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New Strategies of Screening and Treatment for Sleep Apnea Syndrome

WATARU HIDA

The First Department of Internal Medicine, Tohoku University School of Medicine, Sendai 980-8574

The prevalence of sleep apnea syndrome (SAS) is approximately 7.5% in Japanese adults aged 18-68 years old. SAS is characterized by repeated episodes of apnea, especially obstructive apnea, during sleep. Severe SAS has life-threatening complications such as pulmonary hypertension, arrhythmias, right heart failure or brain damage, which could be caused by hypoxemia and/or hypercapnia. Upper airway relaxation is responsible for the obstruction during apnea, and an increase in the activities of the upper airway muscles dilates and stiffens the upper airway wall. Maintaining the activities of the upper airway muscles may contribute to keeping the airway patent. Submental electrical stimulation of the upper airway muscles would be a novel treatment method for obstructive apnea.

Key words--- sleep apnea syndrome; obstructive apnea; upper airway muscles; hypoxia; electrical stimulation

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Lumbar Intradiscal Pressure after Posterolateral Fusion and Pedicle Screw Fixation

EIJI ABE, TROY NICKEL,1 GLENN R. BUTTERMANN,1 JACK L. LEWIS1 and ENSOR E. TRANSFELDT1

Department of Orthopaedic Surgery, Akita University School of Medicine, Akita 010-8543, and 1Bioengineering Laboratory at the Department of Orthopedic Surgery, University of Minnesota, Minneapolis, MN 55455, USA

In vitro biomechanical testing was performed in single-functional spinal units of fresh calf lumbar spines, using pressure needle transducers to investigate the effect of posterolateral fusion (PLF) and pedicle screw constructs (PS) on intradiscal pressure (IDP), in order to elucidate the mechanical factors concerned with residual low back pain after PLF. IDP of 6 calf lumbar spines consisting of L4 and L5 vertebrae and an intervening disc was measured under axial compression, flexion-extension and lateral bending in the intact spine, PS, PLF and the destabilized spine. Relative to the intact spines, the destabilized spines showed increased IDP in all of loadings and moments. IDP under PS and PLF were significantly decreased in axial compression, extension and lateral bending loads (p<0.05). In flexion, IDP under PS and PLF increased linearly proportional to the magnitude of flexion moment and reached as high as IDP of the intact spines. These results demonstrated that despite an increase in the stiffness of motion segments after PLF and PS, significant high disc pressure is still generated in flexion. Flexibility of PS and PLF may cause increased axial load sharing of the disc in flexion and increased IDP. This high IDP may explain patients' persisting pain following PS and PLF.

**Key words**--- biomechanics; intradiscal pressure; lumbar spine; posterolateral fusion; pedicle screw fixation

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**Address for reprints:** Eiji Abe, Department of Orthopedic Surgery, Akita University School of Medicine, 1-11 Hondo, Akita 010-8543, Japan.

e-mail: eijiabe@med.akita-u.ac.jp

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Improved Survival of Children with Advanced Tumors by Myeloablative Chemotherapy and Autologous Peripheral Blood Stem Cell Transplantation in Complete Remission

ATSUSHI SATO,1 MASUE IMAIZUMI,1,2 TAKAKO SAISHO,1 TOSHIKI SAITO,1 MIYAKO YOSHINARI,1 YAN CUI,1 HOSHIRO SUZUKI,1 YOSHITSUGU KOIZUMI,1 TSUNEI ITO,3 YOSHIHIRO TAKAI,4 YUTAKA HAYASHI,2 MAKOTO TAMURA3 and KAZUIE INUMA1,3

1Department of Pediatrics, 2Department of Pediatric Hematology and Oncology, 3Division of Blood Transfusion Service, and 4Department of Radiology, Tohoku University School of Medicine, Sendai 980-8574

