Kolonić SO, Džebro S, Kušec R, Planinc-Peraica A, Dominis M, Jakšić B. Primary mediastinal large B-cell lymphoma: a single-center study of clinicopathologic characteristics. Int J Hematol. 2006;83:331-6.

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Primary mediastinal large B-cell lymphoma (PMLBCL) is a subset of LBCL with unique clinicopathologic features. Some studies have raised the question of differences in biological features and clinical course among patients from different parts of the world. The authors conducted a retrospective clinicopathologic analysis of 24 patients with PMLBCL from a single center in Croatia. They also conducted the first investigation of the frequency of lymphotropic viruses human herpesvirus 6 (HHV-6) and HHV-8 in lymphoid lesions of this disease. The clinical characteristics of the patients were as expected, with high International Prognostic Index scores, elevated serum lactate dehydrogenase (LDH) levels, and bulky disease being adverse prognostic factors. Only 6 patients (25%) showed CD30 expression, and Bcl-6 protein expression was, in this series, prognostically favorable (p=0.0401). One patient's tumor had detectable HHV-6 genome sequence, but no HHV-8 sequences were detected in any tumors. Two thirds of the patients received CHOP chemotherapy (cyclophosphamide, hydroxydaunomycin, vincristine, and prednisone) with a relatively low complete remission rate (43.8%; median follow-up, 33.8 months). This study confirmed the moderate preponderance among PMLBCL patients of young females with B symptoms and elevated LDH levels. The CHOP regimen proved effective as first-line therapy only in patients with limited disease. Therefore, other third-generation chemotherapy protocols may be considered for treatment, especially in patients with bulky and advanced disease.

Ristić S, Lovrečić L, Starčević-Čizmarević N, Brajenović-Milić B, Jazbec SS, Barac-Latas V, et al. No association of CCR5delta32 gene mutation with multiple sclerosis in Croatian and Slovenian patients. Mult Scler. 2006;12:360-2.

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Several studies investigating the role of the CCR5delta32 mutation in multiple sclerosis (MS) have reported varied, often contradictory results. Therefore in the present study the authors have analysed whether the CCR5delta32 mutation is associated with the risk of/or disease process in Croatian and Slovene MS patients. Three hundred and twenty-five MS patients and 356 healthy controls were genotyped by the polymerase chain reaction method. The results showed no significant differences in the distribution of CCR5delta32 mutations between MS and control subjects, indicating that this mutation does not influence susceptibility to MS. Furthermore, the authors did not observe that CCR5delta32 carrier-status could modulate age of disease onset or progression of the disease. In conclusion, CCR5delta32 mutation is neither protective of, nor a risk factor, for MS development.

Horvat S, Mlinarić-Majerski K, Glavaš-Obrovac L, Jakaš A, Veljković J, Marczi S, et al. Tumor-cell-targeted methionine-enkephalin analogues containing unnatural amino acids: design, synthesis, and in vitro antitumor activity. J Med Chem. 2006;49:3136-42.

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A series of new peptides (8-25) containing different unnatural amino acids of the adamantane type (1-6), was synthesized. Possible cytotoxic activity on human cervical adenocarcinoma (HeLa), larynx carcinoma (Hep-2), colon carcinomas (HT-29, Caco-2), poorly differentiated cells from lymph node metastasis of colon carcinoma (SW-620), mammary gland adenocarcinoma (MCF-7), and melanoma (HBL) cells were tested by the MTT assay. The results were compared with the effect of methionine-enkephalin (Tyr-Gly-Gly-Phe-Met, or opioid growth factor, OGF), and its shorter N-terminal fragments. Peptide analogues containing C(alpha alpha)-dialkylated glycine (Aaa1, 1) or C(alpha)-alkylated glycine (Aaa2, 2) amino acid residues showed antitumor activity against melanoma, larynx carcinoma, colon carcinomas, and colon metastasis cell lines in vitro. The pentapeptide Tyr-(R,S)-Aaa2-Gly-Phe-Met (18) was the most effective analogue especially against the most antitumor drug-resistant cell lines HEp-2 and SW-620. Apoptosis as a mode of cell death was confirmed in these tumor cells after exposure to pentapeptide 18.

