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Decades have gone by, still millions are engulfed by deadly tentacles of the cancer. Research and experiments are in progress to limit the genetic change whether spontaneous, or induced by chemicals or viruses that converts a normal cell to an invasive malignant cell. Chemotherapy is one important mode in cancer cure. Antibiotics like actinomycins (dactinomycin), bleomycin, daunorubicin (rubidomycin) and doxorubicin (adriamycin) have justified their use as important anti cancer agents.

Anthracycline antibiotics, is an effective group of chemotherapeutic agents for use against a wide range of solid and haematological malignancies.

Grein et al (1963) isolated an antibiotic from cultures of a mutant streptomyces pencetuis (Streptomyces perctius varcaesive) which was named adriamycin. Its structural formulae is very similar to that of daunomycin from which it differs only in the substitution of a hydrogen atom with a hydroxyl group on the acetyl radical.
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In acid media adriamycin is split into two components, a red pigmented water insoluble aglycone (adriamycinone), and a water soluble base reducing amino sugar (daunosamine). Adriamycin belongs to the anthracycline group, as do daunomycin and rubidomycin (daunorubicin).

The preliminary pharmacological studies were carried out by Di Marco et al (1969) at the National Cancer Institute Milan. Comparative studies showed that at equitoxic dose (2 and 2.5 mg) of adriamycin per Kg and 2.6 - 3.25 mg of daunomycin per Kg, the survival time in C 3H mice bearing lymphosarcoma was higher in animal given adriamycin, while the inhibition dose (ID 50) was found to be 1-5 and 3.3 mg/kg for adriamycin and daunomycin respectively. The conclusion from these preliminary pharmacological studies is that, adriamycin has a higher therapeutic index 1.25 than daunomycin (.67).

Doxorubicin is a principal agent in the treatment of Leukaemias, Hodgkin's and non-Hodgkin's lymphomas, osteogenic sarcoma, breast cancer, ovarian carcinoma, gastric cancer and oat cell carcinoma of the lung. In addition adriamycin has been shown to have some activity in almost all adult tumour types except melanoma, hypernephroma and colon cancer.
Di Marco et al (1965) have demonstrated that mitotic activity and thymidine incorporation are induced by anthracyclines and that RNA synthesis is inhibited. Subsequent studies have shown that both daunomycin and Adriamycin complex with nuclear DNA by intercalation between base pairs, thus causing steric obstruction to DNA-dependent RNA synthesis. These properties apparently explain the molecular basis of the in vitro and in vivo cytotoxic and antimitotic activity exhibited by these antitumour agents against neoplastic and other rapidly dividing cells.

Aside from its promising chemotherapeutic potential, Adriamycin have exhibited undesirable side effects which includes severe bone marrow suppression, alopecia, and oral ulcerations. The most unpredictable and unmanageable toxic manifestation, however, is an insidious cardiomyopathy affecting a variable but significant number of treated cancer patients.

There are two distinctly different types of cardiotoxicity associated with the use of Adriamycin. First, acute arrhythmias, non-specific ST-T wave changes, and even clinically inapparent decreases in left ventricular ejection fractions have been observed. These acute effects are always transient usually asymptomatic, and do require
modifications of the dose or schedule of administration rarely and that too mostly in patients with prior history of arrhythmias. The second and more serious cardiotoxicity, is the late cardiomyopathy clinically indistinguishable from idiopathic or nutritional cardiomyopathies. The congestive heart failure seen may be insidious in onset but frequently occurs abruptly as pulmonary edema precipitated by intravenous hydration associated with cancer therapy.

Heart failure usually develops within two months of the last dose of drug, but instances of cardiomyopathy developing six months to almost a year later have been reported.

Histologically the cardiac lesions induced by anthracyclines are not distinctly different from those associated with many other cardiomyopathies, but they can be readily distinguished from lesions resulting from radiotherapy or arterial occlusions. Initially the damage is focal and scattered throughout the heart. With larger doses of adriamycin, the heart is diffusely involved. The most frequent manifestations of anthracycline damage are myofibrillar lysis and cytoplasmic vacuolization. Fibrosis as typically seen after radiation damages occurs much less frequently, and there is no inflammatory response.
The pathophysiology of this cardiotoxicity is poorly understood. The hearts of rabbits treated with doxorubicin have abnormally high tissue levels of calcium and it has been proposed that adriamycin induced heart changes are due to a calcium mediated necrosis. However, attempts at preventing the cardiotoxicity using chelating agent in animal models have been unsuccessful. Adriamycin has a glycosidic structure and specifically inhibits sodium potassium activated Atpase. This suggests that the doxorubicin effect might occur at the same site as digitalis toxicity or that a common receptor for the anthracyclines and the cardiac glycoside might be necessary for uptake of these drugs into the heart. Currently available data suggests that strophanthin will not block doxorubicin uptake in animal models and there are insufficient data to justify clinical trials using pretreatment with digitalis compounds. In a recently reported study of Bristow et al (1978) on doxorubicin cardiotoxicity in rabbits, alongwith histamine and catecholamine blocking agents used together seemed to prevent the appearance of a cardiomyopathy. This suggests another possible mechanism that might explain both the acute and chronic effects of doxorubicin on the heart.
Folkers et al (1977) in their study concluded that doxorubicin also inhibits Co-Q10 (ubiquinone) enzyme systems in isolated mitochondria and the administration of ubiquinone to rabbits or rats has been found to at least partially block some of doxorubicin's cardiotoxicity. Henderson et al (1980) reported that doxorubicin cardiotoxicity, and possibly even the anthracycline antitumour effect is mediated either through the production of superoxides or by activation of the anthracyclines to a free radical state. It has also been reported by them that lipid peroxidation and histologic changes in murine heart muscle are prevented by pre treatment with alpha-tocopherol, another free radical scavanger.

The study is designed to evaluate the acute effects of the drug on rats heart that may be the first manifestation of a process that ultimately leads to myocyte damage and cardiomyopathy. It is possible that a complete characterization of this process will provide some clue to the pathogenesis, as well as providing a potential model for the evaluation of protective strategies.