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The aim of this study was to better understand the mechanisms that underlie adaptive changes in GABAA receptors following their prolonged exposure to drugs. Exposure (48 h) of human embryonic kidney (HEK) 293 cells stably expressing recombinant alpha1beta2gamma2S GABAA receptors to flumazenil (1 or 5 microM) in the presence of GABA (1 microM) enhanced the maximum number (Bmax) of [3H]flunitrazepam binding sites without affecting their affinity (Kd). The flumazenil-induced enhancement in Bmax was not counteracted by diazepam (1 microM). GABA (1 nM - 1 mM) enhanced [3H]flunitrazepam binding to membranes obtained from control and flumazenil-pretreated cells in a concentration-dependent manner. No significant differences were observed in either the potency (EC50) or efficacy (Emax) of GABA to potentiate [3H]flunitrazepam binding. However, in flumazenil-pretreated cells the basal [3H]flunitrazepam and [3H]TBOB binding were markedly enhanced. GABA produced almost complete inhibition of [3H]TBOB binding to membranes obtained from control and flumazenil treated cells. The potencies of GABA to inhibit this binding, as shown by a lack of significant changes in the IC50 values, were not different between vehicle and drug treated cells. The results suggest that chronic exposure of HEK 293 cells stably expressing recombinant alpha1beta2gamma2S GABAA receptors to flumazenil (in the presence of GABA) up-regulates benzodiazepine and convulsant binding sites, but it does not affect the allosteric interactions between these sites and the GABA binding site. Further studies are needed to elucidate these phenomena.


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The aim of this study was to explore region-dependent changes that occur with aging in trabecular and cortical bone of the human vertebral body. Bone cylinders were drilled with a trephine from three regions (central anterior, central posterior, and lateral) of the third lumbar vertebral bodies of 48 autopsy cases 31 to 76 years old. Two consecutive 5 μm sections obtained 150 μm apart were stained with toluidine blue and Masson trichrome and photographed at 40×. Differences in numerous morphometric factors were evaluated by age and region of the vertebra using repeated-measures analysis of variance and Tukey's Honestly Significant Difference test. Starting at about 50 years of age, significant, linearly progressive decreases occurred in trabecular and cortical bone volume (p<0.005), trabecular surface area (p<0.001), number of trabeculae (p<0.001), and thickness of trabeculae (p<0.001). Space between trabeculae increased from ages 31 to 70 years and then decreased (p<0.001). Trabecular deterioration was significantly more pronounced in central versus lateral regions (p<0.001). Cortical bone thickness decreased significantly with aging in central regions but increased in lateral regions between ages 61 and 70 years (p<0.001). The balance between cortical and trabecular bone maintains the strength of the vertebral body until about the age of 50 years, when irreversible deterioration begins in central regions and subsequently involves lateral regions.


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The aim of this study was to assess how war psychotrauma, refugee status and other factors relate to self-image. Psychotherapeutic-psychiatric interview, the Offer Self-Image Questionnaire (OSIQ), questionnaires for measuring war stressors, posttraumatic stress reactions (PTS-reactions), depression and general data were ad-
ministered. A total of 322 adolescents from Bosnia-
Herzegovina and Croatia were included in the study. In
60.32% of the examinees, more than four war stressors
were encountered. In 13.68% of the examinees, high
PTS-reactions occurred. The refugees had nearly four
times higher odds (aOR=3.66; 95% CI=1.63-8.2; p<0.01) of having a higher Offer score for the sexual attitudes
subscale. Lower war stress had 0.28 times lower odds (aOR=0.28; 95% CI=0.11-0.71; p<0.01) of having a higher Offer score for the emotional tone subscale. War
psychotrauma and refugee status are related to poorer ad-
justment only in some of the OSIQ subscales. Practical
measures are proposed, as well as educational and prevent-
tive/therapeutic psychotrauma models.

