery and radiotherapy, although the use of chemotherapy in the same way has been gaining support. In those circumstances where surgery is not possible on account of the advanced nature of the disease, the use of chemotherapy either before or after radiotherapy has been adopted as a planned treatment. In
addition, a small number of trials have been published, in which chemotherapy has been used at the same time as the administration of radiotherapy. In such circumstances, radiation combined, for example, with bleomycin has given rise to considerable potentiation of the radiotherapy. Perhaps the best known and most used combination of chemotherapy associated with radiotherapy is the regimen suggested by Price and Hill (1978) who have shown that, if it were used before any other form of therapy, their combination induced considerable remission in advanced tumours. This may be extremely beneficial because, as has been explained previously, it is essential to have well-oxygenated tumours to treat with radiotherapy if a cure is to be achieved. There is good evidence to suggest that when the bulk of large tumours has been reduced with chemotherapy, a higher proportion of oxygenated cells remain in the residual tumour. Some of the new cytotoxic drugs, especially some platinum compounds, have shown early promise in the treatment of tumours of the head and neck. Drugs which for many years have been known to enhance the effect of radiotherapy and which still have a place in this type of treatment are methotrexate and bleomycin. These two drugs have been used by many workers to treat advanced cases, such as inoperable neck nodes. The dose of radiation is frequently reduced by both fraction and total dose as a result of the enhanced reactions encountered. It is very important, however, not to compromise a good therapeutic response by either method, although this might be the unfortunate consequence of reducing the radiation dose to the tumour, or the dose of the cytotoxic drug, to levels where either one might have been better used alone in adequate doses than both used simultaneously. The time-dose relationship with regard to radiotherapy may be further disrupted to disadvantage if it is necessary to rest the patient from therapy as a result of the reactions encountered. In the case of the lymphomata, and especially the non-Hodgkin's lymphomata, the primary tumour and any associated lymph nodes are often treated first with radiation and subsequently with the administration of chemotherapy, usually in the form of combination chemotherapy.

Radiation therapy combined with simultaneous administration of multidrug combination chemotherapy, as reported by O'Connor et al (1982) on behalf of the Radiation Therapy Oncology Group (RTOG) gives hope for future trials of multi-agent radiotherapy treatment regimens.

Attitude to the patient

One of the essential factors in the management of patients with tumours of the head and neck is the attitude of the treating physician to the patient. The majority of patients know they have cancer. Those who do not should, usually, be told of the nature of their disease with sympathy and understanding. Most important is that the patient should be encouraged to look forward to the future with some optimism. The words ‘there is nothing we can do to help’ should never be used, for, at best, the patient will be cured and, at worst, after good palliation accompanied by a period of good quality life has been achieved, the patient may be helped to die without pain and with dignity. It might well be expected that such an attitude should apply in the case of all patients with malignant disease. However, by virtue of the site of head and neck cancer, in conjunction with the increased use of very extensive and mutilating surgery with the inevitable disfigurement, it is especially important in such cases. Add to this the loss of hair, the nausea and vomiting, and a general discomfort resulting from chemotherapy, and the above attitude becomes imperative. It is hard to explain away some
of the necessary therapies which a patient has to undergo without their accepting that a serious problems is being dealt with.

The attitude of all concerned, from the most senior to the most junior member of the therapeutic team, must be one of awareness of what the patient understands, about his/her problem and the aims of treatment. The hardest questions are not always asked of the treating doctor. The person confronted with difficult questions is often a student radiographer, a first-year nurse or the new house surgeon or physician. It is important at these times to ascertain the extent of the patient's knowledge by asking what they understand from the information they have been given. The patient's comprehension is often at variance with the meaning which the explanation they were given was intended to convey, and the simple act of talking through what they do understand may provide answers to their questions. If further explanation of a special nature is required then the patient should be referred back to the person who have the original explanation, but if the remaining question is one concerning the treatment details - for example, of the radiation - then a simple answer may be given.

Under no circumstances should the confidence of the patient be lost by evading or contradicting that which has gone before. This takes time but is of the utmost importance, for patients will almost certainly accept therapy which is unpleasant if they know why they need it and if they have understood that need from the outset. Perhaps the most important words in the clinic are those of encouragement. The patient who has undergone a laryngectomy and who has subsequently made progress with pharyngeal speech should be complimented and urged on to do even better. The establishment of laryngectomy clubs associated with the hospital, but with time spent on social activities, will help the shy or those afraid to use their new found voice. Where appropriate, and where the skills are available, young patients who aspire to take part in activities, should be assisted to achieve their goals. With expert help, some laryngectomy patients are able to swim again. This is merely one example, for there are few limits as to what can be achieved by a fit and well-adjusted patient.