INTRODUCTION

Stedman, (1968) reported that cigarette smoke contained several hundreds of substances such as nicotine, carbon monoxide, cadmium and benzopyrine. Many constituents. However, had not been evaluated for their toxicity.

Inhalation of cigarette smoke, whether through active or passive smoking lead to absorption of the toxic component of smoke though the pulmonary vasculature ***(Stillman et al., 1986).***

The high prevalence of smoking among women in their reproductive years continues to be a matter of concern. There is a worrying increase in the smoking prevalence among girls aged between eleven and fifteen. Latest figures indicate that, at the age of fifteen 33% of girls are regular smokers in some countries ***(Augood et al., 1997)***.

A number of epidemiologic studies ***(Olsen et al., 1982; Howe et al., 1985; Daling et al., 1986)*** demonstrated a reduction in fecundity of women who smoke, especially in women smoking at earlier age and women who smoke larger number of cigarettes per day.

Jick et al. (1977) reported that increasing cigarette consumption resulted in decreasing age of menopause by depleting oocyte viability and/or number.

Weigert et al. (1999) stated that smokers undergoing IVF treatment were significantly younger than non smokers and showed a significantly lower oocyte count and a poor oocyte quality. The premature atresia or damaged oocytes might be caused by the harmful components of smoke as cadmium and nicotine.

Although there was a well established link between cigarette smoking and female infertility, early age of menopause and reduced pregnancy rate after IVF treatment, yet relatively few experimental studies were done to demonstrate the effect of cigarette smoking on the primary sex organ in female, the ovary. Therefore, the **aim** of the present study is to study the effect of cigarette smoking on the structure of the ovary of albino rats at different periods of the pre and post-pubertal age.

THE OVARY IN RATS

Brambell (1928) mentioned that the fully grown oocyte of mouse measured about 70 micrometer in diameter. Once the oocyte had attained its maximum size, it did not show further growth until ovulation occurred. Furthermore, the main growth of the follicle and the formation of the theca and antrum took place after the oocyte had completed its growth. The follicles grew rapidly, chiefly by enlargement of the liquour filled antrum, during the 48 hours immediately prior to oestrous period when they reached an average diameter of 550 micrometer. Moreover, the theca interna formed a definite layer measuring about 20 to 25 micrometer. The thickness was more or less uniform around the circumference of the follicle.

Pedersen and Peters (1968) reported a useful classification of the ovarian follicles for the quantitative analysis of the normal distribution of the different follicle stages. The authors classified the ovarian follicles into small, medium and large follicles. The small follicles included type 1, 2 and 3a follicles. The medium follicles included type 3b, 4 and 5a follicles while the large follicles included type 5b, 6, 7 and 8 follicles. Such classification was based on the size of the oocyte as well as the size and the morphology of the follicles.

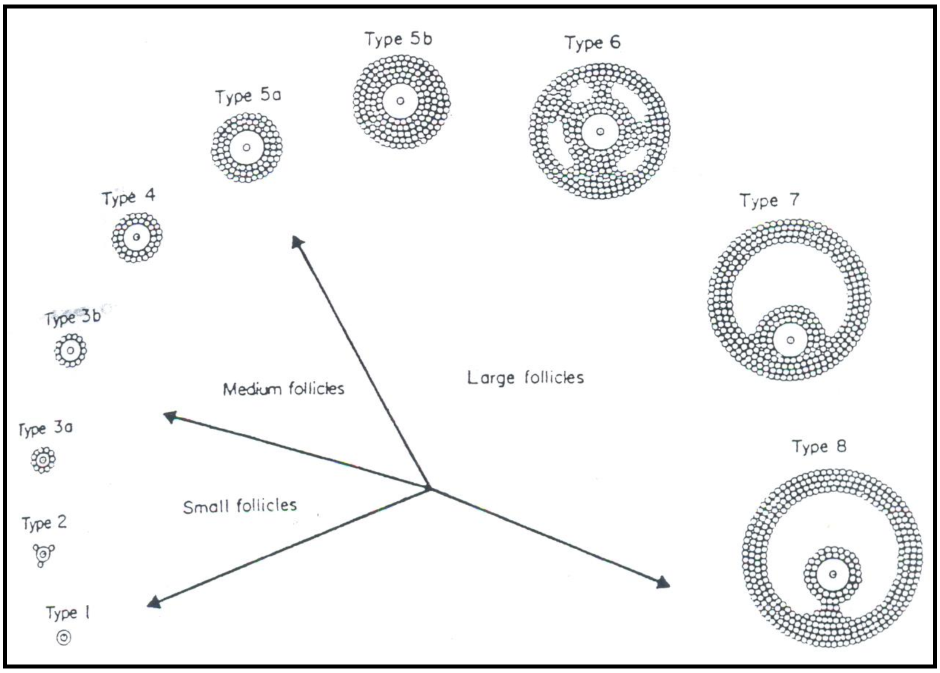

Fig. (1): Pederson and Peter classification of ovarian follicles.

