account of their epidemiological, clinical and pathological findings and surgical results obtained in 35 years.

Methods: In the years 1965–2000 forty-two children under 18 were operated on. Mean age: 14.8 years, two children were under 10. The rate of incidence is 5.1% of that for all thyroid carcinoma operations of the total age group (n = 818). The most frequent case was papillary carcinoma (32), there were 7 follicular and 3 medullary carcinomas. Cervical lymph node metastases occurred in 19 (45%). Characteristic histological changes were revealed in a comparative study for the pre- and post-Chernobyl periods. Cytofluorimetry was used to determine the DNA-content of tumorous cell nuclei for each type.

Results: 30 patients underwent total or near-total thyroidectomy. Surgical management of lymphatic metastases varied from regional node excision to radical neck dissection. Long-term mortality rate: 2.4% (n = 1), 25 years after surgery. Recurrence: local 3, lymph node 10, liver 1. There was significant increase in childhood and juvenile carcinomas after Chernobyl ($p < 0.05$). The moderate aneuploidy in tumor cell DNA-distribution differs from that of adults.

Conclusions: 1. Predominant in the childhood are papillary carcinomas and this structure is getting more frequent after Chernobyl. 2. Regional lymph-node metastases are common, but despite their DNA-aneuploidy do not influence prognosis. 3. Distant metastases are rare, with hardly any metastasis in bone. 4. The benign course of disease necessitates longer than 20 years follow-up.

395 POSTER

Thyroid cancer in children exposed to Ionizing radiation in Belarus as a result of the Chernobyl accident

L. Harabets[1], V. Drozd[1], Y. Demidcik[2], V. Minenko[3]. [1] *Research and Clinical Institute of Radiation Medicine and Endicrinology, Thyroidology, Minsk, Belarus;* [2] *Minsk State Medical Institute, Oncology, Minsk, Belarus;* [3] *Research and Clinical Institute of Radiation Medicine and Endocrinology, Dosimetry and Radiation Situation, Minsk, Belarus*

Non-effective and delayed iodine prophylaxes made possible the accumulation of radioactive iodine in the thyroid gland in population suffered from the Chernobyl accident. The purpose of the study was to analyze an association between thyroid cancer spread (operation data) and estimated dose on the child thyroid in different regions of Belarus.

Subjects and Methods: 265 verified cases of childhood thyroid cancer were analyzed. Female -male ratio was 1,4: 1. Thyroid dose was estimated by using the empirical model. Average age of children at the accident was 3,0 ±0,1 years old, at the moment of diagnosis - 11,0 ±0,2. Latent period was 8,0 ± 0,4 years.

Results: Out of 265 cases 51,7% children operated on for thyroid carcinoma lived in the Gomel oblast the moment of accident, 28,7%- in Brest oblast, 11,7% - Minsk oblast and 7,9% - in the rest three oblasts. According to estimations average thyroid dose was 0,89 ± 0,06 Gy. Children from Gomel oblast received the highest thyroid dose that was 1,38 ± 0,10 Gy ($p<0,001$) compared with those who were from Brest oblast - 0,48 ±0,03 Gy and form Minsk oblast - 0,08 ± 0,01 Gy ($p<0,01$). Distributions of pT categories among children living in different regions of Belarus at the accident showed that the frequency of pT4 was approximately similar in Gomel, Minsk and Brest oblasts - 42,4%, 50% and 48,4%, respectively. There was a tendency of the increase in the pT2 frequency from Gomel oblast (22,7%), Brest oblast (23,7%) to Minsk oblast (35,5%) although it was not significant. The occurrence of pT1 was significantly higher among children from Gomel oblast (34,5%) compared with those from Minsk oblast (16,1%) while the latent periods in children with different pT categories did not differ (7,7-8,4 years).

Conclusion: Received data suggest that there might be an association between doses received to the thyroid and tumor sizes in children operated on for thyroid cancer but further study needs to be done.

396 POSTER

Papillary thyroid carcinoma - importance of elective lymph node dissection in staging and therapy

R. Dzodic, I. Markovic, M. Inic, M. Kocic, M. Juskic, M. Vlajic. *Institute of Oncology and Radiology of Serbia, Surgery, Belgrade, Serbia, YU*

Introduction: The numerous literature data have shown that lymph node metastases in papillary thyroid carcinoma (PTC) strongly impact the occurrence of relapse.

