Introduction

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An intake of vitamin A greatly in excess of the animal requirement results in a toxic syndrome known as hypervitaminosis A. Excess vitamin E appears to protect against hypervitaminosis A. Early signs and symptoms of chronic vitamin A intoxication include irritability, vomiting, loss of appetite, headache and dry skin (Goodman and Gilman (1980).

Hypervitaminosis A has been studied extensively on experimental animals. The most characteristic lesion occurs in bone and cartilage. In general, changes in bone depend on the species, the age of the animal, and the degree of hypervitaminosis. Other manifestations of hypervitaminosis A are anorexia, cutaneous lesions, temporary thickening of skin, deposition of lipid in kupffer cells, exophthalmos, hypoprothrombinemia, and eventually death of animals. Lipoprotein membranes exhibit increased permeability and decreased stability in the presence of excessive concentrations of vitamin A, leading to mitochondrial swelling, lysosomal rupture, and probably the decreased cohesiveness of keratin. Such effects may stimulate mitosis and the proliferation of the basal layer of epidermis, but this area is still controversial (Logan 1972). The chronic intoxication of hypervitaminosis appears after periodic administration of smaller doses of vitamin A. The characteristics of chronic hypervitaminosis A in rats and other experimental animals may be summarized as follows:

Arrest of growth leading to loss in weight, marked emaciation accompanied by anemia, and finally cachexia. According to Rodahl (1950 a) the lowered growth rate results from the reduced appetite caused by overdose of vitamin A. Complete loss of the quills from a hedgehog after about two weeks of subcutaneous administration of ca. 100,000 I.U. vitamin A per day. Hypervitaminosis A in guinea pigs is characterized by reduced keratinization and hyperplasia of the papillae and blood vessels, as well as great increase in surface lipids.

As a result the horny layer finally desquamates, giving rise to a sort of "Wing" formation.

In rats and chick embryo cultures, it was demonstrated that keratinization was suppressed by excess vitamin A. Extensive subcutaneous and intramuscular hemorrhage, especially in the viscera and lungs, and round bone fractures are general phenomenae in hypervitaminosis A and are accompanied by an increased clotting time of the blood (Weslaw et al. 1938 a, Collazo and Rodriguez, 1933 b, Lewis and Reti 1935, Noetzel 1939, Moore and Wang 1945, and Rodahl 1950 b). Other incidental catarrhal lesions such as hemorrhagic rhinitis, enteritis, and conjunctivitis during hypervitaminosis A are often accompanied by hemorrhage. Hypertrophy of the thyroid gland was reported by Takahashi et al. (1925 b), although Noetzel (1939) was unable to demonstrate any histologic changes in this gland.

Further, hypertrophy of both the islets of Langerhans and pancreatic cells as well as the cells of the anterior lobe of the pituitary was reported by Cornil et al. (1939 a) and Cornil et al. (1939 b). According to Masin (1950 a, 1950 b) estrus in female rats is extended after giving 37,000 I.U. Vitamin A per day. Rats in which the pituitary has been removed react like normal rats to a toxic overdose of vitamin A, (Wolbach and Maddock, 1952).

Experimental animals which had received an excess of vitamin A showed degenerative atrophy of various organs. Deposition of fat in the reticuloendothelial system of the liver, i.e. the kupffer cells was reported by Domagk and Dobeneck (1933), Collazo and Rodriguez (1933 a, b) , Drigalski and Laubmann (1933), Uotila and Simola (1938), and Noetzel (1939).

Weslaw et al. (1938 a) described a sort of hypertrophy of the genital organs such as swelling of the testes in rats, which was confirmed by Poumean-Delille (1943 a, b). Degenerative lesions of the testicles as a result of long - continued ingestion of moderate doses of vitamin A were observed in weanling rats, but not in adult animals (Maddock et al., 1953).

Brusa and Testa (1953) studied the effect of hypervitaminosis A on the guinea pig central nervous system. They found a damage in the cerebral cortex, cerebellum, thalamus and mesencephalon.

Of the symptoms of hypervitaminosis A in experimental animals, especially in the rat, are spontaneous fractures and internal hemorrhage. Wolbach and Maddock (1951), Collazo and Rodriguez (1933 b), Papke (1937), Rodahl and Moore (1943) noticed that the skeletal and skin lesions are reversible.

