either due to late onset of adenoma development or noncarrier status, molecular testing may identify affected patients or exclude noncarriers. Since combined clinical/molecular diagnosis can identify affected relatives about twenty years earlier than symptomatic probands, sixty of our probands but none of the presymptomatic relatives presented with colorectal cancer. Restorative proctocolectomy followed by an ileoanal J-pouch procedure prevents colorectal cancer and preserves sphincter function in FAP patients. Although familial adenomatous polyposis accounts for less than 1% of all colorectal cancers, hereditary nonpolyposis colorectal cancer (HNPCC) may account for up to 15%. Presymptomatic molecular diagnosis of FAP and HNPCC and preventive surgical treatment might be effective tools to further decrease mortality due to colorectal cancer.

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COLORECTAL CANCER AND THE NEED FOR SCREENING
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Colorectal cancer is the second commonest killing cancer in Europe. However, there is some cause for hope. First, the adenoma-carcinoma sequence offers a convenient target for screening; intervention during the benign period of the sequence might allow cancer prevention. Second, surgical treatment of colorectal cancer at an early pathological stage is almost always curative. Over the past two decades a major research effort has gone into screening strategies, mainly into faecal occult blood testing. There is guarded optimism while we await the outcome of European RCTs. Another potentially important method of screening in colorectal neoplasia is flexible sigmoidoscopy which, applied once around age 60, might allow cancer prevention by adenoma removal. A very large trial of this modality, involving 200,000 people, is about to start in the U.K.

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THE PHENOMENON OF CANCER CLUSTERING
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There is a long history of disease 'clusters'; although in many reports the term cluster had only an impressionistic meaning without indication of the numbers of cases expected in the time and place in question. A large number of apparent clusters published throughout this century have involved leukaemia and initial reports were essentially non-quantitative and based on astute clinical observations and *ad hoc* investigations. From the 1930s onwards there were a few wide ranging searches for clusters with some elementary statistical analysis. Such was the **Ashington Cluster** involving three cases of AML, one of ALL and one CLL arising in a small mining village. From around 1970 the field was extended with analysis of large computerised databases becoming a reality and statistical methodology emerging. The phenomenon of space-time interaction was developed and demonstrated in childhood leukaemia in the U.K. The most recent phase of cluster research has generally involved sophisticated statistical analysis of aggregations of cases around point sources such as nuclear power installations. Perhaps the most interesting aspect of clustering at the present time is the consensus emerging that the residences at onset of cases of childhood leukaemia show weak evidence of a general tendency for spatial clustering. This is consistent with shared exposure to localised aetiological agents and is providing a clue as to where to look for aetiological factors for childhood leukaemia.

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CANCER AND NUCLEAR INSTALLATIONS
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We describe here the main results of studies of cancer mortality and morbidity in the populations residing in the vicinity of nuclear plants. Reports from the U.K. have described increases in leukaemia and lymphoma risks in children living near nuclear installations. Paternal preconceptional exposure to radiation had been suggested as an explanation, but this explanation has since been dismissed. An infectious aetiology has also been suggested, based on the observation of an excess risk of leukaemia and non-Hodgkin's lymphoma after population mixing both around the sites of some nuclear facilities in the U.K., and in other circumstances.

In all other countries where the problem has been studied (U.S.A., Canada, Germany, France, Sweden), no excess morbidity or mortality has been observed in the vicinity of nuclear installations. The power of these studies were reasonable. For instance in a French study, the expected number of deaths around installations was equal to 200, and therefore the probability of detecting an increase of 25% was 95%, with a type I error of 5%.

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CHILDHOOD CANCER INCIDENCE IN RELATION TO DISTANCE FROM THE FORMER NUCLEAR TESTING SITE IN SEMIPALATINSK, KAZAKHSTAN
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There are few data on cancer risk following atmospheric nuclear explosions. Rates of childhood cancer between 1981 and 1990 in the four administrative zones of Kazakhstan were studied to assess the relationship, if any, with distance from nuclear testing sites. Risk of various cancers among children aged 14 years and younger were estimated in relation to distance from (1) a site where testing in air was performed before 1963, (2) a site where underground testing took place thereafter, and (3) a reservoir, known as "Atom Lake", created by four nuclear explosions in 1965. Risk of acute leukaemia rose significantly with increasing proximity of residence to the testing areas, although the absolute value of the risk gradient was relatively small. The relative risk for those living less than 200 km from the air-testing site was 1.76 compared with those living 400 km or more away from the site. Similar relative risks were observed for the underground site and "Atom Lake". There was also some evidence of increased risk of brain tumours in association with proximity to the test sites. In two of the four zones studied, there was substantial regional variation in acute leukaemia rates which was not attributable to distance from the test site. The findings may be affected by potential confounders, notably urban/rural status and ethnic factors but tend to confirm an association with increased risk of childhood leukaemia and exposure to radioactivity from atmospheric nuclear explosions.

