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# 冻融胚胎移植中辅助孵化对妊娠结局及安全性的影响

赵美 吴海霞 陈智勤 潘家坪 梁珊珊 黄媚媛 滕晓明

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**【摘要】目的** 探讨在玻璃化冻融胚胎移植(FET)中, 激光辅助孵化(AH)操作后对妊娠结局及母婴安全性的影响。**方法** 回顾性分析 2014 年 1 月—2015 年 10 月接受体外受精-胚胎移植(IVF-ET)失败后行 FET 患者的临床资料, 根据患者年龄进行分组后比较 AH 操作后妊娠结局及母儿并发症的发生情况。**结果** 在正常年龄组(<38 岁)的患者中, 未行 AH 操作的对照组中胚胎种植率、临床妊娠率、活产率、多胎率均高于 AH 组, 流产率低于 AH 组, 并且差异有统计学意义( $P<0.05$ ); 在高龄( $\geq 38$  岁)患者中, AH 组的胚胎种植率、临床妊娠率较对照组有增高的趋势( $P>0.05$ ); 分娩周期中, AH 组与对照组早产率、死胎率、母体并发症、新生儿男女比例、胎龄、出生体质量、新生儿缺陷率等均无统计学差异( $P<0.05$ )。**结论** 对于正常年龄患者, 卵裂期 FET 时不建议行 AH 操作; 对于高龄患者, AH 操作可提高胚胎种植率及临床妊娠率, 但不能明显改善其妊娠结局; AH 对母婴安全暂无不良影响。

**【关键词】** 辅助生殖技术(ART); 辅助孵化(AH); 冻融胚胎移植(FET)

· 临床研究 ·

**Effect of assisted hatching on the outcome and security of frozen-thawed embryo transfer** Zhao Mei,

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**【Abstract】Objective** To investigate the effect of laser-assisted hatching (AH) on outcome and security in frozen-thawed embryo transfer (FET). **Methods** The medical information of FET patients was retrospectively analyzed from pregnant cases undergoing *in vitro* fertilization-embryo transfer (IVF-ET) from January 2014 to October 2015. The incidence of pregnancy outcomes and maternal and fetal security were compared between AH group and control group (non-AH group). **Results** In control group with the normal age patients (<38 years old), the embryo implantation rate, the clinical pregnancy rate, the live birth rate and the multiple pregnancy rate were higher than those in AH group, and the abortion rate was lower in control group ( $P<0.05$ ). In elderly patients ( $\geq 38$  years old), the embryo implantation rate and the clinical pregnancy rate were increased in AH group, but there were no significant differences ( $P>0.05$ ). There was no significant difference in premature delivery, stillbirth rate, maternal complications, gender, gestational age, birth weight, birth defects rate between AH group and control group in delivery cycles ( $P>0.05$ ). **Conclusion** There is no benefit to improve pregnancy outcome in the normal age patients when FET used AH. For elderly patients, AH operation may improve the implantation rate and the clinical pregnancy rate, but it did not improve the clinical outcome. The long-term safety need more cumulate data and research.

**【Key words】** Assisted reproductive technology (ART); Assisted hatching (AH); Frozen-thawed embryo transfer (FET)

# 卵巢慢反应患者控制性超促排卵相关因素分析: 一项多中心回顾性研究

高明霞 马晓玲 张学红 邢琪 冯娜 王莉云 曾湘晖 罗宗迪 蔡馥蔓 包俊华 刘丽 滕雪峰

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DOI: 10.3760/cma.j.issn.2096-2916.2017.09.002