Five children with neuroblastoma (NB) stage IV and five children with rhabdomyosarcoma (RMS) stage III were treated with myeloablative chemotherapy and autologous peripheral blood stem cell transplantation (MCT/PBSCT) in the state of complete remission (CR) achieved by conventional therapy. PBSCs were collected in CR status using a cell separator with blood access through a double-lumen central venous catheter. PBSCs With 1.9±0.8×10^5 of CFU-GM per patient weights (kg) were infused following MCT after a period of conventional therapy for 11.1±2.1 or 9.7±0.9 months in NB or RMS patients, respectively. Regimen-related toxicity of MCT was tolerable and peripheral white blood cell count recovered beyond 1.0×10^3/μl 10-12 days after infusion of PBSCs in all patients. All of RMS patients and three of five NB patients survived for an average of 31.6 months (ranged 10.8-58.1). The survival rate of these patients was improved as compared with our historical controls, and presumably, with that of conventional chemotherapy previously reported. Despite a limited number of patients, it appears that MCT/PBSCT may be effective in improving survival by preventing relapse which may occur thereafter if treated with conventional therapy alone. Furthermore, MCT/PBSCT reduced the duration of treatment, as compared with that of conventional chemotherapy. Therefore, this study may suggest the feasibility and promise of the therapy including MCT/PBSCT for children with advanced stages of NB and RMS.

Key words--- PBSCT; children; neuroblastoma; rhabdomyosarcoma; complete remission

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Address for reprints: Masue Imaizumi, M.D., Department of Pediatric Hematology and Oncology, Tohoku University School of Medicine, 1-1 Seiryomachi, Aoba-ku, Sendai 980-8574, Japan.
e-mail: mimaizumi@ped.med.tohoku.ac.jp

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Electromyographic Study of the Elbow Flexors and Extensors in a Motion of Forearm Pronation/Supination while Maintaining Elbow Flexion in Humans

AKIRA NAITO, YING-JIE SUN, MICHIHIRO YAJIMA,1 HIDEHIKO FUKAMACHI1 and KOJI USHIKOSHI2

Department of Anatomy, Shinshu University School of Medicine, Matsumoto 390-8621, 1Kosei-Ren Kakeyu-Misayama Hospital, Maruko 386-0322, and 2Aizawa Hospital, Matsumoto 390-8510

Activities of the elbow flexors (biceps brachii, BB; brachialis, B; brachioradialis, BR) and extensors (triceps brachii, TB) in a motion of forearm pronation/supination with maintenance of elbow flexion (PS-movement) in nine healthy human subjects were studied by electromyography (EMG). The subject performed the PS-movement slowly or quickly with or without a load extending the elbow. In the slow PS-movement, an increase and decrease of EMG activities during supination and pronation, respectively, were seen in BB and the reverse was in B. A clear increment of EMG activities in BB accompanied with a reduction of EMG activities in B and/or BR, and the reverse were often observed. The contraction level and gain with the forearm supine were higher and larger than those with the forearm prone, respectively, in BB and the reverse was in B and BR. In a series of the quick PS-movement, alternating increases of EMG activities between BB and the other flexors (B and BR) were seen. Since TB showed no EMG activities throughout the experiment, it is suggested that reciprocal contractions between BB and the other flexors, which produce a complementary force in flexion direction, enable motions of pronation/supination with maintenance of flexion. Contraction properties of the flexors were discussed.

Key words--- electromyography (EMG); humans; elbow flexors and extensors; pronation/supination; reciprocal contraction

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Present address for Akira Naito, Department of Anatomy, Yamagata University School of Medicine, 2-2-2 Iida-Nishi, Yamagata 990-9585, Japan.
For reprints request to A. Naito at the address above.
e-mail: anaitoh@med.id.yamagata-u.ac.jp

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Erythroid Accelerating Factor Detected in Serum from Rats with Drug Induced Hemolysis

Mikio Kasai, Masaru Yokoyama, Tsutomu Toki, Hidekazu Maruyama, Kei Satoh¹ and Etsuro Itoh

Department of Pediatrics, Hirosaki University School of Medicine, and ¹Department of Pathological Physiology, Institute of Neurological Disease, Hirosaki University School of Medicine, Hirosaki 036-8562

