studies are not informative about risks from childhood exposure to ^{131}I. In contrast, very large increases in the incidence of childhood thyroid cancer have occurred following the Chernobyl accident. Data from the Ukraine, Belarus, and Russia suggest that the risks from childhood ^{131}I exposure are high and may not differ substantially from those associated with external radiation. To date, findings from studies of environmental radiation exposure are inconsistent. Additional data from studies of populations exposed to radiation from nuclear weapons testing and production in the former Soviet Union will become available in the near future. These data should help clarify the role of radionuclides in the etiology of thyroid cancer.

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Thyroid Carcinoma After Chernobyl

D. Williams. *University of Cambridge, Strangeways Research Laboratory, Cambridge, UK*

4 years after the world's worst nuclear accident at Chernobyl an excess of thyroid cancer cases was noted among children who had been exposed to fallout from the disaster. That increase has continued and new cases are still being seen in those who were children at the time of the accident. It is now 15 years since the accident, and so far approaching 2000 cases of thyroid cancer have occurred in the affected area, which involves most of Belarus, the northern part of Ukraine and a small part of the Russian Federation. Collaborative research to study these cases is ongoing, the results so far show that the diagnoses of thyroid cancer are substantiated, with many of the early cases showing marked local invasion. The increase is almost exclusively in papillary carcinoma, so far very few follicular or medullary carcinomas have occurred, there are no reliable reports of increases in non thyroid malignancies, although these cannot yet be entirely excluded. The increase is very largely in those who were children at the time of the accident, with a very marked association of age with sensitivity. The findings after Chernobyl differ greatly from those after the atomic bomb explosion. In Japan the exposure was very largely to whole body radiation from gamma rays and neutrons. After Chernobyl the exposure was to isotopes in fallout, and apart from the inert gas xenon, the largest components were radioactive isotopes of iodine (including Tellurium 132 which decays to Iodine 132).

Exposure to isotopes of iodine gives the thyroid over a 1000 times the average dose to the rest of the body, explaining the specificity for thyroid cancer. Radiation is particularly effective in inducing double strand breaks in DNA, and papillary carcinoma is linked to rearrangement in the ret oncogene, providing an explanation for the specificity for papillary carcinoma, although follicular carcinoma may still show a rise in incidence with a longer latent period than papillary carcinoma. The particular sensitivity of children can be linked to a combination of a higher thyroid dose and the biology of thyroid growth, which falls to a very low level in adult life. The post Chernobyl thyroid carcinomas form the largest group of human tumours of one type, due to a known cause on a known date; to facilitate study of the changes that lead to radiation induced carcinogenesis an international tumour bank has been created. Currently this holds extracted nucleic acids from several hundred tumours and these are now available for study by approved projects. Chernobyl was a major disaster for the population exposed, and for the economies of the countries involved, particularly Belarus. Few of the patients with thyroid cancer have died from the disease, but help is still needed in the affected areas, and continuing study of the occurrence of thyroid cancer and surveillance for other possible effects remains essential.

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Prognostic factors, treatment and follow-up of patients with papillary (PTC) and follicular (FTC) thyroid carcinoma

Martin Schlumberger. *Institut Gustave Roussy, Villejuif, France*

Prognostic factors for PTC and FTC include age at initial treatment, tumor burden (tumor size, extrathyoid extension, lymph node metastases, distant metastases) and tumor histotype.

More than 85% of PTC and FTC patients belong to a low risk group, with specific mortality rates below 2% at 25 y and can be individualized at the time of initial treatment by using the TNM or MACIS scoring systems.

Initial treatment includes surgery (near-total thyroidectomy and in case of PTC central neck dissection). A lobectomy may be sufficient for unifocal micro-PTC and for small minimally invasive FTC. Post-operative radioiodine ablation is performed selectively, i.e. only in high risk patients. Then, levothyroxine treatment is given to all patients with PTC and FTC with the aim to decrease serum TSH to low level.

The search for persistent or recurrent disease is based on neck ultrasonography, serum thyroglobulin (Tg) determination and total body scanning with radioiodine (131I). TSH stimulation can be obtained either by withdrawing levothyroxine therapy for 4 weeks or by intra-muscular injections of recombinant human TSH.