**【摘要】目的** 探讨控制性超促排卵(COH)过程中发生卵巢慢反应可能的相关因素。**方法** 回顾性分析 2014 年 1 月—2016 年 1 月期间于兰州大学第一医院、新疆佳音医院、青海省人民医院、银川市妇幼保健院、广西玉林市妇幼保健院进行促性腺激素释放激素激动剂(GnRH-a)长方案体外受精-胚胎移植(IVF-ET)的 144 例卵巢慢反应患者的临床资料, 与 132 例卵巢正常反应患者(正常对照组)进行对比。**结果** 与正常对照组相比, 慢反应组患者体质量指数(BMI)、促甲状腺激素(TSH)较高, 降调节及促排卵时间较长, 促性腺激素(Gn)使用后 7 d 平均卵泡直径偏小, 雌二醇(E<sub>2</sub>)、黄体生成素(LH)低, hCG 注射日 E<sub>2</sub> 低, IVF 双原核(2PN)卵裂率较高, 临床妊娠率低, 差异均有统计学意义( $P < 0.05$ )。患者年龄、不孕年限、基础卵泡刺激素(FSH)、LH、催乳素(PRL)、E<sub>2</sub>、基础卵泡数、hCG 注射日孕酮(P)、获卵率、胚胎质量、胚胎种植率、流产率、宫外孕率、继续妊娠率及取消移植率组间均无统计学差异( $P > 0.05$ )。**结论** 卵巢慢反应可能与患者 BMI 过高、甲状腺功能降低及 GnRH-a 过度抑制相关, 较长的 Gn 天数仍可使慢反应患者获得较好的妊娠结局。

**【关键词】** 控制性超促排卵(COH); 卵巢慢反应; 体外受精-胚胎移植(IVF-ET)

· 临床研究 ·

**Related factors of suboptimal ovarian response in controlled ovary hyperstimulation: a multicenter retrospective study**

Gao Mingxia, Ma Xiaoling, Zhang Xuehong, Xing Qi, Feng Na, Wang Liyun, Zeng Xianghui, Luo Zongdi, Cai fuman, Bao Junhua, Liu Li, Teng Xuefeng

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**【Abstract】 Objective** To study the related factors of suboptimal ovarian response in controlled ovarian hyperstimulation (COH). **Methods** A total of 144 suboptimal ovarian response patients in *in vitro* fertilization-embryo transfer (IVF-ET) cycles of gonadotrophin releasing hormone agonist (GnRH-a) protocol from January 2014 to January 2016 were reviewed, including Reproductive Medicine Hospital in the First Hospital of Lanzhou University, Jia Yin Hospital in Xinjiang Province, the People's Hospital in Qinghai Province, Maternal and Child Health Hospital in Yinchuan, Maternal and Child Health Hospital in Yulin of Guangxi Province. Totally 132 patients of normal ovarian response were included in control group. The basal indexes, clinical data and results were compared. **Results** Compared with control group, suboptimal ovarian responder group had higher body mass index (BMI), thyrotropic hormone (TSH), longer days of GnRH-a and COH, shorter follicular diameter on the seventh day of COH, lower estradiol (E<sub>2</sub>), luteinizing hormone (LH) on the seventh day of COH, lower E<sub>2</sub> on the day of hCG administration, higher IVF two pronucleus (2PN) cleavage rate and lower clinical pregnancy rate, there were differences between the two groups ( $P < 0.05$ ). No significant differences were found in age, infertility duration, basal FSH, LH, prolactin (PRL), E<sub>2</sub>, antral follicle count, progesterone on the day of hCG administration, oocyte retrieval rate, embryonic quality, embryo implantation rate, abortion rate, ectopic pregnancy rate, ongoing pregnancy rate, implantation cancel rate ( $P > 0.05$ ). **Conclusion** Suboptimal ovarian response is related with higher BMI, lower thyroid function, or excessively GnRH-a depression. Good-quality embryos and satisfied pregnancy outcomes can still be got by extending COH period.

**【Key words】** Controlled ovarian hyperstimulation (COH); Suboptimal ovarian response; *In vitro* fertilization-embryo transfer (IVF-ET)