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RISKS OF EXPOSURE TO RADON GAS
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Radon is a radioactive gas that occurs naturally in the earth's crust as part of the decay chain of uranium-238. It has recently been appreciated that by far the greatest source of exposure to ionizing radiation arises from the inhalation of radon indoors. There is conclusive proof that inhaled radon and its decay products can cause lung cancer, both from animal experiments and from the study of men who have worked in mines of uranium and other igneous rocks where radon levels are exceptionally high. At the present time, estimates of the risk of lung cancer from inhaled radon indoors are based on the miners studies. If these estimates are correct, then radon would be the second most important cause of lung cancer after cigarette smoking. However, there are many uncertainties in extrapolating from the mining to the indoor environment. Direct assessment of the risk of indoor radon exposure is currently in progress.

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CANCER AND ELECTROMAGNETIC FIELDS
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There are several studies on the cancer risk of children exposed to electromagnetic fields. The results are controversial with a majority suggesting an increased risk of childhood cancer to be associated with exposure magnetic fields. The only population-based cohort study until now included all 135,000 Finnish children aged 0–19 years who during 1970–89 lived within 500 m of overhead power lines of 110–400 kV in magnetic fields calculated to be $\geq 0.01\ \mu$T. Cancer cases of these children were picked up from the countrywide Finnish Cancer Registry, and the observed numbers of various cancers were compared with the expected ones based on national incidence rates. In the whole cohort, 140 cancers were observed and 145 expected. The only statistically significant excess was found in nervous system cancer in boys (but not in girls) who were

exposed to magnetic fields of $\geqslant 0.2\ \mu$ or cumulative exposure of $\geqslant 0.4\ \mu$T years. The preliminary results of a similar cohort of adults do not point to an increased cancer risk, either. The number of children exposed to stronger magnetic fields may be too small to draw final conclusions, but that among the adults is not (8,554 cancer cases observed during the follow-up time). An association between the occupational exposure to electromagnetic fields and leukaemia and brain cancer obtained earlier in a Finnish study and some other studies is not confirmed in several more recent studies.

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NO ABSTRACT

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CONSERVATIVE TREATMENT FOR T1T2 SUPRAGLOTTIC SCC
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From 1974 to 1983, 240 previously untreated patients (pts) presenting with T1 or T2 (AJC 1992) supraglottic SCC were treated either by partial surgery (PS = 163 pts: 53 epilarynx, 110 vestibule) or by definitive irradiation (XRT = 77 pts: 52 epilarynx, 25 vestibule). There were 130 supraglottic laryngectomies, 27 hemilaryngopharyngectomies and 6 subtotal laryngectomies while 62 pts had postoperative XRT at primary site and 71 on the neck. There was no postoperative death and local failures occurred in 8% of cases, neck recurrences in 8%, distant metastases in 10% while 31% of pts developed metachronous cancers. The 3 yr survival was 75% (81% for endolarynx vs 50% for epilarynx). The final larynx preservation rate was 93%. In pts treated by XRT, there was no treatment related death and all the 9 local failures (12%) were T2 tumors arising the arytenoid or denuding the epiglottic cartilage. The 3 yr survival was 45% and the larynx preservation was achieved in 90% of pts. We recommend PS for (1) tumors of the laryngeal surface of epiglottis, (2) tumors of suprahyoid epiglottis denuding the cartilage, (3) limited but infiltrating tumors of lateral epilarynx and, (4) tumors reaching the arytenoid, all other cases being suitable for XRT.

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ASSESSMENT OF VOICE RESULTS IN GLOTTIC CARCINOMA TREATED BY IRRADIATION, CO_2 LASER RESECTION AND CORDECTOMY BY MEDIAN THYROTOMY
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The different types of treatment for T1a T1b vocal cord carcinoma: radiotherapy, cordectomy by median thyrotomy and endoscopic CO_2 laser resection offer from the oncologic point of view nearly the same results. When choosing the therapeutical procedure the functional results, regarding voice quality, are of main importance.