Bingel and Schwartiz (1969) noticed that sections of the ovaries of normally cyclic female mice showed that newly formed corpora lutea were basophilic on the morning after ovulation i.e., at estrous where they appeared deep blue. On the morning of the first day after ovulation (metestrus), they began to loose their basophilia appearing purple in color and having lumens of moderate sizes. Then the corpora lutea became increasingly basophilic again. Furthermore, the follicles destined to ovulate at the next estrous were evident on the morning of the third day after ovulation i.e. on diestrus.

Jirasek et al. (1970) studied the postnatal development of the rat ovary by histochemical methods. The authors found, in the ovaries of new born female, superficial epithelium with one layer of cuboidal cells, as well as ovarian cords of epithelial character. The later consisted of oocyte groups and isolated pergranulosa cells and blastematous interstitium composed of gonadal fibroblast like cells. No germ cells were found. At five days, primordial and growing compact follicles were found. The interstitium constituting the thin tunica albugenia and stroma between the follicles was blastmatous in character. At ten days, the first growing follicles with antrum could be seen. Near the granulosa cells of these cavitated follicles the epithelioed theca cells were found. At 15 days, the oocytes of the growing follicles showed a distinct oolemma. Epithelioed cells could be also seen in the interstitium. The capillary system between the epithelioed cells developed at this stage.

The authors described also distinct atretic changes in compact and cavitated follicles of 20 days old rats for the first time.

Perry (1972) revealed that the interstitial tissue formed an important component of the mammalian ovary, its cells had a well defined role in steroido-genesis. It varied greatly in amount in different species. It was very prominent in rabbit and in many species of Insectivora, Rodentia and Carnivora, but sparce in man and primates in general. Concerning the origin of ovarian interstitial cells, the authors said that in rats "primary" interstitial tissue was formed by ingrowing cords of cells derived from the germinal epithelium during early life, whereas near puberty and adult life "secondary" interstitial tissue was formed from the theca interna of atretic follicles.

Byskov (1974) studied atresia of the large follicles of the mouse ovary. The author identified three stages of atresia that represented consecutive stages in a single atretic process. Follicles in stage 1 atresia contained up to 20% pyknotic granulosa cells which usually lied close to the follicular cavity. In stage 2 atresia, leucocytes were always seen among the granulosa cells and the basement membrane was not intact. Follicles in stage 3 atresia were shrunken and in contrast to stage 1 and 2, the follicular cavity were never seen. Furthermore, the author studied the duration of atretic process. Using autoradiography, the time it took a follicle without signs of atresia to reach stage 3 atresia was about 3 or 4 days.

Hummel et al. (1975) described the anatomy of the female genital system of the mouse. The authors recognized the ovaries as small paired spherical bodies located at posterolateral pole of the kidneys, each attached by the mesovarium to the dorsal body wall and enclosed in a thin transparent elastic capsule or bursa. The periovarian space was shut off from the abdominal cavity except for a tiny tunnel like channel through which blood vessels and nerves supported in the mesovarium entered and left the ovary though the hilus. The surface of the ovary was smooth in prepubertal females but became nodular after sexual maturity because of the presence of follicles and corpora lutea. Regarding the oviduct, the authors identified them as a long narrow tube connecting the periovarian space with the uterine horns.

Chiasson (1983) described the anatomy of the female reproductive system of adult white rat. He said that the ovaries of non pregnant female rat appeared as a mass of follicles just caudal to the kidneys and usually buried in a mass of fat. The mature follicle was called Graafian follicle and contained the egg or ovum. Each follicle had an outer limiting layer of cells, the theca externa and a layer of cells, the theca interna, bordering the follicle proper. The theca interna secreted the estrogen hormone. Meanwhile, the granulose cells were present within the follicle supporting the developing ovum. The author also demonstrated that the mature follicle ruptured and the egg was engulfed by the funnel shaped opening of the oviduct i.e. the ostium. In rats, this ostium formed a complete capsule, the bursa ovarica, which enclosed the ovary. The oviducts or Fallopian tubes were small, highly coiled tubes extending from the bursa ovarica to the uteri.

Rowlands and Weir (1984) reported that the process of follicular atresia could take several forms. The commonest form was disintegration of the cellular elements of the follicle and their disappearance or reversion to stromal cells. However, in some animals the theca interna cells hypertrophied and became interstitial cells. The authors added that in many rodents, elephants, and cetaceans the granulosa cells became luteinized although the oocyte had not been released, and these structures were accessory corpora lutea.

Ibrahim (1992) reported that the pergranulosa cells of rats at birth were flat cells present in clusters together with the oocytes. At three days, the pergranulosa cells surrounded the oocytes to form the primordial follicles. At five days, the granulosa cells divided by mitosis and so greatly increased in number forming the multilaminar follicles. By two weeks of age, the granulosa cells of the tertiary follicles could be differentiated into the membrana granulosa cells, the cumulus oophorus cells and the corona radiata cells. At three weeks of age, theca folliculi became differentiated into theca interna and externa. Later, the theca interna became 3 to 4 layers of spindle cells and blood capillaries. After this age, the follicles still grew larger until ovulation took place by the 8^{th} week of postnatal life as proved by the presence of corpora lutea. The author added that the interstitial glandular cells started to appear between the follicles by two weeks of age. These cells increased gradually by age till the 6^{th} week where they formed the gland cell masses. The medulla of the ovary was the small inner part consisting of connective tissue which decreased in amount by age. At 3 weeks of age many blood vessels appeared in the medulla and gradually increased up to the adult age.

