# STUDIES ON THE EFFECTS OF STREPTOMYCIN ON THE PRENATAL AND POSTNATAL DEVELOPMENT OF THE INNER EAR.

## "AN EXPERIMENTAL STUDY ON THE MOUSE"

THESIS

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BY

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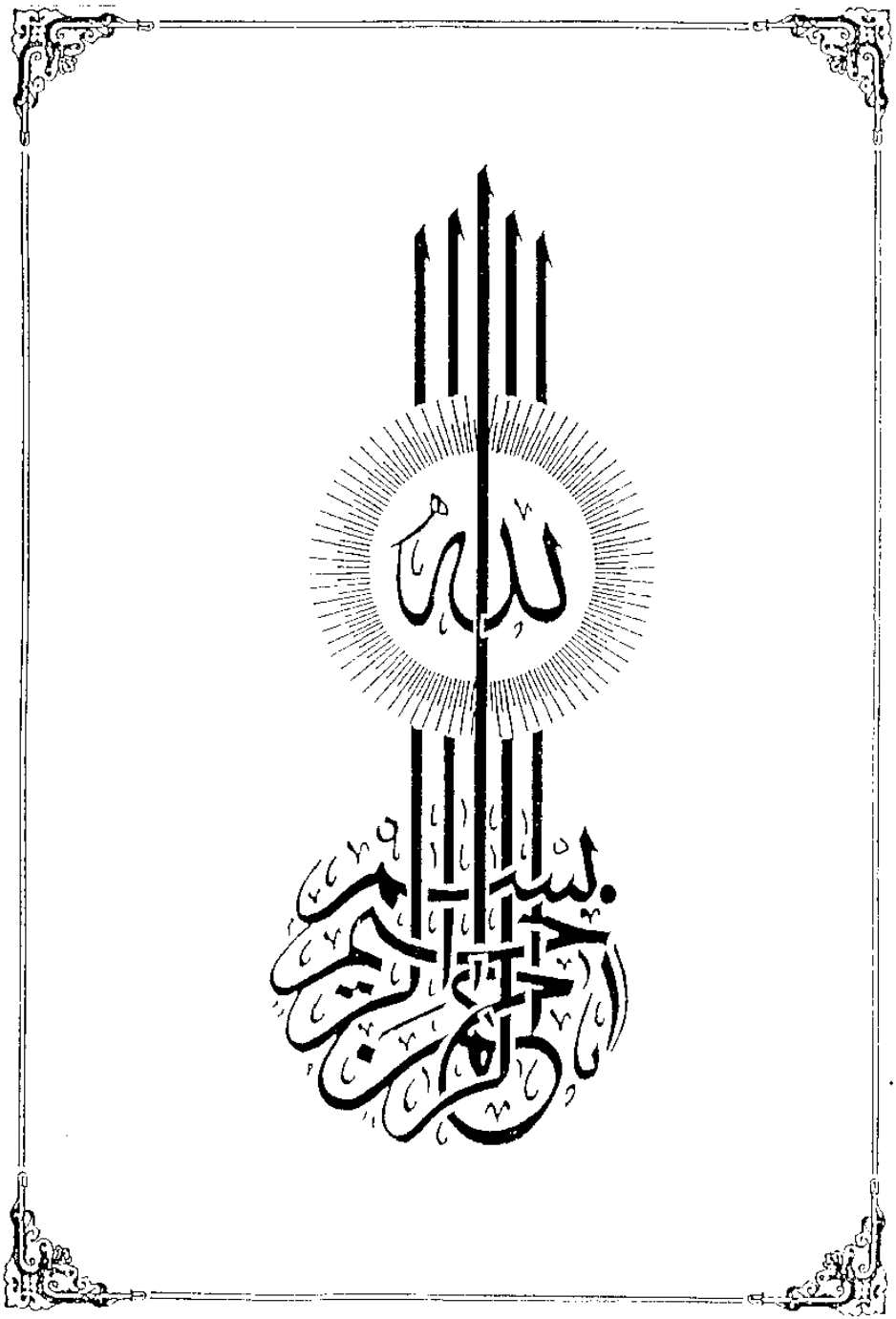