Aim: Aim of this study was to evaluate the impact of elective lymph node dissection in precise staging and therapy of disease.

Patients and Methods: From 1981. to 2000. we have operated 236 patients with PTC. Age: 44.6±14.3 years at diagnosis (Median 44; Rang 7-80). Sex ratio: F/M-3.7/1, a)Total thyroidectomy (TT) with efective dissection of central and lower jugular lymph nodes of the neck for frozen-section histology was performed in 181 (76.7%) pts. b) TT without lymph node dissection was done in 46 pts; c) palliative surgery for locally advanced cancer in 9 pts.

Results: At the time of diagnosis 41% of patients had enlarged lymph nodes in the neck, either palpable or visible on ultrsound. In the group of 181 patients where elective lymph node dissections were peformed lymph node metastases were found in 130 (71.8%) patients. Out of these 116 pts, were presented with metastases in lower jugular nodes, on forzen-section, so modified radical neck dissection (MRND) was performed in the same act. In the group of patients without elective lymph node dissection (46), relapse occurred significantly erlier in 19 years follow-up (p=0.016).

Disscusion: The impact of lymph node metastases on survival rate in PTC is still controversial. Otherwise, lymph node metastases strongly influenced the earlier occurrence of relapse. Approximately 33% to 45% of patients with papillary thyroid cancer has cervical lymph nodes involved at the time of diagnosis. In studies were more extensive surgery with elective lymph node dissections were performed, the incidence of micrometastases in lymph nodes increases up to 80%. In our series the incidence of suspected lymph node involvement at the time of diagnosis was 41%. In the group of patients with elective lymph node dissection the incidence of metastases on definitive histopathology was 71.8%.

Conclusion: Extensive surgery, TT with dissection of central and lower jugular lymph nodes for frozen-section histology, in PTC enables diagnosis of nonpalpable lymph node metastases, precise surgical staging of disease and possible cure in patients with PTC. According to our data, this approach decreases the relapse rate in PTC.

397 POSTER

Thyroid cancer associated with Hashimoto thyroiditis

G. Horvatić Herceg[1], H. Tomić Brzac[1], I. Bračić[1], D. Herceg[2], S. Kusačić-Kuna[1], D. Dodig[1]. [1] *Clinical Department of Nuclear Medicine and Radiation Protection;* [2] *Clinic of Pathophysiology, University Hospital Rebro, Zagreb, Croatia*

The increased incidence of thyroid carcinoma (TC) in patients with Hashimoto's thyroiditis (HT) is well established in the literature, but the previous investigations were based mainly on pathohystologycal findings and only scintigraphic "cold" nodules were suspected as possible TC.

In our study ultrasound (US) and US guided fine needle aspiration biopsy (FNAB) were performed.

HT was diagnosed in 945 patients (pts) and in 36 of them TC associated with HT was found. TC appeared in 30 cases as hypoechogenic nodule, in 4 cases as isoechogenic, in 1 pt as cystic nodule and in 1 as calcified nodule. The size of carcinoma was <1 cm in diameter in 16 cases, 1–2 cm in 11 and >2 cm in 9 cases. Intraglandular dissemination and/or neck lymph nodes metastases were present in 19% of pts, and in the case of small carcinomas (<1 cm) in 37% of pts. All pts with TC underwent total thyroidectomy because of cytological finding. Papillary carcinoma amounted to 32 cases, follicular to 3 and medullary to 1 case. In all cases HT was confirmed hystologically and pts with perineoplastic and nonspecific thyroiditis were excluded.

Conclusions: 1.) We recommend careful US follow-up examinations of pts with HT. 2.) US-guided FNAB has to be performed in all patients with nodular form of HT (especially if the nodules are echographycally displayed as hypoechogenic). 3.) Small nodules (<1 cm) must not be neglected because they also tend to metastasize locally.

398 POSTER

Fine-needle aspiration cytology and frozen-section examination in pre- and intraoperative diagnosis of thyroid cancer

F. Lumachi[1], S. Borsato[2], S. Basso[1], F. Marino[3], M. Montesco[3], D. D'Amico[1], G. Favia[1]. [1] *Endocrine Surgery Unit, Department of Surg & Gastroent Sciences;* [2] *Section of Cytopathology, Department of Pathology;* [3] *Department of Pathology, University of Padua, School of Medicine, 35128 Padova, Italy*

Introduction: In contrast to thyroid nodules thyroid cancer is a rare condition which, in any case, requires an early diagnosis and treatment. In patients with nontoxic solitary thyroid nodules (NSTN) both fine-needle aspiration cytology (FNAC) and intraoperative frozen-section examination (IFSE) are usually requested for the adequate surgical planning. The aim of this study

was to evaluate the usefulness of FNAC and IFSE in patients with NSTN undergoing surgery.