We have previously observed that an erythroid enhancing activity presents in rat serum in the early stage of drug induced hemolytic anemia. The further studies on biological and physicochemical aspects of this erythroid accelerating factor (EAF) is described in this paper. Hemolytic anemia was induced in rats by single intraperitoneal injection of acetylphenylhydrazine (APH) and serum was obtained from the rats on day 1 after APH injection. It was first fractionated by ultrafiltration on Amicon Diaflo membranes to give a series of fractions lying in the following ranges of molecular weight: 10-30 kDa, 30-50 kDa, 50-100 kDa, and >100 kDa. Among those fractions, largest increase in the number of colony forming unit erythroid (CFU-E) colonies was shown in the fraction of >100 kDa that was subsequently fractionated by fast protein liquid chromatography (FPLC) system. EAF activity for CFU-E proliferation was detected in a FPLC fraction corresponding to a molecular weight of about 160 kDa. An addition of EAF significantly increased with dose dependent manner in the number of CFU-E colonies from rat bone marrow mononuclear cells. EAF alone had no burst promoting activity and exhibited no distinct activity to proliferate burst forming unit-erythroid even when interleukin-3 (IL-3) and high concentration (2 U/ml) of erythropoietin (Epo) were added together to the culture. The stimulating effect of EAF on CFU-E was markedly dependent on the presence of adherent cells in the culture. Partially purified protein was relatively heat-unstable (60% at 75°C, 30 minutes) and sensitive to treatment with trypsin and alpha-galactosidase. These results suggest that EAF is a novel factor, possible glycoprotein to reinforce Epo function and is different from various cytokines previously documented because of differences of approximate molecular weight.

Key words--- serum effects on erythropoiesis; erythroid accelerating factor (EAF); drug induced hemolytic anemia in rats
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Address for reprints: Masaru Yokoyama, M.D., Department of Pediatrics, Hirosaki University School of Medicine, 5 Zaifucho, Hirosaki 036-8562, Japan.

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Prognosis of Accidental Low Back Pain at Work

SATOSHI SHINOHARA, MITSUSHI OKADA, TOHRU KEIRA, MAKIKO OHWADA, MASATO NIITSUYA and YOSHIHARU AIZAWA

Department of Preventive Medicine and Public Health, Kitasato University School of Medicine, Kanagawa 228-8555

Accidental low back pain at the workplace was classified into two groups: 177 cases of the organic type and 176 cases of the non-specific type. Concerning the recuperation period, the length of leave, and the amount of compensation for recuperation, medical cost and leave of absence, a comparison was made between two groups. Regarding age, sex, and the type of work, no difference was found between the organic and the non-specific groups. However, the non-specific group showed lower values than the organic one for the duration of recuperation and leave and the amount of compensation for medical cost and leave of absence. Multiple regression analysis showed that the difference in the type of low back pain had more influence on the duration and cost than that in sex and age. The prognosis of non-specific low back pain is better than that of organic one in terms of cost and duration.

Key words--- low back pain; amount of compensation; cost analysis; duration of recuperation; medical cost
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Address for reprints: Satoshi Shinohara, M.D., Department of Preventive Medicine and Public Health, Kitasato University School of Medicine, 1-15-1 Sagamihara, Kanagawa 228-8555, Japan.
e-mail: aizawa@kitasato-u.ac.jp

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Serological and Histological Features of Anti-HCV-Positive Individuals without Serum HCV RNA

ATSUSHI KANNO, MIKI YAMADA, KAZUHIRO MURAKAMI¹ and NOBORU NUMATA²

Department of Internal Medicine and ¹Department of Pathology, Tohoku Koseinenkin Hospital, and ²Department of Microbiology, Sendai Municipal Institute of Public Health, Sendai 983-8512

Antibody to hepatitis C virus (anti-HCV) in patients who are negative for HCV RNA in serum may indicate a memory of past infection of HCV. However, their clinical features have not been well understood. Fourteen anti-HCV-positive but HCV RNA-negative individuals were examined for serological and histological features. As a result, it was found that they had only antibody to HCV core antigen C22-3 with or without antibody to nonstructural viral antigen C33c on a recombinant immunoblot assay (RIBA), and that an concentration of anti-C22 was low. Liver biopsy showed two having no evidence of an obvious hepatic injury, two having a minimal change, and two having portal fibrosis. HCV RNA was not found in the liver. These results corroborate an idea that the anti-HCV in HCV RNA-negative individuals implies a past infection of HCV. Furthermore, it is suggested that a combination of an appearance pattern of antibody to HCV antigens on RIBA and anti-C22 titer are an useful marker to distinguish anti-HCV-positive individuals without viremia from those with viremia.

Key words--- anti-HCV; HCV RNA; RIBA; anti-C22

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Address for reprints: Atsushi Kanno, M.D., Department of Internal Medicine, Tohoku Koseinenkin Hospital, 12-1 Fukumuro 1-cho-me, Miyagino-ku, Sendai 983-8512, Japan.