Neck recurrences are treated with 131I and surgery, typically using an intra-operative probe. Lung metastases are treated with 131I in case of uptake; and bone metastases are treated by surgery when feasible, followed by radioiodine and external radiotherapy; embolisation and cement injections may also be useful. Bio- and chemotherapy are not effective and should be given only to patients with progressive disease in the frame of controlled trials.

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Prophylactic surgery in patients with multiple endocrine neoplasia type 2a

S. Wells[1], J. Moley[2], M. Skinner[1], M. DeBenedetti[2]. [1] *Duke University, Surgery, Durham, USA;* [2] *Washington University, Surgery, St. Louis, USA*

Patients with the type 2 Multiple Endocrine Neoplasia(MEN)syndromes, MEN 2a, MEN 2b and Familial Medullary Thyroid Carcinoma(FMTC)inherit dominant/negative mutations in the RET protooncogene. The diseases have distinguishing phenotypes,which are characterized by medullary thyroid carcinoma,(MEN 2a, MEN 2b and FMTC)pheochromocytomas(MEN 2a and MEN 2b), hyperparathyroidism (MEN2a) and a generalized neural hypertrophy (MEN 2b). Virtually all patients with these syndromes express medullary thyroid carcinoma (MTC), which is the most common cause of death.

However, the time of onset and the biological agressiveness of the MTC vary, being earlier and more rapid in patients with MEN 2b but later and more indolent in patients with FMTC. The MTC cells secret calcitonin (CT), which is an excellent tumor marker. With direct DNA analysis for mutations in the RET protooncogene it became possible to detect members of MEN 2a, MEN 2b or FMTC kindreds who had inherited a mutated alleal. We advised total thyroidectomy in family members who had distinctive RET mutations. The operation was a total thryoidectomy with removal of lymph nodes in the central zone of the neck. Stimulated plasma CT levels were determined before and immediately after surgery, and at yearly intervals thereafter. Since 1970 we have accrued 83 families (1186 patients) with MEN 2a,38 families (57 patients) with MEN 2b and 9 families (147 patients) with FMTC. We have performed thyroidectomies on 83 patients based on genetic testing. Postoperative evaluation ranges from one month to eight years (mean 4.6 years). Preoperative stimulated plasma CT levels were in the normal range in 30 (36%) patients and in 75 (90%) patients stimulated plasma CT levels were in the normal range, postoperatively. On histologic evaluation of thyroidectomy specimens in 5(6%) patients had no evidence of a C-Cell disorder and in 16 (19%) patients only C-Cell hyperplasia was present. In MEN 2a, MEN 2b or FMTC direct DNA analysis for mutations in the RET protooncogene is the method of choice for identifying kindred members who have inherited a mutated alleal. Measurement of stimulated plasma CT levels in the postoperative period is an excellent method of determining the success of the surgery and for evaluating recurrent and persistent disease. In this setting total thyroidectomy appears to be curative in patients with early disease and represents a model of preventative oncology.

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Low dose hyper-radiosensitivity

M.C. Joiner[1], S.C. Short[2], B. Marples[1], M.I. Saunders[2]. [1] *Gray Cancer Institute, Northwood, United Kingdom;* [2] *Mount Vernon Hospital, Northwood, United Kingdom*

Purpose: To review the phenomena of low-dose hyper-radiosensitivity (HRS) and increased radioresistance (IRR) and explore the possible impact of HRS on clinical radiotherapy. Materials and Methods: Clonogenic survival of cell populations has been determined accurately by automated microscopy or FACS. Experiments have been carried out on more than 45 cell lines, altering the size, timing and dose rate of one or more radiation exposures. The effect of HRS has also been determined in mouse normal-tissue models and in human tumour xenografts. Measurements of basal-cell density have been made in skin biopsies exposed to successive small radiation doses from patients undergoing radiotherapy. Results: HRS has been demonstrated in more than 78% of the cell lines tested. It also occurs in some tumours and normal tissues in vivo. It produces increased cell kill per unit dose at doses below one gray which is more apparent in more radioresistant cell lines compared with both sensitive cell lines and