intended to study the monitoring of heavy metals(Cd, Pb, Hg), endocrine disruptors, in korean people with study of 104 korean normal adults and 47 placentas.
This showed that the concentration of Cd was arithmetic mean 1.44±0.65㎍/L, that of Pb was arithmetic mean 31.70±14.12㎍/L and that of Hg was arithmetic mean 6.30±3.08㎍/L in blood, the concentration of Cd was arithmetic mean 1.53±1.04㎍/L, that of Pb was arithmetic mean 18.96±7.35㎍/L and that of Hg was arithmetic mean 2.72±3.16㎍/L in urine and the concentration of Cd was arithmetic mean 94.45±33.69ng/g, that of Pb is arithmetic mean 92.63±24.44ng/g and that of Hg is arithmetic mean 43.24±30.78ng/g in dried placentas.
From these results, the concentrations of Pb and Hg in blood were higher than in urine and the concentration of Cd in blood accords with that of Cd in urine.
The concentrations of Cd, Pb and Hg in blood and urine were within the reference ranges of American and Japanese clinical laboratories.
Comparing the relative concentration ratio of Cd to Pb in blood and urine with that of Cd to Pb in placenta was relatively much higher than in blood and urine. It suggested that the placenta acted as a barrier to Cd.

[PB1-1] [ 04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3] ]

## Involvement of cyclic nucleotide pathway in regulation of gastric motility by ethanol

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To investigate underlying mechanism of ethanol in gastric smooth muscle relaxation, we examined the effect of ethanol on gastric motility and cyclic nucleotide pathway. Ethanol dose-dependently inhibited amplitude and frequency of spontaneous phasic contraction of cat gastric smooth muscle, whereas elicited tonic contraction at concentrations of more than 0.5%. Both spontaneous phasic contraction and 2% ethanol-induced tonic contraction were significantly inhibited by forskolin and sodium nitroprusside. Ethanol dose-dependently inhibited basal cyclic AMP levels and forskolin-induced cyclic AMP formation. On the other hand, ethanol significantly increased the basal cyclic GMP levels and sodium nitroprusside-induced cyclic GMP formation at low concentrations of less than 0.25%. However, ethanol at concentrations of more than 1% significantly inhibited sodium nitroprusside-induced cyclic GMP levels. These results suggest that regulation of gastric motility by ethanol is in part mediated via cyclic nucleotide pathway.

[PB1-2] [ 04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3] ]

## Role of cyclooxygenase-2 in chloroquine-induced apoptosis in A172 human glioblastoma cells

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Role of cyclooxygenase-2 in chloroquine-induced apoptosis in A172 human glioblastoma cells

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Chloroquine, widely used for the treatment of malaria as well as a variety of inflammatory diseases including rheumatoid arthritis, has been reported to induce neuromuscular complications. However, little information is available regarding the mechanism of chloroquine toxicity on the nervous system We have examined the in vitro effects of chloroquine on DNA fragmentation, lipid peroxidation,

cytochrome C reduction, the expression of cyclooxygenase (COX) in A172 human glioblastoma cells, a cellular model of neuronal system. Chloroquine induced apoptosis of the cells in a time- and concentration-dependent manner. Treatment with chloroquine significantly suppressed lipid peroxidation in the cells. In addition, chloroquine significantly enhanced the expression of COX-2 assed by western blot analysis.

[PB1-3] [ 04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3] ]

## Expression of HIF-1 inducible genes in the aged rat brain

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Hypoxia-reperfusion generates reactive oxygen species (ROS). Some ROS have been suggested to play important roles as a second messenger in normal and diseases conditions. Recent findings on hypoxia established the induction of a DNA binding protein synthesis called hypoxia inducible factor-1 (HIF-1), which promotes transcription of multiple genes. HIF-1 plays a major role in adaptive responses essential to hypoxia as the case in angiogenesis to maintain O2 homeostasis. HIF-1 has also been shown to activate transcription of genes encoding inducible nitric oxide synthase (iNOS) and heme oxygenase 1 (HO-1) which are important for the regulation of cerebral blood flow by synthesizing NO and CO, respectively. At present, it is no information on the HIF-1 inducible genes expression and DNA binding activity in aged tissues. We investigated expression of HIF-1 inducible genes in brain isolated from Fischer 344 rats at 6, 12, 18, and 24 months of age. We quantified the age-related changes in four genes, vascular endothelial growth factor (VEGF), HO-1, iNOS, and HIF-1? in rat whole brain. Quantitation of DNA binding activity was carried out by EMSA. Results showed that the protein levels of VEGF, HO-1, iNOS, and HIF-1? were increased with age. These changes are attributed to the age-related increase in HIF-1 DNA binding activity. Significances of our findings are the hypoxic induction of HIF-1 inducible genes may be critical factors in the maintenance of cerebral O2 homeostasis and angiogenesis during aging. Our results warrant further investigation on molecular mechanisms underpinning cerebral blood circulation under hypoxic conditions occurring during aging.

[PB1-4] [ 04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3] ]

## Effect of phospholipase A2 inhibitor on ATP-induced histamine release in rat peritoneal mast cells

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To investigate whether phospholipase A2 pathway is involved in histamine release of rat peritoneal mast cells, we measured ATP-induced histamine release in the presence of various enzyme inhibitors that involved in eicosanoid pathway, such as phospholipase A2, cyclooxygenase and lipoxygenase. ATP dose-dependently increased histamine release at a concentration of up to 100 μM but gradually decreased at concentrations of more than 100 μM. P2-purinergic receptor antagonists significantly inhibited ATP-induced histamine release but adenosine (P1-purinergic) receptor antagonists did not. Also adenosine did not cause histamine release from rat peritoneal mast cells. Phospholipase A2 inhibitors, manoalide and OPC, significantly inhibited ATP-induced histamine release. Cyclooxygenase inhibitors, ibuprofen and indomethacin, significantly inhibited ATP-induced histamine release and lipoxygenase inhibitors, baicalein and caffeic acid, also significantly inhibited. From the above results, it is suggested that ATP-induced histamine release is mediated via purinergic receptor, in which all enzymes of phospholipase A2, cyclooxygenase and lipoxygenase are involved.