Labar B, Sucić S, Zittoun R, Muus P, Marie JP, Fillet G,
et al. EORTC Leukemia Group. Allogeneic stem cell
transplantation in acute lymphoblastic leukemia and
non-Hodgkin's lymphoma for patients < or =50 years
old in first complete remission: results of the EORTC

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In the EORTC ALL-3 trial, the efficacy of allogeneic trans-
plantation was compared with that of autologous mar-
row transplantation and maintenance chemotherapy in
patients < or =50 years who reached CR. Among 340 pa-
patients who entered the study, 279 were < or =50 years
old. Out of these, 220 reached CR, 184 patients started
consolidation and were HLA typed; 68 had a donor and
116 had no sibling donor. The median follow-up was 9.5
years; 93 patients relapsed, 26 died in CR, and overall
116 patients died. Allogeneic transplantation was per-
fomed in 47 (68%) patients with a donor while auto-
logous transplantation or maintenance chemotherapy
was given to 84 (72%) patients without a sibling donor.
The 6-year disease-free survival rate was similar in the
groups with and without donor [38.2% (SE = 5.9%) vs.
36.8% (SE = 4.6%), hazard ratio 1.01, 95% CI 0.67-
1.53]. Comparing the donor group with the no donor
group, the former had a lower relapse incidence (38.2%
vs. 56.3%, p = 0.001), but a higher cumulative incidence
of death in CR (23.5% vs. 6.9%, p = 0.0004). The 6-year
survival rates were similar [41.2% (SE = 6.0%) vs. 38.8%
(SE = 4.6%)]. This trial did not show that allogeneic trans-
plantation, when a sibling donor is available, produces a
better outcome than the policy of offering autotrans-
plantation or chemotherapy in the absence of a donor.

Baričević M, Forčić D, Gulija TK, Jug R, Mažuran R.
Determination of the coding and non-coding
nucleotide sequences of genuine Edmonston-Zagreb
master seed and current working seed lot. Vaccine.

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To confirm the genetic stability of the Edmonston-
Zagreb vaccine strain, the authors determined and com-
pared the nucleotide sequences of genuine Edmons-
ton-Zagreb master seed (EZ D22) and current working
seed lot (EZ D24 2/99). Sequence analysis and compar-
son of the two sequences confirmed that these two se-
quences are the same at the molecular level. The ob-
tained sequences were also compared to reference
strains, i.e. Edmonston wild-type (Edmonston Wt)
AF266288 and Edmonston-Zagreb (EZ) AF266290 vac-
cine strain. The sequence of EZ D22 differed from the
Edmonston Wt in 32 nucleotides. EZ D22 differed from
EZ AF266290 in six nucleotides. Coding substitution at
position 441 and two silent substitutions at positions
11999 and 14612 in the L gene are unique to EZ D22.
The differences found between EZ from different
sources can be a good reason for periodical sequence
analysis of the same strain in the hands of different man-
ufacturers.

Pivac N, Kozarić-Kovačić D, Muck-Šeler D.
Olanzapine versus fluphenazine in an open trial in
patients with psychotic combat-related
post-traumatic stress disorder. Psychopharmacology

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The aim of an open, comparative 6-week study was to
compare olanzapine and fluphenazine, as a monothera-
py, for treating psychotic combat-related PTSD. Fifty-
five male war veterans with psychotic PTSD (DSM-IV
criteria) were treated for 6 weeks with olanzapine
(n = 28) or fluphenazine (n = 27) in a 5-10 mg/day dose
range, once or twice daily. Patients were evaluated at
baseline, and after 3 and 6 weeks of treatment, using
Watson’s PTSD scale, Positive and Negative Syndrome
Scale (PANSS), Clinical Global Impression Severity
Scale (CGI-S), Clinical Global Impression Improvement
Scale (CGI-I), Patient Global Impression Improvement
Scale (PGI-I) and Drug Induced Extra-Pyramidal Sym-
toms Scale (DIEPSS). RESULTS: At baseline, patient’s
data (age, duration of combat experience and scores in
all measurement instruments) did not differ. After 3 and
6 weeks of treatment, olanzapine was significantly
more efficacious than fluphenazine in reducing symp-
toms in PANSS (negative, general psychopathology
subscale, supplementary items), Watson’s PTSD (avoid-
ance, increased arousal) subscales, CGI-S, CGI-I, and
PGI-I scale. Both treatments affected similarly the symp-
toms listed in PANSS positive and Watson’s trauma
re-experiencing subscales. Fluphenazine induced more
extrapyramidal symptoms. Prolongation of the treat-
ment for 3 additional weeks did not affect the efficacy of
either drug. These data indicate that both fluphenazine
and olanzapine were effective for particular symptom

angiogenesis was tested using a between clinicopathological variables and the degree of survival by Kaplan-Meier and log-rank analysis. Correlation MVD was correlated with overall and disease-free surv-