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Modulating Activity of Indomethacin to Vincristine Cytotoxicity in Various Human Carcinoma Cells

SHUNSUKE KOBAYASHI, SHINICHIRO OKADA, TORU HASUMI, NOBUYUKI SATO and SHIGEFUMI FUJIMURA

Department of Thoracic Surgery, Institute of Development, Aging and Cancer, Tohoku University, Sendai 980-8575

The modulating activity of indomethacin to vincristine (VCR) was investigated in thirty human pulmonary carcinoma cell lines (adenocarcinoma 9, large cell carcinoma 9, squamous cell carcinoma 6, small cell carcinoma 6) and five other cell lines (colon carcinoma 2, melanoma 1, teratocarcinoma 1, thymoma 1). The survival of these cell lines treated with VCR with or without indomethacin (2 μg/ml) for 72 hours were examined using MTT assay, and IC\textsubscript{50} Values were calculated. When the cutoff level of potent combined effect in clinical use was set at 2-fold increase of sensitivity, the positive rate was 100% for adenocarcinomas and large cell carcinomas, 25% for squamous cell carcinomas, 33% for small cell carcinomas. Mean modulating index was 2.91 in adenocarcinomas, 1.92 in squamous cell carcinomas, 3.06 in large cell carcinomas and 1.67 in small cell carcinomas. Of the cell lines of other tumors, three cell lines (colon carcinoma 1, melanoma 1, teratocarcinoma 1) showed the potent combined effect of VCR and indomethacin, while indomethacin was not effective in modulating activity to VCR in a thymoma cell line and fibroblast cells. In conclusion, it is considered that modulating activity of indomethacin for VCR is a general effect for various human cancer cells, and combined use with VCR and indomethacin may be a useful modulation therapy for the advanced lung cancer.

Key words--- indomethacin; modulator; vincristine; cell line; pulmonary carcinoma

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Address for reprints: Shunsuke Kobayashi, M.D., Department of Thoracic Surgery, Institute of Development, Aging and Cancer, Tohoku University, 4-1 Seiryomachi, Aoba-ku, Sendai 980-8575, Japan. e-mail: kobayashi-tu@mve.biglobe.ne.jp

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Quantitative Analysis of Hepatitis B Virus Precore Mutant in Hepatitis Type B

TAKESHIICHIKAWA, HITOSHI TAKAGI, MORITOSHI KINOSHITA, RYUYA SHIMODA, TAKEAKI NAGAMINE and MASATOMOMORI

The First Department of Internal Medicine, Gunma University School of Medicine, Gunma 371-8511, IDiagnostic Research Institute, Otsuka Pharmaceutical Co., Ltd., Tokushima 771-0132

Active liver disease has been detected in chronic hepatitis B after seroconversion from positive HBe antigen to positive anti-HBe antibody. Active replication of HB virus (HBV) containing a precore stop-codon mutation has been implicated in this condition. The usual methods, such as direct sequencing, to characterize the responsible mutant of HBV are not suitable for routine clinical use. Here we employed the competitive mutation site specific assay (CMSSA) to detect precore mutant HBV-DNA in patients with positive HB surface antigen. In patients with HBe antigen, precore mutant HBV-DNA was significantly higher than in patients with HBe antibody. The level of precore mutant HBV-DNA in patients with elevated serum ALT was significantly higher than in patients with normal serum ALT. Sex, age and the level of serum HBV-associated DNA polymerase levels were not correlated with levels of precore mutant HBV-DNA. Ten of 11 negative patients for the precore mutant by polymerase chain reaction followed by restriction fragment length polymorphism assay (PCR-RFLP) were positive for the precore mutant by CMSSA. These results suggest that the precore mutant has already emerged in the HBeAg-positive phase as determined by CMSSA, which is more sensitive than PCR-RFLP and is useful for evaluating the clinical course of patients with chronic hepatitis B.

Key words--- hepatitis B virus; precore mutant; competitive mutation site specific assay

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Address for reprints: Takeshi Ichikawa, M.D., The First Department of Internal Medicine, Gunma University School of Medicine, 3-39 Showamachi, Maebashi, Gunma 371-8511, Japan.
e-mail: htakagi@sb.gunma-u.ac.jp

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