Pajtler M, Audy-Jurković S, Škopljanac-Macina L, Antulov J, Barišić A, Miličić-Juhas V. Rapid cervicovaginal smear screening: method of quality control and assessing individual cytotechnologist performance. Cytopathology. 2006;17:121-6.

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The aim of this study was to validate the method of rapid screening (RS) in the detection of cervical lesions and false-negative results as well as in quality control of cytotechnologist performance. The RS method was validated on Papanicolaou-stained and initially conventionally analysed vaginal, cervical and endocervical (VCE) smears collected in an opportunistic programme for the detection of cervical carcinoma. The study included 3680 VCE smears from the Department of Gynaecologic Cytology, University Department of Gynaecology and Obstetrics, Zagreb University Hospital Center, Zagreb and from the Department of Clinical Cytology, Osijek University Hospital, Osijek. Histologically verified abnormal findings accounted for 10% of the study samples. Thirteen cytotechnologists, with no previous experience in RS, performed the test. Each slide was examined using the 'step' technique for 1.5 minutes, the findings were classified as negative or abnormal, and the abnormal ones were also classified according to differential cytological diagnosis. The results were compared with those obtained on initial screening. Abnormal findings from a group of initially negative findings were reanalysed using conventional methods to make definitive cytological diagnosis. RS yielded a sensitivity of 83.7%, specificity of 93.7%, positive predictive value of 62.4%, negative predictive value of 97.9% and diagnostic accuracy of 92.6%. Relative to the initial abnormal differential cytological diagnosis, the diagnostic value of RS increased with lesion severity [54.8%, 68.0% and 91.3% for cervical intraepithelial neoplasia (CIN) I, CIN II and CIN III respectively]. RS detected 38 additional positive findings; 94.2% of these were atypical squamous cells of undetermined significance (ASCUS)/abnormal glandular cells undetermined significance (AGUS) and CIN I. The rate of additional positive findings was 1.14% (38/3135). The false-negative rate of initial screening was 9.4% (38/406), and individual cytotechnologist sensitivity was 60.0-100.0%. In conclusion, RS could be introduced as an efficient method of quality control to improve the sensitivity of cytological screening as well as for quality control of cytotechnologist performance.

Pavelić K, Dedivitis RA, Kapitanović S, Čaćev T, Guirado CR, Danić D, et al. Molecular genetic alterations of FHIT and p53 genes in benign and malignant thyroid gland lesions. Mutat Res. 2006;599:45-57.

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Human FHIT (fragile histidine triad) gene is highly conserved gene whose loss of function may be important in the development and/or progression of various types of cancer. The authors undertook this study to analyze FHIT and p53

gene status in different benignant and malignant thyroid tumors. Status of these genes as well as intensity of apoptosis was analyzed in tumor tissues by molecular genetic methods, immunohistochemistry, and FACS-scan analysis. The majority of the malignant thyroid cancers displayed aberrant expression of FHIT gene, concominant with p53 gene inactivation. This is followed by low rate of apoptosis, which may be important in the development and/or progression of thyroid cancer. They found higher incidence of p53 mutation and aberrant processing of FHIT mRNA in malignant tumors (papillary, follicular, medullary and anaplastic carcinomas) and in those tumors with distant metastasis. The growth of p53(-)/FHIT(-) follicular carcinoma of human origin was much faster in nude mice than p53(+)/FHIT(+) follicular carcinoma, and mice had shorter survival rate. These results show a correlation between aberrant FHIT and p53 expression, low rate of apoptosis, and malignancy. Concomitant aberration of FHIT gene and p53 could be responsible for development of highly malignant types of thyroid cancer and may be considered as a prognostic marker for these tumors.

Baudoin T, Ćupić H, Geber G, Vagić D, Grgić M, Kalogjera L. Histopathologic parameters as predictors of response to endoscopic sinus surgery in nonallergic patients with chronic rhinosinusitis. Otolaryngol Head Neck Surg. 2006;134:761-6.