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# INTRODUCTION

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Several authors studied the toxic effects of streptomycin on the fully developed inner ear in man and in experimental animals. Hinshaw and Feldman (1945) were the first to report the phenomenon of ototoxicity of streptomycin after using the crude preparation of that drug for the treatment of patients suffering from tuberculosis. In addition, Brown and Hinshaw (1946) described disturbances of equilibrium in tuberculous patients treated with streptomycin. Such pheonomena were confirmed both clinically and experimentally by numerous authors on the fully developed inner ear (Hawkins and Mushett, 1947; Caussé, 1949; Renta, 1959; El-Serafy,1964;Watanuki,et al 1971;Hamed and Abd-El Rahman, 1974; Martinez et al,1977). Although some studies were concerned with the effect of streptomycin on the developing ear (Watson and Stow, 1948; Boletti and Croato, 1958; Conway and Birt 1965; Tuchmann-Duplessis, 1970), yet a thorough histological investigation of the effects of that drug, on the prenatal & postnatal development of that organ was not reported. Accordingly, it became the aim of the present work is

to study the histological effect of streptomycin administration on the prenatal and post-natal development of the inner ear. For this experimental study the inner ear of the mouse was chosen.

## DEVELOPMENT OF OTIC LABYRINTH

## OF THE MOUSE

Wada (1923) had studied the maturation of the cochlea of albino rats, and found that the appearance of the Preyer reflex was found to occur when two changes had taken place in the cochlea. The first was when the tectorial membrane had reached the outermost part of the outer hair cells; the second change was in the tunnel of corti when all its turns had been opened.

Larcell, MacCready, and Jerself (1944) studied the cochlear potential in the maturing opossum. These workers found that the first cochlear potentials occurred in a narrow frequency range. As the animals matured, the frequency range increased. They found that the cochlear potential was associated with the development of the tunnel of corti and the maturation of the three scalae.

Alford and Ruben (1963) reported that the

auditory function in the mouse became evident about the 10th day after birth. They were able to record cochlear potential from the round window on the 11th day after birth, while the action potential from the eighth nerve could be recorded 12.5 days after birth. The Preyer reflex could be elicited from the 9th - 14th days.

Mikaelian and Ruben (1965) studied some aspects of the postnatal anatomical development of the inner ear of the mouse, and reported that the stria attained its normal adult dimensions on the eighth postpartum day.

Kikuchi and Hilding (1965) used phase contrast and electron microscopy to study the maturation of the organ of corti in mice from birth to adulthood. They found that, the internal and external hair cells, Deiter's cells, pillar cells, nerve fibres and afferent nerve endings were identified at birth. The tunnel of corti began to open at the basal end as early as the 6th day after birth and moved upward towards the apex. They reported that the kinocilia of the hair cells were apparent at the first postpartum day. On the 10th day, the efferent nerve endings appeared, and by the 14th day the organ of corti was well developed by light and

electron microscopy. These authors concluded that the inner ear of the mouse at birth was so immature that it resembled that of a human foetus of 15 weeks.

Kikuchi and Hilding (1966) studied by electron microscope the development of the stria vascularis in the mice after birth; they reported that the differentiation of the stria vascularis proceeded from base to apex and that by the 10th day after birth the adult pattern was reached.

Ruben (1967) studied the developmental pattern of terminal mitosis in the membranous labyrinth by radioautographs of specimens exposed to tritiated thymidine at different stages during development. The terminal mitosis of most of the cell types of the organ of corti occurred during a short period of time from the 13th to 15th day of gestation. The terminal mitosis of the hair cells and supporting cells of the posterior labyrinth occurred over a relatively longer period of time, from the 14th to the 18th day of gestation. This difference in the length of the period of terminal mitosis between the organ of corti and the posterior labyrinth was considered as a possible factor to account for the preservation of the vestibular response in some congenitally deaf patients. The spatial distribution of the cells of the organ of

corti occurred so that those cells which underwent terminal mitosis on the 12th and 13th days of gestation were located in the apical segment of the adult cochlea, and those cells of the organ of corti which underwent terminal mitosis on the 15th and 16th days of gestation were located in the basal segment of the adult cochlea. The spatial distribution of the cells of the spiral ganglion was the reverse of that of those of the organ of corti. The older cells were located in the basal segments and the younger cells were located in the apical segments.