Patients and Methods: We retrospectively analyzed a series of 606 patients with a SNTN who underwent both preoperative FNAC and IFSE prior to partial or total thyroidectomy. There were 118 (19.5%) men and 488 (80.5%) women, with an overall median age of 44 years (range 16-81 years). Final pathologic examination showed 500 (82.5%) benign nodules, including 239 (39.4%) follicular adenomas, and 106 (17.5%) thyroid carcinomas, of which 80 (75.5%) papillary, 18 (17.0%) follicular, 5 (4.7%) undifferentiated, and 3 (2.8%) medullary carcinomas. Patients with benign tumors were significantly ($p<0.05$) younger

Results: In the preoperative differential diagnosis between hyperplastic thyroid nodules and thyroid tumors, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of FNAC was 93.6%, 98.9%, 92.1%, 99.4%, and 95.9%, respectively. In the detection of malignancy sensitivity, specificity, PPV, NPV, and accuracy were 94.3%, 99.8%, 98.8%, 99.0%, and 98.8% for FNAC, and 95.3%, 100%, 99.0%, 100%, and 99.2% for IFSE (p=NS, chi-squared test). The combination of FNAC and IFSE did not improve significantly (p=NS) the results. In fact, IFSE suggested a thyroid cancer in only one of the 6 patients with false negative FNAC, and failed to detect malignancy in 5 of 18 (27.8%) follicular carcinomas.

Conclusions: In patients with NSTN and an adequate FNAC suggesting malignancy IFSE may be unnecessary, and in those with follicular tumors the results of both FNAC and IFSE should not affect the final intraoperative decision-making.

399 POSTER

Results of Interferon alpha 2b (Introna) treatment in 22 patients with metastatic progressive differentiated endocrine tumors

C. Baiseau Corrieri[1], J.Y. Scoazec[2], O. Boillot[1], C. Dumanoir[3], C. Barel[1], J.C. Saurin[1], J. Dumortier[1], J.A. Chayvialle[1], C. Lombard-Bohas[1].
[1] Hopital Edouard Herriot, Digestive Diseases Federation, Lyon, France; [2] Hopital Edouard Herriot, Pathology Department, Lyon, France; [3] Schering Plough, Laboratory, Paris, France

Digestive endocrine tumors (ET) are uncommon tumors; treatment of metastatic disease is not well established. Oberg and Collegues first described the potential role of Interferon alpha 2-b in the treatment of non curable progressive disease. We report here the results in 22 consecutive patients (pts) with progressive histologically proven ET treated with interferon alpha 2b (Introna): 14 men - 8 women, median age 57,8 years (40 - 75). Eleven were enterochromaffin ET (1 bronchial, 1 rectal, 8 ileal); 8/11 patients had carcinoid syndrom and 11 high serotonin levels. Eleven were pancreatic ET, 5/11 with clinical functional syndrome and high hormonal blood levels (1 vipoma, 1 glucagonoma, 1 insulinoma, 2 gastrinomas). All had documented progressive disease in the past six months before Interferon treatment. They all had been pretreated: surgery (20) including liver transplantation (2), octreotide (13), chemotherapy (10) and hepatic chemoembolisation (7). The median time beetween first diagnosis and interferon treatment was 3.9 years (1 month - 17.4 years). Interferon was given subcutaneouly three times a week first at 1.5 MU per injection and escalated to 5 MU until progression.

Results: Median follow -up was 23 months (6 - 80). Among 12 patients with secretory syndromes, 10 (83%) had objective responses (OR): 3 complete (CR) and 7 partial (PR), including 7/8 carcinoid syndromes (2 CR) and 3 pancreatic ET (1 CR). Hormonal responses were evaluated in 13 patients, with 8 OR (3 CR). Effects on tumeur burden could be assessed in 20 patients. These were 2 OR (9%), 11 stable disease (SD, 50%), 7 progressive disease (PD, 41%), with similar profiles in enterochromaffin and pancreatic ETs. Eleven patients are still on treatment. As regards toxicity, 2 patients discontinued Interferon at 2 and 6 weeks, respectively. Other effects included neutropenia, anemia, elevated transaminases, dysthyroidism, sexual dysfunction and flux-like syndrome, each in 4 patients at most.

