to be reduced after reserpine treatment of the hypothalamic and sensory-nerve systems. The release of adrenaline by stimulation of the suprarenal medulla of cats, and of the vascular system of rat after adrenals are removed, affects the vascular response to peptides. 

MATERIALS AND METHODS

Healthy albino rabbits (1.2 to 1.5 kg) and mongrel puppies (2 to 3 kg) of either sex, anaesthetized with pentobarbitone sodium 35 mg/kg intraperitoneally, constituted the subject material for this study. Half an hr after the induction of anaesthesia, the ECG (standard leads I, II and III) of these animals were recorded and the effect of 0.5, 1, 2 and 4 U/kg of SLO* injected intravenously at 30 min intervals in rabbits and similarly of 0.5 to 8 U/kg of SLO in puppies, on their ECG was measured.
studied. Three animals of each species were used for each dose of SLO. In order to investigate whether pretreatment of animals with antistreptolysis 'O' (ASO)* could protect them against the cardiotoxic and lethal effects of SLO, the effect of challenging doses of SLO (4 to 10 U/kg i.v.) on ECG in 8 rabbits pretreated with ASO (4 IU/kg intraperitoneally), has also been studied.

RESULTS

ECG changes in Puppies: The effect of SLO on ECG in puppies is shown in Fig. 1. The initial heart rate was 240 to 360/min (mean 290±1.6 SE, n= 12). The intravenous administration of small doses of SLO (0.5 to 4 U/kg) immediately produced a reduction of 26 to 48 percent in the heart rate, which was dose dependent (Fig. 2); this effect persisted for 3 to 5 min only. In higher doses (8 U/kg) SLO instantaneously caused marked sinus bradycardia (percent mean reduction in heart rate 78±4.7 SE), soon followed by nodal rhythm and intraventricular conduction defects terminating in cardiac standstill 5 to 7 min after the injection.

ECG changes in rabbits: The initial heart rate in rabbits was 310 to 400/min (mean 360±1.2 SE, n= 20). Intravenous administration of 0.5 to 2 U/kg of SLO immediately caused a mean (SE) reduction of 32 to 80 percent in the heart rate, which was dose dependent (Fig 2); it persisted for 5 to 7 min followed by complete recovery. In all the animals a dose of 4 U/kg of SLO instantaneously caused intense sinus bradycardia (percent mean reduction in heart rate 91±4.8 SE) and ST elevation, followed by progressively increasing intraventricular blocks and reduction in voltage.

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*ASO per intraperitoneally

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Fig. 1: ECG (lead I) changes in a puppy after i.v. injection of SLO. The initial heart rate was 300/min (A). Sinus bradycardia at 30 sec after 0.5 U/kg SLO (B), 30 sec and 2 min after 2 U/kg SLO (C and D) and 3 min after 4 U/kg SLO (E and F); intense sinus bradycardia at 30 sec (G), 1 min (H) and 3 min after 8 U/kg SLO, followed by nodal rhythm and intraventricular conduction defects (J), terminating in cardiac standstill 5 min after 8 U/kg SLO (K).
In order to investigate, *Streptolysin O* (SLO) could protect them against the lethal effects of challenging doses of SLO (4 to 10 U/kg i.v.), has also been studied. Intraperitoneal administration of SLO (4 IU/kg i.p.) did not produce any ECG changes in the rabbits. However, pretreatment of rabbits with ASO completely protected them against the cardiotoxic and lethal effects of challenging doses (4, 8 and 10 U/kg, i.v. administered at 30 min interval) of SLO (Fig. 2).

**DISCUSSION**

The present study has demonstrated that both in the puppies as well as the rabbits, the i.v. injection of small doses of SLO immediately caused transient sinus bradycardia, which was dose dependent. In higher doses SLO produced progressively increasing defects in intracardiac conduction processes, terminating in cardiac standstill. Similar ECG changes have also been demonstrated in rabbits and mice after the administration of streptococcal preparations containing SLO, by other workers (5-8). However, the doses of SLO used in these studies (5-8) had been much higher than employed by us; this could be due to the use of a relatively more purified preparation of SLO in our experiments.

An interesting observation of the present study has been that in the rabbits, SLO besides causing changes in cardiac conductivity, also caused ST elevation, a feature highly suggestive of acute myocardial damage. The demonstration of morphological cardiac damage in animals after the parenteral administration of SLO (1,2,5), supports this observation.

Total protection of the rabbits pretreated with ASO against the cardiotoxic and lethal effects of challenging doses of SLO, as observed in the present study, would suggest that the cardiotoxic moiety of SLO is antigenic.
From the above discussion it will be clear that SLO is cardiotoxic and is capable of causing derangements of cardiac activity and myocardial damage in animals. On the basis of these observations and keeping in view that the patients suffering from acute rheumatic carditis do not infrequently present with various disorders of cardiac activity, it would be fair to suggest that this streptococcal component may be involved in the causation of derangements of cardiac activity during acute rheumatic fever in man.

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