400x magnification on 3 microscopic fields per patient. brand factor antibody and microvessels were counted at
ttive immunohistochemical study. Sections from diagnos-
tic biopsies were immunostained using anti-von Wille -
tive of angiogenesis in osteosarcoma. Thirty-nine pa-

The aim of this study was to investigate prognostic signifi-
cance of angiogenesis in osteosarcoma. Thirty-nine pa-


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Finding disease markers (classifiers) from gene expression data by machine learning algorithms is characterized by a high risk of overfitting the data due the abundance of attributes (simultaneously measured gene expression values) and shortage of available examples (observations). To avoid this pitfall and achieve predictor ro-


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The aim of this study was to investigate prognostic signifi-
cance of angiogenesis in osteosarcoma. Thirty-nine pa-


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The aim of this study is to compare the Lich-Gregor procedure and antireflux ureterocystoneostomy at the ver-
tex of the bladder (AUVB) based on 20 years’ clinical experience. Over a period of 20 years (1978-1998), a total of 1280 children were operated on, 368 bilater-
ally, which resulted in 1648 antireflux ureterocystoneo-
stomies being performed. Of the total of 1648 antireflux ureterocystoneostomies, AUVB was performed in 1032 ureteric units and the Lich-Gregor procedure in 616 ureteric units. Between 1978 and 1992 the authors per-
formed only AUVB, and from 1992, both AUVB and the Lich-Gregor procedure. The final result was evaluated 2 years after the operation. Satisfactory results were achieved in 93.5 % with AUVB and 96 % with the Lich-Gregor procedure. The postoperative failure rate was 6.5 % for the AUVB and 4 % for the Lich-Gregor
Operations. The recurrence rate was higher with AUVB (5 %) than with the Lich-Gregoir procedure (1.5 %), but postoperative stenosis was more frequent with the Lich-Gregoir procedure (2.5 %). The authors recommend the Lich-Gregoir procedure as the preferred operative method. If the results of the Lich-Gregoir procedure are unsatisfactory, the authors recommend the AUVB for the first and second recurrence operation. Finally, in cases of repeated VUR recurrence of postoperative stenosis, as the last operation, the authors perform antireflux ureteroulocystoplasty with an intussuscepted segment of the ileum.


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Occult hepatic metastases from colorectal cancer result in an increase of the ratio of arterial hepatic blood flow to total hepatic blood flow, described as the Doppler perfusion index. Whether this alteration is due to an increase in arterial blood flow or a decrease in portal venous inflow has not yet been unequivocally determined. The purpose of this study was to analyze changes in hepatic perfusion in patients with liver metastases from colorectal cancer by standardization of hemodynamic parameters to body surface area. Hemodynamic parameters (crosssectional area, blood flow, and congestive index) were measured for the common hepatic artery and portal vein with duplex color Doppler sonography in 20 patients with liver metastases and 20 healthy control subjects and evaluated relative to body surface area. No statistically significant differences in age, body surface area, cross-sectional area of the common hepatic artery, and congestion index of the common hepatic artery and portal vein were observed between control subjects and patients with liver metastases. Patients with liver metastases had significantly greater arterial hepatic blood flow and Doppler perfusion index and significantly smaller portal cross-sectional area portal blood flow as well as total liver blood flow (p<001). This study supports the theory that the primary mechanism of alteration in liver perfusion is the reduction of portal inflow with subsequently increased arterial hepatic blood flow.


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The primary challenge in the management of a multinodular thyroid gland is to rule out malignancy. The present study was undertaken to assess the value of preoperative ultrasound-guided fine needle aspiration cytology (FNAC) in diagnosing tumors of the thyroid gland. Of the 80 patients operated for multinodular lesions, malignant tumors were found in 29 and benign tumors in 36 patients (81%) and non-tumorous lesions in 15 (19%) patients. Compared with the histopathological postoperative diagnosis, the overall sensitivity of FNAC was 85% and specificity 88%. Current morphological diagnosis of the nodules in multinodular goitre requires thorough preoperative examination, including ultrasound-guided FNAC in order to establish the appropriate management.