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Abnormal cortical activity and brainstem functioning are considered the possible etiopathogenetic factors of migraine. Monoamine oxidase A and B (MAO-A and -B) regulate the levels of monoamine neurotransmitters, so changes in their activity could participate in migraine pathogenesis. We have investigated the possible association of MAO-A and -B alleles and haplotypes with two common types of migraine, ie migraine without aura (MO) and migraine with aura (MA), on the sample of 110 migraineurs (80 MO and 30 MA) and 150 controls. MAO-A promoter and MAO-B intron 13 polymorphisms were genotyped by the PCR-based methods. In addition, we have reevaluated the reported association between MAO-B intron 13 polymorphism and platelet MAO-B activity. The platelet MAO-B activity was determined fluorimetrically using kynuramine as a substrate. The authors found a tendency toward association of the shorter variant of MAO-A gene promoter with migraine without aura in male subjects. Regarding investigated MAO-B polymorphism, no association with migraine or with platelet MAO-B activity was found. The suggestive association of the variant in MAO-A gene with migraine is considered worthy of independent replication. On the other hand, further studies on MAO-B polymorphism in migraine do not seem promising.


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One of the underemphasized supportive criteria for the diagnosis of prostatic cancer is the presence of retraction clefting around neoplastic glands. We analyzed a series of 152 prostatic cancer cases to determine the frequency, extent, and correlation of periacinar retraction clefting between needle core biopsies (NCB) and corresponding matched radical prostatectomy (RP) specimens. Clefting was significantly more frequent in neoplastic compared to nonneoplastic acini in NCB and RP (p<0.05). There was no significant difference in the frequency of retraction clefting in neoplastic acini between NCB and corresponding RP (p>0.05). We have also found a concordance in matched RP and NCB (kappa=0.582). We conclude that periacinar retraction clefting appears more frequently in neoplastic acini and could serve as a reliable criterion in the diagnosis of prostatic adenocarcinoma.


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The aim of this study was to evaluate the efficacy and toxicity of ifosfamide and cisplatin administered concomitantly with low-dose-rate brachytherapy followed by consolidation chemotherapy in the treatment of locally advanced squamous cell cervical carcinoma (LASC). Forty-four patients with biopsy-proven LASC were enrolled. FIGO stages IB2 bulky to IVA were entered into this study. Patients were assigned to receive external radiotherapy (50 Gy in 25 fractions); then ifosfamide 2 g/m2 plus cisplatin 75 mg/m2 was applied during two low-dose-rate brachytherapy applications, and 4 cycles of consolidation chemotherapy with the same drug combination were given after completion of radiotherapy. The planned dose to point A was 85 Gy. All patients received both courses of concomitant chemobrachytherapy and at least 1 cycle of consolidation chemotherapy. The average duration of radiation was 45.1 days. The clinical complete response rate was 100%. Grade 3 and 4 leukopenia occurred in 25% and...
11% of the cycles, respectively. After a median follow-up of 34 months (range, 20-34 months), the recurrence-free and the overall survival rates were 84% and 91%, respectively. Major delayed local complications occurred in 7 cases (16%). These results indicate that concomitant chemoradiotherapy with ifosfamide and cisplatin is a feasible combination for patients with LASCC of the cervix uteri. A randomized trial is planned.


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Congenital myasthenic syndromes (CMS) result from mutations in various synapse-associated genes. Mutations in the choline acetyltransferase (CHAT) gene cause a presynaptic CMS associated with episodic apnea (CMS-EA). The authors present two unrelated Croatian children affected by CMS-EA. Beside other clinical findings characteristic for CMS, both patients manifested intermittent apneas since early infancy. Whereas the course of disease is mild in the female patient (pt.#2), the male patient (pt.#1) experienced recurrent and severe episodes of apnea despite adequate treatment with AChE-inhibitors and shows a global developmental delay with delayed myelination and signs of hypoxic-ischemic injury in brain imaging. Interestingly, sequencing of the CHAT gene revealed identical, compound heterozygous mutations S694C and T354M in both children. These findings are in line with a remarkable clinical heterogeneity observed in patients with CHAT-mutations and emphasize the potential role of apnea crises for the development of secondary hypoxic brain damage and psychomotor retardation.