# 薄型子宫内膜合并甲状腺功能减退不孕患者的辅助生育治疗结局

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**【摘要】目的** 探讨薄型子宫内膜合并甲状腺功能减退不孕患者行辅助生育治疗后的效果。**方法** 165例因新鲜周期内膜 $\leq 7$  mm而取消胚胎移植的不孕患者,在拟行冻融胚胎移植前,对游离甲状腺素T4(FT4)正常、促甲状腺激素(TSH) $>2.5$  mIU/L的患者进行左旋甲状腺素片干预治疗。经治疗4~8周后,患者依据TSH水平分为A组( $n=70$ ), TSH $>2.5$  mIU/L; B组( $n=95$ ), TSH $\leq 2.5$  mIU/L。所有患者均采用相同剂量激素替代方案准备子宫内膜,分析子宫内膜情况及辅助生育结局。**结果** A组与B组相比,虽然子宫内膜下血流数量和阻力指数(RI)组间无统计学差异( $P>0.05$ ),但B组内膜下血流数量的均值高于A组,RI均值低于A组。且B组的子宫内膜厚度、临床妊娠率显著高于A组( $P<0.05$ ),流产率显著低于A组( $P<0.05$ )。**结论** 薄型子宫内膜合并TSH升高的不孕患者,给予干预至TSH $<2.5$  mIU/L后,行辅助生育治疗可改善这些患者的妊娠结局。

**【关键词】** 甲状腺功能减退; 薄型子宫内膜; 体外受精(IVF); 冷冻胚胎; 不孕症

· 临床研究 ·

**Clinical outcome of infertile women with thin endometrium and thyroidism after assisted reproductive treatment** Feng Fan, Ni Yali, Zhu Dalin, Zhang Lin, Wang Yan, Wang Jialing

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**【Abstract】 Objective** To investigate the clinical outcome of infertile women with thin endometrium and thyroidism after assisted reproductive treatment. **Methods** Totally 165 infertile women with thin endometrium and thyroidism were enrolled into this study. These women had their fresh embryo transfer canceled due to their endometrial thickness  $\leq 7$  mm, and had normal free thyroxin 4 (FT4) and thyroid stimulating hormone (TSH)  $> 2.5$  mIU/L. Then they received L-thyroxine for one or two months treatment in order to prepare their frozen-thawed embryo transfer. Based on their TSH levels, 165 infertile women were divided into two groups: group A,  $n=70$ , TSH  $> 2.5$  mIU/L; group B,  $n=95$ , TSH  $\leq 2.5$  mIU/L. All cases were given the same dose of estrogen replacement treatment to ready endometrium. Both endometrial status and clinical outcome were compared between the two groups. **Results** Although the number of endometrial blood flow and resistance index (RI) were not significantly different between groups A and B ( $P > 0.05$ ), the mean value of endometrial blood flow in group B was higher than that in group A, and the mean value of RI in group B was lower than that in group A. The clinical pregnancy rate and endometrial thickness in group B were significantly higher than those in group A ( $P < 0.05$ ). Besides, group B had lower abortion rate than group A ( $P < 0.05$ ). **Conclusion** Infertile women with thin endometrium and thyroidism could improve their clinical outcome by using assisted reproductive techniques after they underwent L-thyroxine treating and reached normal TSH levels.

**【Key words】** Hypothyroidism; Thin endometrium; *In vitro* fertilization (IVF); Frozen embryo; Infertility



# 维生素 D 与不孕女性卵巢储备标志物的相关性分析

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**【摘要】目的** 探讨血清维生素 D 水平与卵巢储备标志物抗苗勒管激素(anti-Müllerian hormone, AMH)和窦卵泡数(antral follicle count, AFC)之间的关系。**方法** 回顾性分析 2016 年 5 月—2017 年 6 月第一次接受辅助生殖助孕技术治疗的不孕症患者共 2 391 例, 根据患者血清 25(OH)D<sub>3</sub> 水平分为 ≤ 30 nmol/L 组(A 组,  $n=417$ )、30.1~49.9 nmol/L 组(B 组,  $n=626$ )和 ≥ 50 nmol/L 组(C 组,  $n=1 348$ )。分析患者血清 25(OH)D<sub>3</sub> 水平与不孕女性卵巢储备标志物血清 AMH 水平和 AFC 之间的相关性。**结果** ①各组患者间的年龄、体质指数(BMI)、基础 FSH、不孕原因构成比及不同季节的维生素 D 水平的差异均无统计学意义( $P>0.05$ ); ② 3 组患者的 AMH 水平分别为(4.07 ± 3.53) ng/mL、(4.12 ± 3.43) ng/mL 和(4.10 ± 3.18) ng/mL; AFC 分别为 14.0 ± 6.7、13.7 ± 5.9 和 14.1 ± 6.1, 组间差异均无统计学意义( $P>0.05$ ); ③调整潜在的混杂因素后, 运用相关因素多重线性回归分析显示, 血清 AMH 水平的偏回归系数( $B$ )=-0.005, 标准误差( $s_x$ )=0.007,  $P=0.506$ ; AFC 的  $B=-0.122$ ,  $s_x=0.019$ ,  $P=0.214$ , 与血清 25(OH)D<sub>3</sub> 水平之间均无相关性( $P>0.05$ )。**结论** 不孕女性维生素 D 和卵巢储备标志物血清 AMH 水平及 AFC 之间不存在相关性, 对维生素 D 缺乏的不孕女性通过补充维生素 D 以改善卵巢储备功能可能没有作用。

