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278 Interindividual Variation in Cytogenetic Adaptive Response of Cultured Human Lymphocytes to Mitomycin C, Bleomycin, Co^{60} γ-rays, Quinacrine and Hyperthermia.

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Background: Adaptive response (AR) is a phenomenon by which cells exposed to low non-cytotoxic doses of a genotoxicant become significantly resistant to a subsequent higher dose of the same or another genotoxicant. The present work contains cytogenetic data on the AR induced by 2 antineoplastic agents mitomycin C (MMC), bleomycin (BLM), BLM induced cross resistance to Co^{60} γ-rays (Cγ), hyperthermia (HT) induced AR to these antitumour agents, and quinacrine dihydrochloride (QDH) which acts by an S-independent mechanism, like ionizing radiation, examined under different time schedules as well as comparisons between the donors and between the schemes. If treatment with antineoplastic drugs is pursued for long periods, depending on the doses employed, the AR of the cells and tissues involved may not be excluded. This might modify the efficacy of the treatment. **Methods:** The AR, if any, induced in human lymphocytes in vitro was analysed, 1) in 6 donors by an adaptive dose (AD) of MMC 0.001 µg / ml or BLM 0.001 units / ml, at 26 h, subsequent exposure to challenge dose (CD) of MMC 0.1 µg / ml or BLM 0.01 units / ml at 48 h, using 3 different cytogenetic endpoints (sister chromaid exchanges - SCEs and micronuclei – MN for MMC, chromosome aberrations - CA and MN for BLM); 2) in 2 donors after an AD of BLM at 48 h and CD at 69 h; 3) in 2 donors by an AD of BLM at 24 h and CD of 1 Gy Cγ or BLM at 48 h on CA and MN; 4) in 2 donors HT pretreatment at 26 h (41^0C, 1 h) and CD of BLM or MMC at 48 h on MN frequencies; 5) in 3 donors by an AD of QDH 0.006 µg / ml at 24 or 48 h followed by CD of 0.6 µg / ml at 48 or 69h on CA and MN. **Results:** AD of BLM or MMC caused an inhibition of 30-67, 46-58 % in CA, MN and 25-36, 52-62 % in SCE and MN frequencies respectively, induced by CD. Interindividual variability in AR was evident. The AD of BLM at G_2 caused 55-57, 76-84 % decrease in CA and MN frequencies. BLM showed 55-59, 62-63 % decrease in CA, MN frequencies and 42 % increase in acentric fragments in one donor, induced by CD of Cγ. HT caused 50-66, 53-54 % decrease in MN frequencies induced by MMC and BLM respectively. AR was not detected in 2 donors with QDH. Third donor showed 20 % inhibition in MN frequencies under the 24-48 h time scheme. Increased Proliferative rate index (PRI) and Nuclear division index (NDI) values indicated reversal of cell division delays caused by CD of MMC, BLM and Cγ. **Conclusions:** 1) Significant difference between the protective effects induced by BLM and MMC in the lymphocytes of the same donors was noticed. 2) The BLM AD delivered at G_2 stage resulted in statistically significant AR. 3) Lymphocytes adapted to BLM and HT showed cross resistance to the induction of chromosome damage by Cγ and induction of MN by BLM and MMC respectively. 4) With respect to the AR cytogenetic data, contradictions pertain to the biomarkers which can be affected by AD, time schedules of AD and CD and the extent of individual variability in AR expression to different genotoxicants. The role of DNA glycosylase, alkyltransferase, BLM hydrolase and DNA repair enzymes in the resistance and cross resistance observed in human lymphocytes needs to be elucidated.

279 Atypical Features of Leptospirosis – A Study at Pondicherry, India.

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Background: Typical presentation of leptospirosis is that of Weil's disease caused by *Leptospira icterohemorrhagiae*, where the patient has high fever with jaundice with conjunctival and other mucosal hemorrhage and renal failure, *and multiorgan failure in severe cases*. **Methods:** Thirty three patients admitted with acute febrile jaundice in our hospital from July, 1999 to May, 2002 were diagnosed to have leptospirosis by IgM ELISA method. Clinical and laboratory parameters were observed in these patients for atypical features. **Results:** One patient developed aphemia late during the course of illness. Aphemia is an articulation defect which is seen in strokes of left cerebral artery origin. Aphemia as a late complication of leptospirosis has not been described before. Hemiplegia with anisocoria was seen one patient. Platelet count was normal in this patient. This patient developed Cheyne Stoke respiration and expired. These phenomena might have been due to vasculitis in the cerebral circulation. Subarachnoid hemorrhage was seen in one patient. This patient also had other bleeding manifestations. Out of two patients with massive pleural effusion, one patient had frank pus in the pleural fluid (empyema), this has not been documented before. Coomb's positive hemolytic anemia was seen in one patient. Antinuclear antibodies were not detected in this patient. Patient recovered once the acute febrile illness subsided. This has been described in leptospira infection in animal (rhinoceros), but not in human being. Pancytopenia was observed in two patients. Two patients developed transient leucopenia which subsided with clinical recovery. Disseminated intravascular coagulopathy was observed in one patient. Ultrasonogram of abdomen done in 12 patients with severe leptospirosis revealed shrunken liver in two patients. Widal test was found positive in three patients, which could have been due to anamnestic reaction; however two patients had very high O & H titres suggesting true salmonella infection along with leptospirosis.