This study is directed to establish the differences of voice quality between patients treated by radiotherapy, conventional cordectomy and CO_2 laser resection.

Since the T1 vocal cord carcinomas is not a homogenous group of tumors and because the treatments are also different in some aspects comparison between the three groups could be erroneous. To avoid it we select a group of patients, treated by each one of the treatment types, of nearly the same characteristics on size and degree of infiltration. (Phonatory results by objective acoustical, etc.)

Phonatory results by objective acoustical analysis, visual evaluation by stroboscopy and perceptual evaluation by the patient and voice experts are presented.

The relationship between all degree of surgical resection on voice quality are discussed.

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SUPRAGLOTTIC CANCER-COMBINED RADIOTHERAPY/CHEMOTHERAPY AND/OR NEW FRACTIONATION SCHEDULES. DO THESE APPROACHES IMPROVE THE RESULTS COMPARED TO CONVENTIONAL RADIOTHERAPY? A REVIEW OF THE SITUATION IN 1995
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The principal goals in the management of laryngeal cancer are eradication of disease with preservation of function. The optimal treatment should be chosen for each patient. Several points will be emphasized.

—The results of conventional radiotherapy in several studies, including results of supraglottis in Institut Curie. The effects of dose-time-fractionation on local control.

—The results of clinical trials using altered fractionation schedules such as hyperfractionation, accelerated fractionation, treatment with split course, or with concomitant boost-Studies comparing altered schemes to conventional radiotherapy will be reviewed.

—The role of chemotherapy as part of combined modality programs and as part of larynx preservation. Results of clinical trials, especially with induction or concomitant chemoradiotherapy will be discussed.

—The value of cell kinetics measurements to predict radiosensitivity: labeling index, length of S-phase, potential doubling time and therapeutic implications.

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PROGNOSTIC FACTORS FOR ORGAN PRESERVATION IN PATIENTS WITH ADVANCED LARYNGEAL CANCER
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The effectiveness of induction chemotherapy combined with radiation therapy as an organ preservation treatment strategy would be enhanced by improved methods to select for patients with a high likelihood of success. Detailed analyses of prognostic factors for chemotherapy response and ultimate organ preservation were undertaken in 166 patients randomized to 3 cycles of cisplatin/5-FU and definitive radiation (66–76 Gy). Overall tumor size and histologic pattern of growth were significant predictors of complete response after chemotherapy. Successful organ preservation was significantly associated with T class, performance status, and p53 overexpression. In patients with supraglottic cancers treated surgically, disease-free and overall survival were significantly associated with histologic growth pattern. Organ preservation after chemotherapy and radiation was predicted by performance status, prior tracheostomy and chemotherapy response. Until better molecular markers of chemo/radio sensitivity are available to optimize patient selection for organ preservation, histologic response to induction chemotherapy appears most reliable.

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NO ABSTRACT

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INHIBITION OF 3′, 5′-CYCLIC NUCLEOTIDE PHOSPHODIESTERASE AS A NOVEL CONCEPT IN TUMOUR THERAPY
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A wide spectrum of human and animal tumour cell lines exhibit significantly lower cAMP levels than normal cells, as a consequence of strongly enhanced activities of a cAMP-specific phosphodiesterase isoenzyme (PDE). Inhibition of this isoenzyme by selective inhibitors results in a long lasting, concentration-dependent rise of intracellular cAMP, accompanied by marked growth inhibition. At higher concentrations of the inhibitor (>3 μM), induction of apoptosis becomes apparent, as detected by flow cytometry, confocal microscopy and ELISA-based determination of fragmented DNA in intact cells. Thus tumour-associated overexpression of a cAMP-specific PDE-isoenzyme in proliferating tumours offers a novel cellular target for selective antineoplastic therapy.

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NEW CONCEPTUAL AND METHODOLOGICAL APPROACHES TO ANTICANCER DRUG DEVELOPMENT
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Although cancer chemotherapy and hormonal treatment may have significant palliative effects in the systemic treatment of malignant disease, major steps towards a cancer cure by drugs cannot be expected from these therapies. Therefore, the originally successful empirical approach to drug discovery should probably be substituted by a more rational drug design. Molecular genetics have produced enormous progress in our understanding of the principles of tumor development and tumor growth. For the first time in the history of anticancer drug development it now