such as blackfoot disease, atherosclerosis and hypertension, but the exact mechanism has not been elucidated yet. In order to investigate one of the possible causes toward cardiovascular disease by arsenic, we examined the effects of arsenic on platelets which play an important role in development of cardiovascular disease. Addition of sodium arsenite (AsIII), trivalent inorganic arsenic, to rat platelets did not induce either aggregation or cytotoxicity to platelets directly, whereas AsIII treatment potentiated platelet aggregations induced by various agonists, such as thrombin, collagen, ADP and arachidonic acid in concentration- and time-dependent manners. Thrombin-induced platelet aggregation was also enhanced by relatively higher concentration of sodium arsenate (AsV) or monomethylarsonic acid (MMA) compared to AsIII. Treatment with AsIII resulted in a dose-dependent elevation of thrombin-induced serotonin levels from platelets, while the formation of thromboxane A2 from platelets did not altered significantly. Consistent with these findings, the in vivo studies revealed that ingestion of drinking water containing AsIII in mouse increased blood serotonin levels significantly, which is indicative of platelet aggregation in vivo. These results suggest that AsIII exposure makes platelets more susceptible to agonist-induced aggregation mediated through serotonin secretion from platelets and thus these effects by AsIII may contribute to the pathogenesis of cardiovascular disease.

[PA4-16] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Studies on DNA damage by single cell gel electrophoresis and endocrine disrupting activity by transcriptional assay of dibutyl phthalate

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A wide range of phthalates have been produced for use as plasticizers and softeners in many synthetic products. Among phthalate esters, Di-n-butyl-phthalate (DBP) may act as xenoestrogens or antiandrogens. Also, DBP was reported to be genotoxic on human mucosa. To elucidate the relationship between endocrine disrupting activity and DNA damage of phthalate esters, DBP was studied by yeast-based steroid hormone receptor gene transcription assay and single cell gel electrophoresis. We have used a yeast-based assay to assess the interactions of DBP with the estrogen, androgen, and progesterone receptors. DBP ranging from 10^{-16} to 10^{-11} M was active in the estrogen receptor assay, but it did not show the effect on β-galactosidase activity in the progesterone and the androgen receptor assays. Also, to determine whether DBP induces DNA strand breakage, single cell gel electrophoresis (comet assay) was performed using mouse lymphoma L5178Y cell lines. The induction of strand breaks by DBP was not significantly different from control. In these assays, we found that DBP does not induce DNA single strand breakage in the single cell gel electrophoresis and DBP has estrogenic activity in the gene transcription assay of yeast-based steroid hormone receptor.

[PA4-17] [10/19/2000 (Thr) 10:00 - 11:00 / [Hall B]]

Establishment of assay to screen estrogenic activity of chemicals

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To establish the rapid and easy-to-perform methods to screen estrogenic activity of many compounds, we determined 5'-ERE-regulated transactivation and cell proliferation in MCF-7 cells by luciferase assay and SRB assay, respectively. MCF-7 stable cells which are stably transfected with phERE-Luc were treated with many chemicals and then luciferase activity were determined. Estradiol (E2) and synthetic estrogen, diethylstylbesterol (DES) were induced luciferase activity in