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The aim of this study was to estimate the predictable value of histopathologic parameters in chronic rhinosinusitis (CRS) for response to endoscopic sinus surgery (ESS). Symptomatology was rated in 100 patients prior to as well as 12 and 24 months after surgery. Specimens taken during the procedure were examined and scored for goblet cells, subepithelial thickening, mast cells, and eosinophils. Multiple regression analysis was performed to predict the total score of subjective symptoms before treatment by histopathologic parameters. The correlation between histopathologic parameters and postoperative symptoms was then evaluated. Goblet cells were the best predictor correlating with 5 symptoms. Subepithelial thickening correlated with 4 symptoms. Mast cell infiltration correlated with 3 symptoms. Eosinophilic infiltration correlated with only one symptom ($p<0.05$). In conclusion, certain histopathologic parameters in CRS are predictive of favorable response to ESS. Pathologic evaluation may help the ENT surgeon to predict the persistence of certain CRS symptoms after ESS, even in patients at low risk for surgical failure.

Musani V, Gorry P, Basta-Juzbašić A, Stipić T, Miklić P, Levanat S. Mutation in exon 7 of PTCH deregulates SHH/PTCH/SMO signaling: possible linkage to WNT. Int J Mol Med. 2006;17:755-9.

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The novel PTCH mutation and clinical manifestations within Gorlin syndrome family links PTCH haploinsufficiency and aberrant activation of the Wnt pathway. Here the authors report a family case with Gorlin syndrome, characterized by the usual phenotype features such as widespread basocellular tumors and craniofacial and bone malformations, but also including a less common appearance of craniopharyngioma. These clinical manifestations might be associated with a novel constitutional mutation of the PTCH gene, 1047insAGAA, which we found in exon 7. It changes the normal amino acid sequence leading to termination of the PTCH protein at exon 9. The analyzed tumors of the family show extensive loss of heterozygosity in the PTCH region, both basocellular and in particular craniopharyngioma, and in the latter a high expression of beta-catenin was detected. These findings suggest involvement of the SHH/PTCH/SMO pathway in pathogenesis of the analyzed disorders, including its possible contribution to aberrant activation of the Wnt pathway in craniopharyngioma.

Vulić-Prtorić A, Macuka I. Family and coping factors in the differentiation of childhood anxiety and depression. Psychol Psychother. 2006;79(Pt 2):199-214.

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The purpose of this investigation was to explore whether specific contextual (perception of family relationships) and personal (coping strategies) factors are more likely to be associated with anxiety or depression. The research was conducted on a sample of 331 children and adolescents ranging

in age from 10 to 16 years who completed measures of the anxiety symptoms, depressive symptoms, coping strategies, and family interactions. Data were analysed according to gender differences. Among family variables, perceived father rejection was found to be best predictor of anxiety, and father and mother rejection, together with family satisfaction, was best predictor for the depression. Avoidance is a coping strategy that best predicts anxiety, and expressing feelings is a significant predictor of depression. This research strongly indicates that problems in family interactions are more associated and better predictors of depression than anxiety. Results support the argument that the two disorders are distinct and that they are characterized by unique coping and family profiles. Knowledge that anxiety and depression could be distinguished on the basis of family and coping variables may facilitate clinical assessment and treatment planning.

Ivetić Tkalčević V, Bošnjak B, Hrvačić B, Bosnar M, Marjanović N, Ferenčić Z, et al. Anti-inflammatory activity of azithromycin attenuates the effects of lipopolysaccharide administration in mice. Eur J Pharmacol. 2006;539:131-8.

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The authors investigated the ability of azithromycin to attenuate the deleterious effects of lipopolysaccharide (LPS) in three different LPS-induced inflammatory models. The results show that azithromycin (10 and 100 mg/kg) significantly attenuated the intraperitoneal LPS-induced increase in plasma TNF-alpha concentration. It also increased survival rate in a septic shock model in mice challenged with intravenous LPS. Oral treatment with azithromycin (up to 300 mg/kg) was less effective in suppressing neutrophil infiltration into the lungs 24 h after intranasal LPS challenge, possibly because of a slower onset of action or inadequate dosing. In the same model, azithromycin given intraperitoneally significantly improved inflammatory markers (total cell number, neutrophil percentage and MIP-2 concentration) in bronchoalveolar lavage fluid. In conclusion, azithromycin exhibits significant anti-inflammatory properties but the potency of such effects varies depending on the experimental model and route of administration.