**【关键词】** 维生素 D; 卵巢储备标志物; 抗苗勒管激素(AMH); 窦卵泡数(AFC)

· 临床研究 ·

**Correlation analysis between vitamin D and ovarian reserve markers in infertile women** Sun Lijun,

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**【Abstract】 Objective** To investigate the relationship between serum vitamin D levels and ovarian reserve markers anti-Müllerian hormone (AMH) or antral follicle count (AFC). **Methods** Totally 2 391 cases infertility patients who received assisted reproductive technology for the first time were retrospectively analysed. According to the serum 25(OH)D<sub>3</sub> level, they were divided into  $\leq 30$  nmol/L group (group A,  $n=417$ ), 30.1–49.9 nmol/L group (group B,  $n=626$ ),  $\geq 50$  nmol/L group (group C,  $n=1 348$ ). The relationship were analysed between serum 25(OH)D<sub>3</sub> levels and AMH or AFC among the above three groups. **Results** 1) There was no significant difference in age, BMI, basic FSH, infertility cause and vitamin D level in different seasons among the three groups ( $P>0.05$ ). 2) There was no significant difference in AMH mean level [ $(4.07 \pm 3.53)$  ng/mL,  $(4.12 \pm 3.43)$  ng/mL and  $(4.10 \pm 3.18)$  ng/mL, respectively] and AFC ( $14.0 \pm 6.7$ ,  $13.7 \pm 5.9$  and  $14.1 \pm 6.1$ , respectively) among the three groups ( $P>0.05$ ). 3) After adjusting the potential confounding factors, we used the multivariate linear regression analysis and found that there was no correlation between AMH ( $B=-0.005$ ,  $s_x=0.007$ ,  $P=0.506$ ) or AFC ( $B=-0.122$ ,  $s_x=0.019$ ,  $P=0.214$ ) and serum 25(OH)D<sub>3</sub> level ( $P>0.05$ ). **Conclusion** There was no correlation between serum vitamin D and ovarian reserve marker AMH or AFC for infertile women. For infertile women lacking vitamin D, it may have no effects on improving ovarian reserve function by supplementing vitamin D.

**【Key words】** Vitamin D, Ovarian reserve markers; Anti-Müllerian hormone (AMH); Antral follicle count (AFC)

· 临床研究 ·

## 电针对重复周期患者卵细胞质量的影响

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**【摘要】目的** 观察控制性促排卵期间电针对重复周期患者卵细胞质量以及胚胎情况的影响。**方法** 将重复控制性卵巢刺激(COS)的患者 94 例, 分为观察组(48 例)和对照组(46 例)。两组患者再分别按女方年龄进行分组, 分为 3 个亚组: A 组(<35 岁)、B 组(35~39 岁)和 C 组( $\geq 40$  岁)。所有对象均采用改良方案进行 COS, 观察组在促排卵第 1 日开始进行电针治疗, 直到 hCG 注射日, 选用穴位为子宫、关元、中极、三阴交、太溪; 对照组不加用电针干预。**结果** 观察组 A 组 hCG 注射日  $E_2$  峰值、临床取卵数和  $M_{II}$  卵子数与自身前一周期和同年龄组对照组相比差异具有统计学意义( $P < 0.05$ ), Gn 剂量及使用时间、双原核(2PN)数、获胚数和优质胚胎率则差异无统计学意义( $P > 0.05$ )。B 组和 C 组与自身前一周期和同年龄组对照组相比则差异无统计学意义。**结论** 电针可改善重复周期患者卵细胞质量, 提高卵巢反应性, 其效果可能与女方年龄有关。