From the numerous reviews on mammalian spermatogenesis (Albert, 1961, Clermont, 1960, 1962, 1963 & 1972, Clermont and Leblond, 1953 & 1955, Clermont and Perey, 1957 and Courot, et al., 1970), it is evident that the seminiferous epithelium of various mammals has once more come under intensive investigation.

Clermont and Leblond (1953) based the quantification of the cells of the seminiferous tubules on the development of the acrosomic system.

The seminiferous epithelium of the adult mammalian testis consists of a complex yet ordered arrangement of germ cells in intimate contact with a population of Sertoli cells.

Studies reviewed by Clermont (1972) on the morphology of the seminiferous epithelium and the kinetics of spermatogenesis have demonstrated the organization of the germ cells into defined cellular associations, each representing a stage in the process of spermatogenesis which together constitute the cycle of the seminiferous epithelium. In the rat 14 such stages have been described (Leblond and Clermont 1952) and it is believed that the hormonal regulation of spermatogenesis is mediated by the Sertoli cells which partially or completely

surround every germ cell (Fawceet 1975, Kerr and Krester 1981, Purvis and Hansson 1981, Ritzen et al., 1981 a).

In various recent studies on the seminiferous tubules of mammals, two distinct trends have emerged in the choice of criteria for the identification of the stages.

The first method uses the nuclear morphology of spermatids simultaneously with the position of the more mature spermatids within the seminiferous epithelium. These mature spermatids, arranged in fascicles, plung deeply into the epithelium toward the sertoli cell nuclei and then migrate toward the lumen of the tubule to be finally released. In this approach various staining methods are employed. Such classification resulted in 8 stages in rat (Roosen, Runge, 1952 & 1955, Roosen Runge, and Giesel 1950), ram (Ortavant. 1958), bull (Ortavant, 1959), rabbit (Swierstra, and Foote, 1963) and boar (Swierstra, 1968). More stages were reported, however, for example 14 stages in the rat (Clermont, and Perey, 1957; Leblond, and Clermont 1952; Ortavant, 1959), 13 stages in the hamster (Clermont, 1954) and guinea pig (Clermont, 1960) and 12 stages in the mouse (Oakberg, 1956 a) and monky (Clermont and Leblond, 1959).

A classification resulting in many stages has the advantage of offering a tool that facilitates analysis of the neumerous cytological and cytochemical phenomena taking place within the seminiferous epithelium. Summer sterility resulting

in cow and buffaule bulls under climatic conditions in Upper Egypt (El-Sherry et al., 1977) is a representation for the two factors operating in Summer stress (i.e.), Photoperiod (Courot et al., 1968) and relative humidity (Patrick, et al. 1954).

The mouse has provided much of the important information on irradiation effects on the testis (Oakberg, 1955 a, b, 1956, 1975 and Withers et al., 1974), while the rat in particular has furnished information on the qualitative and quantitative aspects of normal spermatogenesis (Leblond and Clermont 1952, Clermont, 1962, Clermont and Bustos-Obregon 1968, Huckins 1971 a & b and Clermont and Hermo, 1975).

In both rat and mouse, a new concept of spermatogonia stem cell renewal and differentiation has recently been evolved (Oakberg, 1971, Huckins, 1971 a & b, Clermont and Hermo 1976). The identification of the various stages of the seminiferous epithelial cycle based on the morphological changes of the germ cell mnuclei and the local arrangement of the spermatids in the seminiferous tubules was applied in the present investigation. Each stage of the seminiferous epithelial cycle was identified when the entire cross section of the seminiferous tubule include germ cells in the same stage.

From reviewing the literature, it is evident that there is no available references dealing with the effect of hypervitaminosis A on the testis of the albino rat. Therefore, the main aim of the present work is to describe the spermatogenic

cell cycle in normal mice and it's quantification using the Sertoli cell ration together with the estimation of the diameter of the seminiferous tubules and compare it with the treated mice injected with overdoses of vitamin A.

The skin has been considered in most of the experimental works done with regards to vitamin A. It was thought that it may be of benifit to take the ear pinna of the mouse fed excessive vitamin A to examine the skin as well as the elastic cartilage.