



TRACE ELEMENTS IN FOLLICULAR FLUID AND THEIR EFFECTS ON REPRODUCTIVE FUNCTIONS

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ABSTRACT

Environmental pollution plays an important role in affecting the internal milieu of animals and humans. The amount of trace elements in the environment is generally low, but these chemicals can interfere with physiological systems. Thus, the health and welfare of individuals could be compromised by exposure to environmental levels of pollutants. In order to understand risk and effects of various chemicals on the animal and human organism, the input of pollutants into biological systems has to be defined. Trace elements, mainly the toxic ones, can adversely affect animal health and reproductive system and its functions, through either direct or indirect effects on numerous organs and systems.

Keywords: trace elements, environment, follicular fluids, reproduction

INTRODUCTION

Expressions of toxicity for any xenobiotic material are related directly to the amount absorbed into the body, its metabolism and accumulation in target organs, and cellular vulnerability to irreversible toxic change. Metals absorbed into the body interact and compete for binding sites on carrier proteins, and that when protective mechanisms afforded by key

metal-binding proteins like metallothioneins and epidermal barrier function become saturated, toxic changes occur (**Lansdown et al., 2001**). The accumulation of toxic substances in the tissue of animals is studied almost world-wide. Studies concern not only the degree of contamination of the whole animal body or particular tissue but also the influence of accumulated elements on the condition, growth and reproduction of individuals (**Samiullah, 1990**). One of the most important aspects of environmental pollution is the intake of toxic substances in the diet. Since this should be limited to an unavoidable minimum monitoring programmes have been conducted in many countries. All heavy metals are toxic at certain levels of intake (**Lopez-Alonso et al., 2000**). The major source of heavy metal pollution are processes, such as smelting of non-ferrous ores, waste incineration and the disposal of sewage sludge onto land that releases toxic metals into the environment resulting in enhanced levels of lead, mercury, cadmium and arsenic (**Beresford et al., 1999**). The level of toxic substances in muscle is generally low. Liver and kidney of animals shows higher concentrations (**Khalafalla et al., 2011; Capcarova et al., 2008; Kolesarova et al., 2008a, 2008b; Koréneková et al., 2008; Arpasova et al., 2007; Andreji et al., 2006; Cigánková et al., 2010**). Exposure to environmental concentrations of pollutant has been shown to perturb ovarian development in the sheep (**Mandon-Pepin et al., 2009**) and follicle status (**Amezaga et al., 2009**). Direct effects on components of the reproductive system are often among the most noticeable adverse effects of pollutants. Lead may have negative effect on porcine ovarian granulosa cells when added to culture medium (**Capcarova et al., 2009**). Cobalt (Co) was able to induce changes in porcine granulosa cells in response to various Co concentrations and caused numerous effects in ovarian granulosa cells (**Kolesarova et al., 2010**).

Trace elements in follicular fluid affecting human and animal reproduction

Scientific and technical development contributed on the one hand greatly to easier living conditions, on the other hand there is however substantially greater danger threatening not only the life of man but also of nature, of the entire living environment. At present the problem of the possible part played by this phenomenon in reproductive disorders is in the foreground. Via the food chain heavy metals, toxic trace elements and polyhalogenic hydrocarbons penetrate into the organism. They accumulate in the organism and thus also in the reproductive tract and may have an impact on fertility. Toxic elements comprise cadmium (Cd), lead (Pb), mercury (Hg), and arsenic (As) (**Drbohlav et al., 1998**). Concentrations of

elements in follicular fluid of small follicles can differ from those of large follicles. When follicles grow they become filled with fluid of an elemental composition similar to blood. Concentrations of elements in small follicles may represent longer term element exposure, whereas those of growing follicles represents the coincident blood concentrations (**Silberstein et al., 2009**). Where identical contaminants were found in both sera and follicular fluids, the levels were about twofold higher in serum and were positively correlated in both fluids (**Younlai et al., 2002**). According to **Menezo et al. (2011)** no correlation was found between zinc and oestradiol concentrations in serum and zinc concentrations in follicular fluid were significantly lower than serum concentrations.

According to **Silberstein et al. (2009)** the most abundant elements found in women follicular fluid were calcium (Ca) and magnesium (Mg), followed by copper (Cu), zinc (Zn), iron (Fe), chromium (Cr), rubidium (Rb). **Ng et al. (1987)** found the mean levels of calcium, copper and zinc in amounts: $86.9 \pm 11.6 \text{ mg.l}^{-1}$, $1.16 \pm 0.29 \text{ mg.l}^{-1}$, and $0.72 \pm 0.12 \text{ mg.l}^{-1}$. Authors concluded that the concentrations of these elements do not seem to reflect oocyte status or maturity.