**【关键词】** 电针; 控制性卵巢刺激(COS); 重复周期; 女方年龄

· 临床研究 ·

**Effect of electro-acupuncture on the ovarian response in repeated *in vitro* fertilization cycles**

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**【Abstract】 Objective** To assess the effect of electro-acupuncture (EA) on the ovarian response in patients who underwent several cycles of controlled ovarian stimulation-*in vitro* fertilization/intracytoplasmic sperm injection (COS-IVF/ICSI). **Methods** Ninety-four COS-IVF/ICSI patients who underwent several cycles were divided into two groups: EA group and control group. Each group were divided into three subgroups according to women's ages: group A (<35 years), group B (35-39 years) and group C ( $\geq$ 40 years). The EA group was treated with EA during COS, and no intervention to the controls. **Results** The number of oocytes, M<sub>II</sub> oocytes, and embryos were all significantly higher than those in the previous cycles and also the control ( $P<0.05$ ) in group A. However, no significant difference was noted in the dosage and days of Gn used as well as the number of two pronucleus (2PN) embryos and the high-quality embryo rate ( $P>0.05$ ). Groups B and C showed no significant difference in the measurements above compared with themselves in last cycle and the control with the same age. **Conclusion** Our study preliminarily suggested that acupuncture treatment would have the efficacy in improving the quality of the oocytes which may relate with women's age.

**【Key words】** Electro-acupuncture (EA); Controlled ovarian stimulation (COS); Repeated cycles; Women's age

# 囊胚内细胞团和滋养外胚层基因表达研究

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**【摘要】**目的 研究人胚胎植入前囊胚内细胞团和滋养外胚层细胞基因的表达。方法 收集辅助生殖来源人受精后 6 d Gardner 评分 5AA 囊胚, 显微镜下微吸管机械分离内细胞团和滋养外胚层细胞, 单细胞测序检测, 选取筛选的差异表达基因并进行无监督层次聚类分析和 Gene Ontology(GO)功能分类分析。结果 对 3 枚受精后 6 d 的 5AA 囊胚内细胞团 14 个单细胞和滋养外胚层 19 个单细胞测序, 结果显示内细胞团 1 283 个基因表达上调, 其 GO 生物学功能主要是参与 DNA 依赖的转录、生物种间相互作用、抗原加工和表达、免疫反应、信号转导、氧化还原、细胞分化、抗凋亡、神经系统发育、细胞黏附等, 参与丝裂原活化蛋白激酶(MAPKs)信号通路、肌动蛋白细胞骨架、黏附、轴引导、Jak-STAT、Wnt 信号通路。滋养外胚层 1 073 个基因表达上调, 其 GO 生物学功能主要是参与转录、DNA 依赖的转录、细胞周期、蛋白分解代谢、蛋白氨基酸磷酸化、蛋白质运输、细胞分裂、有丝分裂、泛素依赖性蛋白分解、细胞内蛋白质转运等; 参与泛素介导蛋白水解、鞘脂代谢、缬氨酸、亮氨酸和异亮氨酸降解、果糖和甘露糖代谢、氨基磷酸酯代谢、类固醇的生物合成、抗原处理和表达等信号通路。结论 从空间维度揭示囊胚内细胞团和滋养外胚层的基因表达, 显示两者相互协调, 精细调节囊胚发育和胚胎植入过程, 进一步数据分析有望寻找到调控胚胎植入的内源性关键特异分子。