THE OVARY IN HUMAN

Mossman and Duke (1973) mentioned that 4 stages of ovarian follicles were usually recognized. These were; primordial, primary, secondary and tertiary (Graafian) follicles. In the primordial follicle, the oocyte was surrounded by a single layer of squamous cells. The simple squamous cells eventually enlarged to form a simple low columnar epithelium converting the follicle into primary follicle. The simple columnar cells multiplied forming first a double and finally a stratified cuboidal follicular epithelium or granulosa. These were the secondary follicles. Graafian follicles were formed by progressive formation of large intercellular fluid filled spaces in the secondary follicles. The spaces coalesced into a large cavity, the follicular antrum.

Harrison and Wei (1977) reported that the growth of the ovarian follicles was divided into two phases relative to that of the oocyte. During the first phase the oocyte grew rapidly until almost adult size while the follicle increased only slowly in size and were a solid sphere. During the second phase, the follicle grew rapidly in size while the oocyte increased only slowly in diameter. The follicle also developed an antrum and the theca interna enlarged. The authors also mentioned that the follicular fluid was not of consistent appearance. The primary liquor was formed by the granulosa cells. It was secreted between the cells in the coalescing central cavities and exhibited a marked reticulum. Moreover, a secondary liquor was secreted rapidly just before ovulation and was less viscous. Tertiary liquor was formed after ovulation and plugged the cavity of the ruptured follicles.

Victor (1993) demonstrated that, the ovary had a peripheral cortex and a central medulla. The cortex was constituted from one half to two third of the ovarian thickness during life and had numerous ovarian follicles in various stages of development. The ovarian medulla was consisted of a dense vascular connective tissue stroma which was continuous with that of the mesovarium.

Junqueira et al. (1995) described the primordial follicles to be the smallest, most primitive and most numerous of the ovarian follicles. Each consisted of a spherical primary oocyte surrounded by a single layer of squamous follicular cells. They were arranged into groups immediately deep to tunica albugenia. A clear basement membrane demarcated the peripheral boundary of the follicle from the surrounding interstitial tissue. During each ovarian cycle, a number of primordial follicles were activated under the effect of the follicle stimulating hormone (FSH) to begin the process of maturation, in order to provide sufficient hormonal secretion. In addition, they mentioned that progressive growth of the follicle resulted in stratification of the follicular epithelium, forming multilaminar primary follicles in which the follicular cells acquired secretory granules forming granulosa cells and the surrounding theca layer became prominent.

Micheal et al. (1995) reported that the onset of the growth of ovarian follicles was marked by morphological changes in the oocyte, their surround-ding follicular epithelium and the ovarian stroma adjacent to the follicles. The oocyte was enlarged with marked increase in the number of cytoplasmic organells augmenting the synthetic capacity of the oocyte which started the secretion of PAS-positive amorphous refractile layer of glycoprotein, the zona pellucida. In early growing follicles, epithelial cells assumed a greater height and were designated the unilaminar primary follicles. The surrounding connective tissue became more compactly and circumferentially disposed around the follicle, forming the theca folliculi.

Roland et al. (1996) postulated that with progressive growth, the follicle increased markedly in diameter with the accumulation of fluid in the intercellular spaces of the granulosa cells and the formation of a single space termed the follicular antrum. At this stage, the growing follicles were designated as secondary or vesicular follicles. The theca layer surrounding the secondary follicle increased in thickness and was differentiated into inner and outer layers termed theca interna and externa respectively. The cells of theca interna were found to secrete androstendiol which was transported into the follicle to be aromatized to estradiol by granulosa cells.

Goldfien and Monroe (1997) described the cummulus oophorus as the granulosa cells that attached the oocyte to the wall of the mature Graafian follicle. The layer of granulosa cells, that surrounded the ovum was in close contact with the zona pellucida, formed the corona radiata, which accompanied the ovum after ovulation.

Junqueira et al. (1998) reported that, immediately after ovulation, rupture of thecal capillaries filled the lumen of postovulatory follicle with a blood clot forming a temporary structure, the corpus haemorrhagicum. Later, the basal lamina of the old follicular epithelium broke down with consequent invasion of the granulosa cells and blood clot with the thecal capillaries and connective tissue. The granulosa cells differentiated into granulosa lutein cells while the theca interna cells differentiated into theca lutein cells forming the corpus luteum.

Cormack (2001) reported that, after ovulation, the remaining follicles at various stages of development became atretic. The follicular cells showed pyknosis of the nucleus and dissolution of the cytoplasm. The oocyte also degenerated, leaving behind a prominent zona pellucida which might be folded inward or collapsed.

James and Lesile (2001) stated that the corpus luteum started involution if pregnancy did not occur with regression of its blood vessels and