

Title: Analysis of the influence of selected endocrine active compounds on the developmental competence of porcine oocytes during in vitro aging - hormonal and molecular mechanisms.

Ageing is a natural biological process connected with irreversible changes that accumulate with age. They affect not only physiological functions of the whole organism but also psychological ones. In the modern society natural ageing leads to disturbances in cells, tissues, organs and organ systems, entailing an increased morbidity and finally is the leading cause of death. However, such a process can be initiated earlier than usually as an answer to disturbed homeostasis resulting from constantly increasing level of environmental pollution, overuse of drugs or defined lifestyle. In the case of women, the occurrence of menopause is connected with natural ageing process. Menopause is a physiological period in the life of a woman when menstruation ceases and activity of ovaries is restricted. Mean age of the occurrence of menopause is 51 years, whereas its occurrence before the age of 40 is described as **premature ovarian failure; (POF)**. The causes of POF are diverse (starting from the genetic background, through enzymatic reasons to those caused by recurring infections) and not fully understood. Given that statistically an increasing number of women postpones the decision of pregnancy to the time of gaining economic stability, it is of importance to carry out research providing answer to the causes of their premature reproductive potential decline.

During the last decade researchers, a number of institutions and governments warned the general public against serious health risks connected with the ever increasing presence in the natural environment of chemical compounds called **Endocrine Active Compounds; (EACs)**, that disturb hormonal balance of living organisms. The majority of such substances can be found in commonly used products such as drugs, cosmetics, they are components of plastics, pesticides, and are generated as industrial byproducts e.g. in paints and lacquers fabrication. Among EACs special attention deserve those that when combined with sex steroid hormone receptors located inside cells (androgens, estrogens) can mimic or block their actions. Therefore they may play an important role in the development of reproductive tract diseases such as already mentioned POF or **polycystic ovarian syndrome (PCOS)**. The female reproductive cycle is a complex process involving among others growth and development of ovarian follicles (folliculogenesis), inside which female reproductive cells – oocytes mature. Proper course of folliculogenesis and oocytes maturation ending with their release into the oviduct (ovulation) where fertilization takes place, determines reproductive success of a female. Women are being born with final and non-renewable number of oocytes, constituting so called ovarian reserve. In light of this it seems of importance to study if and in what way selected compounds that block or mimic sex hormones action (an anabolic steroid: nandrolone; a fungicide: vinclozolin) negatively affect the developmental potential and the number of developing oocytes.

Our previous studies with the application of transmission electron microscopy and specific fluorescent markers confirmed that in pig oocytes and follicular cells surrounding them in the presence of selected EACs there is an abrupt decrease in the number of mitochondria and their structure is altered. This may indicate initiation and active course of processes similar to those that occur in ageing oocytes. Based on these results the paramount aim of the presented project is the characterization of the mechanism of action of selected EACs (nandrolone and vinclozolin) in the process of preovulatory maturation of pig oocytes, determining their subsequent ability to be fertilized. The specific aim of the project will be denotation if and in what way oocytes may be protected against harmful influence of the compounds applied. The answer to such a question is especially important in the light of constantly developing techniques of assisted reproduction that may contribute to the increase in the reproductive potential of a female.

Recently carried out research indicate that pig thanks to its special similarity to the human both in the anatomy of internal organs and physiological processes is the most suitable model animal used in biomedical research. According to that in the presented project the source of both follicular cells and oocytes will be ovaries of pigs collected in a slaughterhouse. During ageing of the organism there is a decline in all protective and reparative mechanisms, thus results obtained in the carried out experiments will allow to follow signaling pathways operating between follicular cells and oocytes and possible disturbances in them that lead to the premature cessation of their function. Finding and understanding mechanisms of action of selected compounds expressing endocrine activity in the ovary of a pig will complement and enrich the present state of knowledge concerning reproductive potential of a female what seems important in the light of reports indicating an increased exposure to such hormonally active substances present in the environment.