**【关键词】** 囊胚; 内细胞团; 滋养外胚层; 基因; 单细胞测序

**基金项目:** 国家自然科学基金面上项目(81070493)

· 实验研究 ·

**Global gene expression of the inner cell mass and trophectoderm of the human blastocyst** Zhao Liang,

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**【Abstract】Objective** To investigate the global gene expression of inner cells mass and trophectoderm of the human primplantational blastocyst. **Methods** We used blastocysts which was 6 d after fertilization, and Gardner score 5AA. Microcapsules were used to separate the inner cells mass and trophectoderm. Single cell sequencing was performed. And the gene expression was analyzed by bioinformatics software. The unidentified hierarchical clustering analysis and Gene Ontology (GO) functional classification were used to analyze the differentially expressed genes. **Results** The 11 single cells from inner cells mass and 16 single cells from trophectoderm in 5AA preimplantational blastocysts were sequenced. We found there were 1 283 genes up-regulated in inner cell mass compared with trophectoderm. The GO biological function was mainly involved in DNA-dependent transcription resistance, signal transduction, cell differentiation, anti-apoptosis, nervous system development, cell adhesion, etc. These genes involved in MAPKs signaling pathway, actin cytoskeleton, adhesion,axis guidance, Jak-STAT, Wnt signaling pathway. We found there were 1 073 genes with up-regulated expression in trophectoderm compared with inner cell mass. Its GO biological function was mainly involved in transcription, DNA dependent transcription, cell cycle, protein catabolism, protein amino acid phosphorylation, protein transport, cell division, mitosis, ubiquitin-dependent protein decomposition, intracellular protein transport, etc. Those genes involved in ubiquitin-mediated proteolysis, sphingolipid metabolism, valine, leucine and isoleucine degradation, fructose and mannose metabolism, aminophosphonate metabolism, steroid biosynthesis, antigen processing and expression signal pathways. **Conclusion** The global gene expression of inner cells mass and trophectoderm of the human preimplantational blastocyst is revealed from the spatial dimension, indicating that they are coordinated with each other, and the process of embryo implantation are finely regulated. Further data analysis is expected to find the endogenous specific molecules for regulating embryo implantation.

**【Key words】** Blastocyst; Inner cells mass; Trophectoderm; Gene; Single cell sequencing

**Fund program:** Surface Project of National Natural Science Foundation of China (81070493)

## *ssp411* 基因敲除小鼠生育表型的初步研究

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**【摘要】目的** 对 *ssp411* 基因的生育功能进行初步研究。**方法** 利用 PB 转座子插入建立小鼠模型 *ssp411* 基因敲除小鼠各基因型之间交配后, 检查雌鼠生殖道是否见栓。记录出生小鼠的窝仔数, 性别, 出生 20 d 仔鼠体质量、基因型等数据; 记录出生后 90 d 雄仔鼠的睾丸重量, 进行组织形态学研究, 并对附睾尾精子进行活力分析。**结果** *ssp411* 缺陷型雌鼠可以正常生育, 而雄鼠无自然生育能力。*ssp411* 基因敲除雄鼠能够与母鼠自然交配形成阴道栓, 但是没有子代出生, 且在交配后母鼠输卵管壶腹部未见精子。睾丸的组织形态学研究和睾丸称量结果表明, *ssp411* 蛋白缺失可以影响精子的生成。*ssp411* 基因敲除雄鼠的附睾精子活力也明显差于对照组。**结论** *ssp411* 基因缺陷不影响雌性生殖, 但影响雄鼠的精子生成功能, 造成少弱精子症, 并引起雄性不育。

**【关键词】** 转基因动物模型; *ssp411*; 雄性不育

**基金项目:** 国家自然科学基金(81471503)

· 实验研究 ·

**Preliminary exploration of reproductive phenotype in *ssp411* gene knockout mice** Tang Jianan,

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**【Abstract】Objective** To study reproductive phenotype of *ssp411* gene deficiency. **Methods** By using mouse model with inserted PB transposon after natural mating between different genotypes, females were examined for the presence of vaginal plugs. The data such as litter size, genders, genotypes and body weights of pups were recorded. Testicular weights of adult mice were also recorded. Histomorphological analysis of testes and activity analysis of cauda epididymal sperms were performed. **Results** Male *ssp411* knockout mice showed infertile, while female mice showed same degree of fertility as that of wild types. Although male mice could normally perform mating, their sperms were not capable to reach to ampulla of fallopian tube. Their testis weights, cauda epididymal sperm concentration and activity were significantly low. Histomorphological analysis suggested that spermatogenesis was injured in *ssp411* deficient males. **Conclusion** Females with *ssp411* deficiency are fertile. *ssp411* deficiency could negatively affect spermatogenesis, which will lead to oligoasthenospermia and male sterility.