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In a prospective study, 68 patients in the initial stage of the infertility treatment were examined by hysterosonosalpingography using saline NaCl infundible and Echovist as contrast media. Subsequently, further status of the tubes and uterine cavity was assessed by the “gold standards”, laparoscopy and hysteroscopy. Sensitivity and specificity of hysterosonosalpingography using NaCl infundible for evaluation of the uterine cavity was 100 and 88.8%, respectively. Negative predictive value was 100% and positive predictive value 97%. Sensitivity and specificity of the method for the assessment of the tubal status was 100 and 66%, respectively, negative predictive value was 100% and positive predictive value was 61%. For the assessment of tubal patency using positive contrast Echovist the method has shown 100% sensibility and negative predictive value again but it reached a specificity of 77% and a positive predictive value of 70%. There were no evident complications during or after the procedure. In conclusion, hysterosonosalpingography is useful in making decisions regarding further procedures for the diagnosis and treatment of infertility. Uterine cavity evaluation using saline is the method of choice. Tubal patency can be assessed only under ideal sonographic conditions. The method is feasible for early assessment of the reproductive status of uterine cavity and fallopian tubes as a simple, safe and cheap outpatient method prior to any following invasive procedure or even hysterosalpingography.


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The authors analyzed the verrucae areae entorhinalis (VAE) in 60 neurologically normal subjects ranging from 23 to 85 years of age using a casting method. In 10 of these subjects the total number of neurons in the entorhinal islands was estimated stereologically using the optical fractionator. The number and surface area of VAE were higher in the left hemisphere compared with the right, and this leftward asymmetry was highly significant. Regression analysis showed a negative correlation between average VAE area and age in both hemispheres, representing a rate loss of about 800 microm² per year. The estimated number of neurons obtained with the optical fractionator showed no significant difference between the left and the right hemisphere (468,000144,000 vs. 405,000117,000). There was a highly significant negative correlation between neuron numbers and age in both sides. In addition, clusters of small, undifferentiated layer II neurons (‘heterotopias’) were frequently observed in the rostral part of the entorhinal cortex in young and elderly adults. Layer II entorhinal neurons are among the first to show neurofibrillary changes during normal aging. The present data confirm the occurrence of age-related neuron loss in the entorhinal cortex. Considering the consistent projections from ipsilateral auditory association areas that, together with Broca’s motor-speech area (Brodmann areas 44 and 45), show leftward asymmetry from early infancy (such as Brodmann area 22, planum temporale, and area 52 in the long insular gyrus), the authors speculate that functional lateralization of the human entorhinal cortex may be associated with specialization for memory processing related to language. Due to the dependence of hippocampal formation on entorhinal projections, this finding is also consistent with the greater capacity of the left hippocampus for verbal episodic memory.
The aim of this study was to investigate whether the reduction of core number in first-line PB from 6-12 to 4 in patients with presumed advanced PC leads to loss of clinically relevant information. The authors retrospectively studied 113 men that underwent PB, classified in two groups: “H” (high) and “L” (low likelihood of having advanced PC), according to PSA, digital rectal and transrectal ultrasound findings. Pathological results of 6-12-core PB and QPB were retrospectively compared for the presence of malignancy, percentage of positive cores, Gleason score (GS), and the presence of high-grade prostatic intraepithelial neoplasia (HGPIN). PC detection rate was not impaired in group H but dropped significantly in group L, and the percentage of positive cores was not significantly changed in group H (p=0.39), but decreased in group L (p=0.04), due to sampling scheme reduction. No HGPIN was missed with QPB in group H, while 2 HGPINs were missed in group L. No significant change in GS in either group was observed (p=0.12, p=0.13) due to reduction to QPB. The authors conclude that in patients with presumed advanced PC, reduction of the number of cores in PB may be an acceptable diagnostic strategy, but further studies are needed to analyze the impact of PB scheme reduction on other relevant pathological information obtained from PB.


