SUMMARY AND CONCLUSION

Streptomycin, gentamycin and tobramycin are structurally related to the aminoglycosidic group of antibiotics. The members of this group are known for their side effects. The most important of which is peripheral arrest of respiration and cardiac arrest. There is disagreement in the literature about the antagonists of these side effects which is the result of the vague ideas of action of these antibiotics upon neuromuscular transmission and cardiac vascular function. The effect of streptomycin, gentamycin and tobramycin on neuromuscular transmission was reinvestigated in an attempt to explore further their neuromuscular effect as well as to determine the eligible antagonists. The present work was designed to study the effect of these aminoglycosidic antibiotics on the cat-sciatic gastrocnemius muscle preparation, the rat phrenic nerve-diaphragm preparation and the isolated rectus abdominis preparation of toad.

Analysis of the results obtained from the experiments done on the cat-sciatic gastrocnemius muscle preparation revealed clearly that:

- The three studied aminoglycosidic antibiotics were capable of inhibiting twitches of the muscle evoked by sciatic nerve stimulation on their own without initial twitch augmentation (Figs. 1, 2, and 3).
- Intravenous prostigmine (Neostigmine) was not capable of reversing streptomycin, gentamycin and tobramycin induced depression of indirectly stimulated muscle contraction although it appeared that prostigmine relatively hastened the rate of recovery of the muscle (Figs. 1, 2 and 3).
- Intravenous calcium gluconate was effective in reversing the inhibition of indirectly stimulated muscle contraction induced by these aminoglycosidic antibiotics. Moreover, intravenous calcium gluconate protected the muscle against the characteristic inhibitory effect of these antibiotic when subsequently administered (Figs. 1, 2 and 3).
- Pre-exposure to each studied aminoglycosidic antibiotic markedly potentiated the degree of depression of the indirectly stimulated muscle contraction produced by subsequent injection of the same antibiotics (Figs. 1, 2 and 3).

The ability of calcium gluconate and not prostigmine to restore the neuromuscular transmission as well as to protect the preparation against the inhibitory effect of subsequent injected doses of the three antibiotics leads to assumption that these aminoglycosidic antibiotics interfere with the process of acetylcholine release by nerve impulse antagonising calcium ions.

Analysis of the results obtained from the experiments on the isolated toad's rectus abdominis clearly showed:

- A significant antagonistic effect of each tested aminoglycosidic antibiotics on the control tetanic contracting response of acetylcholine (Figs. 4, 7 and 10).
- The action of each antibiotic became more persistent and prolonged on increasing the test dose levels.
- Addition of prostigmine was capable of reversing the inhibitory effect of streptomycin, gentamycin and tobramycin respectively on the control response to acetylcholine (Figs. 5, 8 and 11).
- The curarizing effect of d-tubocurarine was increased when given in conjugation with subeffective doses of each studied antibiotic (Figs. 6, 9 and 10).

- Both streptomycin and gentamycin were capable of reducing the amplitude of contraction of the muscle produced by stimulation of the phrenic nerve, an effect which was proportional to the administered doses (Figs. 14 and 17).
- Addition of prostigmine was not capable of reversing streptomycin and gentamycin induced depression of the indirectly stimulated muscle contraction, also prior addition of prostigmine was not able to prevent the inhibitory effect of these antibiotics (Figs. 16 and 19).
- Addition of calcium gluconate was effective in reversing streptomycin and gentamycin induced inhibition of indirectly stimulated muscle contraction (Figs. 16 and 19), also prior addition of calcium gluconate was effective in preventing such inhibitory effect of streptomycin and gentamycin (Figs. 16 and 20).
- Streptomycin and gentamycin were capable of reducing the amplitude of contraction evoked by both nerve and direct muscle stimulation. It was noticed that the percentage of reduction of indirectly muscle contraction induced by these drugs was more intensified than that for directly stimulated muscle contraction (Figs. 15 and 18).

The present findings lead to assumption that the mechanism involved in this respect could be mediated through:

1) Interference with the process of acetylcholine release by nerve impulse.
2) A direct depressant effect.

The role of tobramycin on the amplitude of contraction of rat diaphragm evoked by both nerve and direct muscle stimulation was of controversial effects. In some experiments, a significant inhibitory effect of indirectly stimulated muscle contraction was initially obtained (Fig. 21). It was noticed that addition of calcium gluconate was effective in preventing such tobramycin induced inhibition. In other experiments, it was noticed that addition of tobramycin potentiated the amplitude of contraction evoked by both nerve and direct muscle stimulation by almost equal extent. Increasing the dose level of tobramycin to 6 mg/ml solution produced initial potentiation in the amplitude of contraction followed by gradual reduction in the amplitude of both indirectly and directly stimulated muscle contraction (Fig. 23).

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The present finding drew the attention to that the initial potentiating effect of tobramycin which appeared in some experiments could be explained on basis of direct nonspecific effect. The inhibitory effect of tobramycin could be mediated through similar mechanisms to streptomycin and gentamycin.

Comparing the effect of equilevel doses of these aminoglycosidic antibiotics on the amplitude of contraction of indirectly stimulated rat diaphragm revealed that the order of potency is as follows:
gentamycin > streptomycin > tobramycin.