SUMMARY AND CONCLUSION
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The anthracycline antibiotics are an effective group of chemotherapeutic agents for use against a wide range of solid and hematologic malignancies. Their use is limited, however, by cardiac toxicity. The precise mechanisms of cardiac toxicity have not yet been identified. Because the anthracyclines have multiple biologic effects including alterations of vasomotor tone and interactions with membrane lipids and with membrane and mitochondrial enzyme system, there are numerous potential mechanisms of damage. The emphasis of most clinical and experimental investigations of adriamycin cardiotoxicity has been the delayed dose dependent degenerative cardiomyopathy. An acute toxicity, however, manifested by fibrinous pericarditis left ventricular failure and arrhythmias has been described in some patients treated with anthracyclines and in animal models. The purpose of the present investigation was to study the acute effects of adriamycin on the heart of rats and to assess the probable mechanism leading to the cardiac injury.

The present work comprised of an experimental study of cardiotoxicity, using doxorubicin. The cardiac injury was produced by the intraperitoneal injections
of doxorubicin in various dosage schedules. The experiments were performed on 42 healthy Swiss albino rats. They were divided into 3 groups (A, B & C) of 12 animals each. 6 untreated animals served as healthy control. The salient features of this study are as follows:

GROUP 'A':

Group A animals were administered with single i.p.i. of 10 mg/kg of doxorubicin. In all the animals there were dilated and congested blood vessels few of them showing leakage and extravasation of blood. The vascular changes were more marked in the subepicardial zone. Out of eleven animals three showed papillary muscle involvement. Most of the animals (9/11) showed multiple small areas of haemorrhages while two rats sacrificed on day 1 and 7 respectively showed large areas of interstitial haemorrhage. Pericarditis and valvulitis with or without involvement of the valve ring was encountered in 7 out of 11 animals. The intensity of myocardial injury gradually increased as the animals sacrificed on day one, showed only cytoplasmic vacuolization whereas those sacrificed at day 3, 4, 7 had myofibre necrosis although the severity of cardiac injury regressed at day 14 after the administration of the drug however, occasional foci of myofibre necrosis were still seen in these animals.
GROUP 'B' :

Animals in this group received 5 mg/kg i.m.i. of doxorubicin for 2 consecutive days. In all the animals there were some dilated and congested blood vessels, few of them showed leakage with extravasation of blood, these vascular changes as in the previous group were more pronounced in the subepicardial zone. Out of 12 animals in this group 5 showed papillary muscle involvement. The extent of myofibre necrosis was reduced in animals sacrificed later but the extent of inflammatory reaction showed little change. Most of the animal (9/12) showed multiple small areas of interstitial haemorrhage while one rat sacrificed at day fourteen after the administration of the drug showed large areas of interstitial haemorrhage. Pericarditis and valvulitis was seen in ten out of twelve animals.

GROUP 'C' :

Animals in this group received doxorubicin in doses of 1 mg/kg i.p.i. for ten consecutive days. All the animals in this group showed mild degree of myofibre necrosis. Of the twelve animals four showed moderate degree of inflammatory reaction while eight showed mild inflammation. Pericarditis was seen in nine animals and valvulitis was observed
in most of the animals (11/12). Six animals showed papillary muscle involvement. Small and large foci of haemorrhage were seen as in previous groups. The blood vessels were dilated with or without congestion and rupture.

Contraction band necrosis was a frequent feature in the animals of group A, where (4/11) animals exhibited the contraction band necrosis. Only single animal in group B while none in group C showed contraction band necrosis. The injury score data reveals that the intensity of myocardial injury in group A and B was almost similar while group C animals had the most pronounced cardiac injury.

It is believed that doxorubicin causes direct endothelial damage with extravasation of blood; this leakage of the drug in the myocardium causing myofibre necrosis. The type of valvular damage, valve ring involvement, and lesions involving the papillary muscle shall help in assessment of possible relationship between structural damage and cardiac dysfunction which has a direct bearing in clinical assessment of patients on doxorubicin therapy.