Introduction
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Chromium is one of the naturally occurring heavy metal found in environment in many forms, the commonest stable oxidation states being trivalent (Cr III) and hexavalent (Cr VI). Cr(VI) compounds have been declared as a potent occupational carcinogen by IARC (1990) through epidemiological studies among workers in chrome plating, stainless-steel, and pigment industries. The major non-occupational source of chromium for humans is food such as vegetables, meat etc. (Hertel, 1986). Other potential non-occupational sources include urban air, hip or knee prostheses and cigarettes (U.S. EPA 1984). The reduction of Cr(VI) to Cr(III) results in the formation of reactive intermediates that contribute to the cytotoxicity, genotoxicity, and carcinogenicity of Cr(VI)-containing compounds.

Chromium enters the body through the lungs, gastro-intestinal tract, and to a lower extent through skin (Hamilton and Wetterhahn, 1988). Inhalation is the most important route for occupational exposure, whereas non-occupational exposure occurs via ingestion of chromium containing food and water (Langard, 1982; Hertel, 1986). Most of the chromium absorbed by the body is distributed in the lungs, liver, kidneys, RBC, plasma, spleen and bone marrow (Langard, 1982). Cr (VI) enters into the cells through membrane anionic transporters while Cr (III) does not. Intracellular Cr (VI) is metabolically reduced to the ultimate Cr (III). It is therefore in the interest of the body to reduce the toxic Cr (VI) to less toxic form, the Cr (III).

Dengue is a mosquito-borne virus infection which is found in tropical and sub-tropical regions around the world, predominantly in urban and semi-urban and now in rural areas also. The virus produces a benign self-limiting illness, the dengue fever (DF) or a life-threatening serious illness, the dengue haemorrhagic fever (DHF). The prevalence of dengue has grown dramatically in recent decades. The disease is now endemic in more than 100 countries.
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Some 2500 million people – two fifths of the world's population – are now at risk from dengue. WHO currently estimates there may be 50 million cases of dengue infection worldwide every year. An estimated 500 000 cases of DHF require hospitalization each year, of whom a very large proportion are children (Halstead, 2002; Agarwal et al., 1999). Dengue is endemic in India with frequent epidemics of DF and DHF.

Viral virulence and immune responses have been considered as two major factors responsible for the pathogenesis of DHF. The immunopathological mechanisms appear to include a complex series of immune responses. A rapid increase in the levels of cytokines and chemical mediators apparently plays a key role in inducing plasma leakage, shock and haemorrhagic manifestations (Chaturvedi et al., 1999a; 2000). Dengue continues to be a Global challenge because the pathogenesis of DHF is not fully understood.

The cells of the immune system form a strong line of defence against foreign substances. Following entry into body Cr (VI) reaches the cells of the immune system which try to eliminate it and in the process their functions may also be adversely affected.

Cr (VI) is highly toxic to all forms of living organisms and is mutagenic in bacteria (Losi et al., 1994). The presence of chromate in the environment inhibits most microorganisms but also promotes the selection of resistant bacteria. The processes by which the microorganisms interact with the toxic metals enabling their removal/and recovery are biosorption, bioaccumulation and enzymatic reduction. Microorganisms have evolved resistance mechanism to select resistant variants to deal with metal toxicity as the result of exposure to metal contaminated environments. The commonest route of entry of chromium is through drinking water and food. Intestines have a huge population of bacteria and the caecum harbours the largest number (Siman and Gorbach, 1986). Further, some of the bacteria bioaccumulate large quantity of
Cr and bring down the residual concentration of Cr (VI) in 24 h (Srinath et al., 2002). Thus, bacteria may play an important role in protecting body from the toxicity of ingested chromium. The resident bacterial flora of the gastrointestinal tract is exposed to Cr through ingestion but the literature on the effect of Cr on resident gut microflora is scarce (Francisco et al., 2002; Viti et al., 2003). It was, therefore, considered important to investigate the effect of chronic ingestion of chromium on the resident gut microflora of Wistar rats.

**Aims and Objectives of the study:**

Dengue is endemic all over India so is the occupational and non-occupational exposure to hexavalent chromium. The pathogenesis of dengue depends upon the immune response of the body. The intermediary products generated during reduction of chromium (VI) kill the target cells including leucocytes by apoptosis. This effect of chromium compromises the immune response of the host. It is, therefore, possible that the chromium toxicity may affect the disease process during dengue virus infection. There are no reports in literature on the outcome of dengue virus infections during chromium toxicity, therefore, the present study was undertaken.

**Questions that have been addressed are:**

1. What are the effects of subtoxic dose of Cr (VI) on the peripheral blood cells of mice during dengue virus infection?

2. Does Cr (VI) toxicity enhance the ill effects of dengue virus on macrophage functions and proliferative responses of lymphocytes?

3. Can the cells of immune system detoxify Cr (VI)?

4. Can the intestinal cells and the gut microflora help in detoxifying the ingested Cr(VI).
In the present study an attempt has been made to answer the above question using mice (which has been used most for dengue virus studies) and rats (used extensively for Cr (VI) studies). This may lead to better understanding of Cr (VI) toxicity and dengue virus infection.