CHEMISTS AND CARCINOGENS -- EXOGENOUS AND ENDOGENOUS

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Reports from several countries indicate that chemists have an increased risk of developing neoplasms of the pancreas or lymphatic system. Laboratory chemists are usually exposed to small amounts of numerous substances, a condition which obscures pinpointing the compounds responsible. However, epidemiologic studies on production workers in chemical, mining, and allied industries have indicated that approximately 30 compounds or processes are carcinogenic in humans. The great majority of these 30 compounds are metabolized in the body by enzymes of the P-450 system to activated electrophilic forms which in turn react with cellular nucleophiles such as proteins, DNA, RNA, lipids, or other constituents. During the process of carcinogenesis, there may be substantial changes in P-450 levels, as well as in components of the P-450 system such as phospholipids. Control of cholesterol synthesis may also be diminished, leading to an increase in bile acid production, which in turn may enhance the action of exogenous carcinogens. The current investigation showed that feeding the nephrotoxic hepatocarcinogen 2-aminoanthraquinone to rats led to increases in cholesterol and triglyceride levels in liver, kidney and plasma of male rats. Female rats showed a similar trend, except for kidney values. In both sexes total and individual phospholipid levels of hepatic mitochondrial and microsomal fractions increased. In males total and individual phospholipids, namely phosphatidyl ethanolamine and

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phosphatidyl choline, of kidney mitochondrial and microsomal fractions increased. In females, which are more susceptible to the nephrotoxic effect, the total and individual phospholipid values tended to decrease. N-Butyl nitrosourea, a carcinogen with markedly different structure, causes intestinal tumors in mice. However, it also led to increases in cholesterol and triglycerides of liver, kidney, spleen and plasma from male mice. Total phospholipids and the individual phospholipids increased, as did total microsomal and mitochondrial phospholipids of liver and kidney. Thus, despite their variant sites of action, the two carcinogens had a similar effect on triglyceride, cholesterol and phospholipid levels.

INTRODUCTION

In 1969 there was an initial report of a higher than expected incidence of malignant neoplasms of the pancreas and lymphatic system among chemists, members of the American Chemical Society.\textsuperscript{1} Within the past several years there have been confirmatory reports from Sweden\textsuperscript{2} and Great Britain,\textsuperscript{3} all serving as warning signals to chemists to evaluate carefully their working habits and possible exposure to toxic materials. The identification of the responsible substances is complicated since laboratory chemists usually work with numerous compounds in the course of a day.

However, production workers in chemical and allied industries are more likely to be exposed to larger total amounts of single chemicals, as are persons using certain drugs on a chronic basis. These populations are more suitable for epidemiological studies which evaluate on a retrospective basis the possible long-term toxic effects of such exposures. Such endeavors have shown that approximately 30 substances or processes are associated with a carcinogenic effect in humans (Tables I & II). Most, but not all, of these substances also are carcinogenic in properly conducted animal tests.\textsuperscript{4} Nevertheless, occupational carcinogenesis due to exposure to chemicals is not a recent development. Highly publicized is the fact that in 1775 Sir Percivall Pott ascribed scrotal cancer in chimney sweeps to their occupational exposure to soot. However, in 1700 Bernardino Ramazzini, the author of "De Morbis Artificium" attributed the high incidence of breast cancer in nuns to their celibate life, inherent to their occupation. Current epidemiological studies concur in the higher risk of this cancer among nuns.\textsuperscript{5} Moreover in 1531 Paracelsus and later Agricola described a disease among miners in the Schneeberg region of Germany. The ailment, thought to be tuberculosis of the lung, was later recognized as carcinoma of the lung.\textsuperscript{6} Bladder cancers due to exposure to aromatic