Sher (1971) mentioned that, on the 11th day of gestation, the otocyst appeared as a closed ovoid sac. On the 12th day, the endolymphatic duct developed as an evagination from the medial wall of the otocyst about one third of the way from its dorsal to its ventral ends. As regards the development of semicircular ducts, he reported that the superior semicircular duct was the first one to develop. It appeared in its most rudimentary form between the 12th and 13th days of gestation as a pouch of epithelium projecting from the dorsal wall of the otocyst. The opposite walls of the pouch came together in the centre, but the pouch remained patent along its rim. The superior semicircular duct was completed by the

13th day of gestation. On that day, the posterior duct was represented by an evagination from the ventral part of the caudal end of the utricle, but no crus communies was present at that time. However, on the 14th day of gestation, all the three semicircular ducts were present, the crus commune was formed, and there was an ampulla on each of the three ducts together with a crista.

On the other hand, the first step towards separation of the membranous labyrinth into utricle and saccule occurred on the 15th day of gestation. A constriction appeared in the region of the origin of the endolymphatic duct indicating the beginning of the formation of the utriculo-saccular duct. The macula of both utricle and saccule were differentiated on the 14th day of gestation. Although Otoconia were detected for the first time on the 17th day, yet their number increased considerably on the 18th and 19th days. On the day of birth, both maculae have thick otolithic membrane with a large number of otoconia.

The development of the cochlear duct was reported by the author as follows :

(1) The formation of cochlear duct and ductus reuniens: The former started to develop between the 12th

and 13th days of gestation as an extension of the ventral part of the otocyst. On the 13th day, the embryo had about one-half turn of the cochlear duct. However, there was no ductus reuniens at that stage, and a wide channel connected the cochlear duct with the vestibular labyrinth. The cochlear duct, on the 14th day, was about one and one quarter coils long, and became one and one half coils in length. However, the ductus reuniens became well defined on the 16th day of gestation. Between the 17th and 18th days of gestation the cochlear duct might sometimes reach one and one-three quarters coils, with no further coiling after that.

(2) The differentiation of the organ of corti :-
The cochlear duct on the 13th day has two types of walls. The rostral wall consists of epithelium with two to three layers of tightly packed nuclei. The caudal wall has six layers of tightly packed nuclei.

The caudal wall of the cochlear duct was the site of differentiation of the organ of corti. On the 14th day, the caudal wall had differentiated into a layer of supporting cells containing five to six strata of nuclei.

However, the appearance of the caudal wall does not change significantly on the 15th and 16th days of gestation. The sensory cells in the cochlear duct had

more cytoplasm than the supporting cells. On the 17th day the sensory cells in the lateral portion of the basal third of the duct showed signs of differentiation into three outer hair cells, one inner hair cell, and phalangeal cells. The hair cells rest on a layer of supporting cells that had one to two strata of nuclei. The area which will form the tunnel of corti had became apparent in the basal and middle coils on the 18th day of development. The cytoplasm was vacuolated and gave the appearance of a space. Three outer and one inner hair cells flank the tunnel. They rest on a layer of supporting cells which, in the basal coil, had a single layer of nuclei. In the middle portion of the cochlear duct there were two to three layers of supporting cell nuclei beneath the hair cells. The outer and inner hair cells had differentiated throughout the length of the cochlear duct on the 19th day of gestation.

The tectorial membrane appeared on the first postpartum day, as a thin strip of pale eosinophilic material over the cells in the region where the sulcus spiralis internus formed. The pillar cells attained their mature shape on the 10th postpartum day. The tunnel of corti became wider between the eighthand tenth days after birth.

The Deiters cells and inner phalangeal cells became very vacuolated on the eighth and ninth postpartum days. On the tenth day, these cells were very cylinder, and there were large spaces between them.

(3) Differentiation of the limbus spiralis :
In the 18th day embryo, the development of the limbus was limited to the basal coil of the cochlear duct. On the 19th day the middle coil was starting to differentiation into limbus. On the first day after birth the limbus was differentiated throughout the cochlear duct except for the extreme apex. On the fourth day after birth the limbus spiralis had formed throughout the cochlear duct.

(4) Differentiation of the sulcus spiralis internus :
The sulcus spiralis internus started to develop after the first postpartum day. By the tenth postpartum day the sulcus spiralis internus was completed throughout the cochlear duct.

(5) Differentiation of the stria vascularis :
The stria vascularis started to differentiate on the 17th day of gestation. A vascular condensation of mesenchyme started to develop adjacent to the outer part of the rostral wall of the cochlear duct. On the first day after birth the boundary between the epithelial