Cd, Pb and Hg have been identified in human follicular fluid and ovarian tissue, and have been associated with adverse reproductive outcomes in epidemiologic studies; however few studies have examined the relationship between blood metal levels and reproductive hormones (**Jackson et al., 2011**). The lead (Pb) levels found in follicular fluid in women were $11.29 \pm 1.38 \text{ mg.l}^{-1}$ (**Paksy et al., 2001**). **Zha et al. (2008)** measured in human follicular fluid the average concentration of Pb in amount 151.06 mg.l^{-1} , cadmium (Cd) 2.02 mg.l^{-1} , Zn 0.54 mg.l^{-1} , Mg 28.54 mg.l^{-1} . Raised blood level affects infertility and intervention to reduce the Pb exposure might be needed for women of reproductive age (**Al-Saleh et al., 2008**). Pb levels within follicular fluid were found to be significantly higher in non-pregnant women compared to pregnant patients suggesting that elevated concentrations of the environmental toxicant lead adversely affect female reproduction (**Silberstein et al., 2006**). The mean level of follicular fluid cadmium was higher in smokers than in non-smokers, and with a dose-effect of smoking. Cd also could accumulate in oocytes of smokers in a dose-dependent manner, in oocytes of cadmium-treated rats (**Zenzes et al., 1995**).

CONCLUSION

Environmental chemicals are thought to adversely affect animal and human reproductive functions. The possible cause of fertility disorders in conjunction with toxic

elements is probably in damage of the granulosa cells and thus their dysfunction as regards production of steroid hormones with full impact on female fertility (hormone disruptor). Very significant are the differences in the blood and follicular fluid levels, the levels in follicular fluid being significantly lower. There is a protective barrier of the oocyte formed by the follicle (probably the cells of the granulosa) against blood (**Drbohlav et al., 1998; Jackson et al., 2011**). The presence of contaminants in follicular fluid may compromise the quality of oocytes.

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REFERENCES

- AL-SALEH, J. – COSKUN, S. – MASHHOUR, A. – SHINWARI, N. – EL-DOUSH, I. – BILLEDI, G. – JAROUDI, K. – AL-SHAHRANI, A. – AL-KABRA, M. – EL DIN MOHAMED, G. 2008. Exposure to heavy metals (lead, cadmium and mercury) and its effect on the outcome of in-vitro fertilization treatment. In *International Journal of Hygiene and Environmental Health*, vol. 211, 2008, no. 5-6, p. 560-579.
- AMEZAGA, M.R. – SPEERS, C.J.B. – BELLINGHAM, M. – EVANS, N.P. – MANDON-PEPIN, B. – COTINOT, C. – SHARPE, R.M. – RHIND, S.M. – FOWLER, P.A. 2009. Sudden changes in exposure to environmental chemicals perturbs ovarian development. *Proceedings of the Society for Reproduction and Fertility*, 2009, Edinburgh, UK, p. 37.
- BERESFORD, N.A. – MAYERS, R.W. – CROUT, N.M.J. – MACEACHERN, J.P. – DODD, B.A. – BARNETT, C.L. – STUART LAMB, C. 1999. Transfer of cadmium and mercury to sheep tissues. In *Environmental Science and Technology*, vol. 33, 1999, p. 2395-2401.
- CAPCAROVA, M. - KOLESAROVA, A. - ARPASOVA, H. - MASSANYI, P. - LUKAC, N. - KOVACIK, J. - KALAFOVA, A. - SCHNEIDGENOVA, M. 2008. Blood biochemical dynamics and correlations in laying hens after experimental nickel administration. In *International Journal of Poultry Science*, vol. 7, 2008, p. 538-547.
- CAPCAROVA, M. – KOLESAROVA, A. – LUKAC, N. – SIROTKIN, A. 2009. Antioxidant status and selected biochemical parameters of porcine ovarian granulosa cells exposed to lead in vitro. In *Journal of Environmental Science and Health, Part A*, vol. 44, 2009, p. 1617-1623.

DRBOHLAV, P. - BENCKO, V. - MASATA, J. - BENDL, J. - REZÁCOVÁ, J. - ZOUHAR, T. - CERNÝ, V. - HÁLKOVÁ, E. 1998. Detection of cadmium and zinc in the blood and follicular fluid in women in the IVF and ET program. In *Ceska Gynekologie*, vol. 63, 1998, no. 4, p. 292-300.

JACKSON, L.W. - HOWARDS, P.P. - WACTAWSKI-WENDE, J. - SCHISTERMAN, E.F. 2011. The association between cadmium, lead and mercury blood levels and reproductive hormones among healthy, premenopausal women. In *Human Reproduction*, vol. 26, 2011, no. 10, p. 2887-2895.

KHALAFALLA, F.K. - ALI, F.H. - SCHWAGELE, F. - ABD-EL-WAHAB, M.A. 2011. Heavy metal residues in Beni-Suef abattoir, Egypt. In *Veterinaria Italiana*, vol. 47, 2011, no. 3, p. 351-361.

KOLESAROVA, A. - CAPCAROVA, M. - ARPASOVA, H. - KALAFOVA, A. - MASSANYI, P. - LUKAC, N. - KOVACIK, J. - SCHNEIDGENOVA, M. 2008a. Nickel-induced blood biochemistry alterations in hens after an experimental peroral administration. In *Journal of Environmental Science and Health, Part B*, vol. 43, 2008a, p. 625-632.