Conclusion: were observed 59% stabilisation with 9% OR in patients with progressive endocrine tumors after previous therapy. Tolerance was fair. Interferon in useful in a substantial proportion of patients with ETs, and should be prospectively evaluated against other treatment modalities.

Tumour biology/Human genetics

400 POSTER

Isolation of human leukocyte antigen (HLA)-associated peptide(s) in the absence of HLA-restricted specific cytolytic T lymphocytes (CTL)

A.M.E. Nouri, N. Torabi-Pour, R.T.D. Oliver. *Departments of Medical Oncology, Bart's and The London Trust, London, UK*

The human leukocyte antigens (HLA) class I and class II are critical molecules for T cell recognition of endogenous and exogenous non-self antigens and hence are the major players in immune surveillance. As bladder cancer is one of the most immune sensitive tumours, based on their response to BCG, a unique combination of an in-housed established bladder tumour cell lines Fen (the original class I negative and class I positive Fen cells after the restoration of the missing class I antigen by β2-m gene transfection) were used for detail biochemical analysis of the nature of the corrected class I antigens and the associated peptides using various approaches. These included: immuno-precipitation, dot blot, immunocytochemical staining, SDS PAGE and high performance liquid chromatography (HPLC).

The results showed that.

(1) Trasfection of Fen cell line with normal β2-m gene resulted in restoration of missing class I antigens as assessed by HPLC and dot blot assay.
(2) Both interferon alpha (IFNα and IFNγ stimulation of cells led to an up-regulation of class I antigens, more so in the case of IFNγ.
(3) The intact class I antigens could be isolated from lysate of the β2-m gene transfected cells using sepharose CNBr-W6/32 beads and DEA as a dissociation reagent.
(4) Dissociation of class I antigens from heads by DEA and analysis by the SDS PAGE showed the presence of both free heavy and light chains of class I antigens.
(5) More than 20 class I-associated peptides with molecular weight of 700 to 3000 Daltons could be isolated from W6/32-loaded beads but only from lysate of HLA positive Fen cell line. The data also showed that 1×10^6 of positive Fen cells contained about 200 ug total protein of which about 0.10ug was class I of which about 2 ng was class I-associated peptides.

These findings demonstrated that gene transfection approach could be used to restore missing class I antigens on otherwise a class I negative bladder tumour cell line. The results also showed the feasibility of using various immuno-biochemical techniques to isolated HLA-associated peptides form lysate of a class I positive tumour cell line in the absence of specific cytolytic T lymphocyte (CTL). These approaches may provide a realistic possibility for extraction and identification of putative tumour specific peptide(s) from tumour specimens with the aim to use such peptide(s) for immunotherapy in cancer patients.

401 POSTER

Profile of p53 expressions in human tissue biopsies of bladder and head and neck tumours: Effects of various in vitro manipulations of p53 on tumour cell behaviour in vitro

A.M.E. Nouri, H. Cannell, R.T.D. Oliver. *Depts. of Medical Oncology and Maxillofacial Surgery; The Royal London Trusts Hospitals, London E1, UK*

In this investigation the profile of p53 expression in tumour tissue biopsies from bladder and from oro-phamgeal tumours was investigated using immunocytochemical staining method. In addition, various techniques including SDS page gel electrophoresis, colorimetric assay and gene transfection were used to investigate the influence of p53 on the behaviour of established human tumour cell lines in vitro. The results showed that:

(a) positive p53 expression was present in more than 40% of cases from both regions, although their profile of the expression differed.

(b) both gamma radiation and cisplatin treatment of tumour cell lines showed induction of p53.

(c) the susceptibility of two cell lines, one with constitutive expression of p53 and one with no p53 expression, showed that the expressing cells were more sensitive to the gamma radiation.

(d) the insertion of wild type and therefore non-mutated p53 into a bladder tumour cell line showed that the inserted cells apoptosed very rapidly whereas the cells inserted with the mutated p53 survived.

If these data could be translated to an in vivo setting, it would be possible that the introduction of wild type p53 gene by gene transfection into tumour cells independent of their p53 gene mutational status, would prove to be beneficial in that if the cellular p53 gene is mutated, the introduction of the