INTRODUCTION :

Streptomycin (Schatz et al. 1944), neomycin (Waksman and Lechevalier 1948), viomycin (Bartz et al. 1951 and Finlay, et al. 1951), kanamycin (Umezawa et al.1957) and paromomycin (Coffey et al. 1959) and other aminoglycosidic antibiotics represent 'streptomycin group of antibiotics'. These chemical compounds are obtained as metabolities of Actinomycete group of micro-organisms and were developed as antitubercular and broad-spectrum antibiotics. The chemical structure of these antibiotics indicates that the molecule is composed of two components, the central guanido moiety and the two sugar components attached to the guanido moiety by glycosidic linkages. Viomycin which has a guanido group in the main component and aminoacids in place of sugar moieties is also characterised as a polypeptide antibiotic.

The most important side effect of these antibiotics is the inhibition of motor nerve leading to respiratory distress and paralysis (Hinshaw and Feldman 1945; Pridgen 1956; Engel and Denson 1957; Middleton 1957 and Webber 1957). This significant clinical observation led to investigations

on the action of these antibiotics on neuromuscular junction, which became the main topic of interest with pharmacologists (Molitor et al.1946; Molitor and Kuna 1949; Brazil and Corrado 1957; Iwatsuki et al. 1958; Jindal and Deshpande 1958; Pittinger and Long 1958; Brazil et al. 1959; Corrado et al. 1959; Adamson et al. 1960; Brazil 1960; Corrado and Ramos 1960; Bezzi and Gessa 1961; Brazil et al.1961; Osterloh 1963; Goldberg 1964; Speranskaya 1964; Sikh and Sachadev 1965). Similarly the effect on 8th cranial nerve leading to ototoxicity and involving both the cochlear and the vestibular portions has been investigated extensively. Correlation between these two main toxic reactions has been shown with a fair degree of accuracy (Pruett: Unpublished observation).

These antibiotics do not affect the blood pressure of the anaesthetised cat, dog and rabbit to adrenaline and acetylcholine (Molitor et al. 1946; Corrado 1958; Tisch et al. 1958; Veis et al. 1963; Jeske et al. 1964). Streptomycin has been shown to exert depressant action on the isolated rabbit heart (Leaders et al. 1960) and the frog heart (Gomazkov 1963). It also supresses the peristaltic activity of guinea pig ileum and has

antiacetylcholine (Dzoljie and Atanockovic 1956) and antihistamine (Leaders et al.1960; Popovici et al.1965) actions.

Thus although the influence of antibiotics of this group on blood pressure responses to acetylcholine, amd adrenaline and noradrenaline has been studied there are no reports on the blood pressure responses to histamine. In preliminary experiments it was observed that following streptomycin, the depressor response to histamine in cats was changed to a biphasic response that is, an initial depressor followed by a pressor. An attempt has been made in the present investigation to elucidate the mechanism of the secondary pressor response. To this end, experiments were made on the cat and dog blood pressure and nictitating membrane. Though there are many antibiotics which are stucturally similar to streptomycin, only those that are widely used in clinical practice were included in study. In order to get an insight into the part of the streptomycin molecule responsible for this type of action two of its degradation products, streptidine and streptamine were also included. The results of experiments on blood pressure suggested that the guanido group(s) contained in all the compounds

investigated must be responsible for the actions observed. This confirmed the literature reports (Molitor and Graessle 1950; Adamson et al.1960 and 1961; Corrado and Ramos 1960; Vermier and Alleva 1960; Brazil et al.1961; Owada 1962; Ramos et al. 1962; Vies et al.1963; and Goldberg 1964)and prompted the inclusion of a veriety of isolated tissue preparations in the present study in order to confirm further the importance of guanido group(s) in the pharmacodynamic profile of the compounds.