KOLESAROVA, A. - SLAMECKA, J. - JURCIK, R. - TATARUCH, F. - LUKAC, N. - KOVACIK, J. - CAPCAROVA, M. - VALENT, M. - MASSANYI, P. 2008b. Environmental levels of cadmium, lead and mercury in brown hares and their relation to blood metabolic parameters. In *Journal of Environmental Science and Health, Part A*, vol. 43, 2008b, p. 646-650.

KOLESAROVA, A. - CAPCAROVA, M. - SIROTKIN, A. - MEDVEDOVA, M. - KOVACIK, J. 2010. Cobalt-induced changes in the IGF-I and progesterone release, expression of proliferation- and apoptosis-related peptides in porcine ovarian granulosa cells in vitro. In *Journal of Environmental Science and Health, Part A*, vol. 45, 2010, p. 810-817.

LANSDOWN, A.B.G., SAMPSON, B., ROWE, A. 2001. Experimental observations in the rat on the influence of cadmium on skin wound repair. In *International Journal of Experimental Pathology*, vol. 82, 2001, no. 1, p. 35-41.

LOPEZ-ALONSO, M. - BENEDITO, J.L. - MIRANDA, M. - CASTILL, C. - HERNÁNDEZ, J. - SHORE, R.F. 2000. Toxic and trace elements in liver, kidney and meat from cattle slaughtered in Galicia (NW Spain). In *Food Additives and Contaminants*, vol. 17, 2000, no. 6, p. 447-457.

MANDON-PEPIN, B. - LOUP, B. - POUMEROL, E. - FOWLER, P.A. - AMEZAGA, M.R. - SHARPE, R.M. - EVANS, N.P. - BELLINGHAM, M. - RHIND, S.M. - COTINOT, C. 2009. Consequences of in utero exposure to environmental chemicals on ovary

development in sheep. 5th Copenhagen Workshop on Endocrine Disruptors, 2009, Copenhagen, Denmark, Poster, 1pp.

MENEZO, Y. – PLUNTZ, L. – CHOUTEAU, J. – GURGAN, T. – DEMIROL, A. – DALLEAC, A. – BENKHALIFA, M. 2011. Zinc concentrations in serum and follicular fluid during ovarian stimulation and expression of Zn²⁺ transporters in human oocytes and cumulus cells. In *Reproductive Biomedicine Online*, vol. 22, 2011, no. 6, p. 647-652.

NG, S.C. – KARUNANITHY, R. – EDIRISINGHE, W.R. – ROY, A.C. – WONG, P.C. – RATNAM, S.S. 1987. Human follicular fluid levels of calcium, copper and zinc. In *Gynecologic and Obstetric Investigation*, vol. 23, 1987, no. 2, p. 129-132.

PAKSY, K. – GÁTI, I. – NÁRAY, M. – RAJCZY, K. 2001. Lead accumulation in human ovarian follicular fluid, and in vitro effect of lead on progesterone production by cultured human ovarian granulosa cells. In *Journal of Toxicology and Environmental Health*, vol. 62, 2001, no. 5, p. 359-366.

SAMIULLAH, Y. 1990. Biological monitoring of environmental contaminants: animals, MARC Report, 37, University of London, 1990, p. 767.

SILBERSTEIN, T. – SAPHIER, O. – PAZ-TAL, O. – TRIMARCHI, J.R. – GONZALES, L. – KEEFE, D.L. 2006. Lead concentrates in ovarian follicle compromises pregnancy. In *Journal of Trace Elements in Medicine and Biology*, vol. 20, 2006, no. 3, p. 205-207.

SILBERSTEIN, T. – SAPHIER, O. – PAZ-TAL, O. – GONZALES, L. – KEEFE, D.L. – TRIMARCHI, J.R. 2009. Trace element concentrations in follicular fluid of small follicles differ from those in blood serum, and may represent long-term exposure. In *Fertility and Sterility*, vol. 91, 2009, no. 5, p. 1771-1774.

YOUNGLAI, E.V. – FOSTER, W.G. – HUGHES, E.G. – TRIM, K. – JARELL, J.F. 2002. Levels of environmental contaminants in human follicular fluid, serum, and seminal plasma of couples undergoing in vitro fertilization. In *Archives of Environmental Contamination and Toxicology*, vol. 43, 2002, no. 1, p. 121-126.

ZENZES, M.T. – KRISHNAN, S. – KRISHNAN, B. – ZHANG, H. – CASPER, R.F. 1995. Cadmium accumulation in follicular fluid of women in in vitro fertilization-embryo transfer is higher in smokers. In *Fertility and Sterility*, vol. 64, 1995, no. 5, p. 599-603.

ZHA, S.W. – YU, J.Q. – LIU, J.Y. – PAN, L. – LIN, N. – ZHA, J. – YANG, M.M. 2008. Contents of lead, cadmium, zinc and manganese in the follicular fluid and semen of non-professionally exposed infertile couples. In *Zhonghua Nan Ke Xue*, vol. 14, 2008, no. 6, p. 494-497.