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The aim of the present study was to analyse the character and incidence of orofacial clefts in Croatia and to compare the data with reports from other countries. All the material for the epidemiological study was retrieved from the documented files from all the neonatal units and hospitals in Croatia providing surgical treatment. A total of 525,298 livebirths were documented during 11 years (1988-1998); 903 among them with orofacial clefts, 24 (2.7%) of them twins. Sixty (6.6%) infants died between birth and the age of 6 months. The incidence of orofacial clefts during the study period was 1.71 per thousand. When eliminating syndromic clefts, the incidence of non-syndromic clefts was 1.56 per thousand. Analysis of cleft lip with or without cleft palate (CL+/-P) and isolated cleft palate only (CP) revealed their incidence to be 1.05 and 0.66 per 1000, respectively. Of all types of clefting, CL and CLA was found in 17.2%, CL+/-P in 43.9%, CP in 38.2% and atypical facial clefts (AFC) in 0.8% of children. Left-sided clefts were most common (51%), followed by bilateral (30.5%) and right-sided (18.5%) clefts. The male to female ratio was 1.3. CL+/-P predominated in male and CP in female children. In 220 cases (24.4%) orofacial clefts were either associated with other anomalies or the clefts occurred as one feature of a syndrome. The data obtained from different sources yielded a cleft incidence of 1.71 per 1000 in Croatia. There were no differences in the incidences of orofacial clefts in comparison with similar data from other European countries.
CD13, and the enzyme activity. Regulation of CD13/aminopeptidase N (APN), an ectoenzyme processing several signal peptides. Cells of a myelo-monocytic cell line HL-60 were used as a model system, and APN was assayed at the levels of mRNA, its membrane marker CD13, and the enzyme activity. Regulation of CD13/APN by IFN-gamma was found at all three levels. The direction of regulation was time-dependent: an initial down-regulation seen 24 and 48 hrs after the onset of treatment with IFN-gamma was replaced by an up-regulation after 72 and/or 96 hrs. Up-regulation of CD13/APN observed after 96 hrs was preceded by an up-regulation of APN mRNA reaching its maximum after 72 hrs. The IFN-gamma-induced regulation of APN was due to membrane aminopeptidase N, since it could be completely abrogated by an APN blocking antibody WM-15. The delayed up-regulation of CD13/APN (observed after 72 and/or 96 hrs), required de novo protein synthesis as it could be abrogated by cycloheximide, an inhibitor of protein synthesis. Possible role of endogenous (IFN-gamma-induced) TGF-beta in mediating CD13/APN up-regulation could be excluded, since no TGF-beta was found in supernatants of IFN-gamma-treated HL-60 cells. Thus, these data show regulation of CD13/APN on cells of myelo-monocytic origin by a T-cell derived cytokine, IFN-gamma. A similar mechanism might play a role in inflammation.


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The mannose receptor (MR) is involved in the initiation of the immune response and regulation of homeostasis during inflammation and tissue remodeling. Distribution, endocytosis and possible natural ligand tumor associated glycoprotein-72 (TAG-72) for the MR have been examined by immunohistology, immunocytochemistry and flow cytometry at the maternal-fetal interface, characterized by extensive tissue remodeling. Contrary to disseminated distribution of the MR positive (MR+) cells in term placenta, the MR+ cells of early pregnancy decidua intimately surrounded glands and followed tissue distribution of CD14 positive cells. The mannose receptor was present on freshly isolated first trimester decidual mononuclear cells and distributed mostly on macrophages (77.08 +/- 10.55%, mean +/- SD). The expression of the MR on CD14 positive cells decreased following 18 h culture (p<0.01) and was accompanied by the reduction of fluorescein isothiocyanate (FITC)-dextran uptake. PAM-1 anti-MR antibody, mannann and TAG-72 reduced FITC-dextran uptake by decidual macrophages. These data indicate that the MR+ macrophages, surrounding early decidual glands, are able to internalize ligands for carbohydrate recognition domain of the receptor, including decidual secretory phase mucin TAG-72.