**【Key words】** Genetically modified animal models; *ssp411*; Male sterility

**Fund program:** National Natural Science Foundation of China (81471503)



# 冻融牛始基卵泡在体外三维培养的最适藻酸盐浓度

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**【摘要】目的** 探讨冻融的牛始基卵泡在体外三维培养的最适藻酸钠浓度。**方法** 玻璃化冷冻牛卵巢组织后复苏, 加入Liberase DH酶消化, 然后随机挑取始基卵泡, 将其分别培养在二维的培养系统中(对照组, A组)和浓度分别为0.5%(B组)、1%(C组)、2%(D组)的藻酸钠三维培养系统中培养8d, 每隔1d观察卵泡的生长情况, 测量卵泡直径以及雌二醇(E<sub>2</sub>)的分泌。**结果** 随着培养天数增加, 对照组中卵泡的完整性丧失, 卵母细胞和颗粒细胞分离, 而三维培养组中卵泡仍维持其完整性。体外培养8d后, D组的卵泡平均直径为(57.7 ± 8.5) μm, 大于B组和C组(P<0.05); 荧光染色后, D组的未受损卵泡率为68.4%, 较B组、C组高, 但仅B组、D组间有统计学差异(P<0.05); B组、C组、D组的E<sub>2</sub>水平均随培养时间的延长而分泌增加, 其中D组中的E<sub>2</sub>水平(98.5 ± 7.8) pg/mL最高, 较B组、C组高, 但仅B组、D组间有统计学差异(P<0.05)。**结论** 藻酸钠三维培养系统较二维培养系统更适合始基卵泡的体外培养, 体积浓度为2%的藻酸钠凝胶较低浓度的藻酸钠凝胶更适合始基卵泡的生长发育。

**【关键词】** 始基卵泡; 体外培养; 藻酸钠三维培养

· 实验研究 ·

**Investigation of the optimum concentration of sodium alginate in the three-dimensional culture of the freeze-thawed bovine primordial follicles**

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**【Abstract】Objective** To investigate the optimum concentration of sodium alginate in the three-dimensional culture of the frozen-thawed bovine primordial follicles. **Methods** The vitrified bovine ovarian tissues were resuscitated. Liberase DH was added to digest the resuscitated ovarian tissue. Then the primordial follicles were randomly selected and cultured in a two-dimensional culture system (control group, group A) and in a three-dimensional culture system with 0.5% (group B), 1.0% (group C), 2.0% (group D) sodium alginate and cultured for 8 d. The growth of follicles were observed, the diameter of follicles and E<sub>2</sub> hormone secretion were measured every other day. **Results** With the increase of culture time, the integrity of follicles in the control was lost, the oocytes and granules were separated, while the follicles in the three-dimensional culture group maintained its integrity. After cultured primordial follicles for 8 d *in vitro*, the diameter of the follicles in group D was (57.7±8.5) μm, which were higher than those in group B and group C, the difference was statistically significant ( $P<0.05$ ). After fluorescent staining, the number of undamaged follicles in group D was 68.4%, which were higher than those in other two groups, but the difference was only statistically significant with group B ( $P<0.05$ ). The levels of E<sub>2</sub> in the three groups were increased with the prolongation of culture time, and the concentration of group D was (98.5±7.8) pg/mL, which were higher than those in other two groups, but the difference was only statistically significant with group B ( $P<0.05$ ). **Conclusion** The three-dimensional culture system of sodium alginate was more suitable for the *in vitro* culture of the primordial follicles than the two-dimensional culture system. The sodium alginate gel with the concentration of 2.0% was more suitable for the growth and development of the follicles.

**【Key words】** Primordial follicles; *In vitro* culture; Alginate three-dimensional culture

# “全面二孩”政策下湖南省可生育人群生育意愿及影响因素研究

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**【摘要】目的** 了解湖南省可生育人群的生育意愿及其影响因素, 为“全面二孩”政策后湖南省人口预测及政策调整提供科学依据和支持。**方法** 采用问卷调查的方式对湖南省可生育人群进行调查, 按湖南省经济水平的阶梯式分布原则将湖南省划分为经济发达地区、经济中等地区和经济欠发达地区, 从这三类地区中随机抽取经济发达的长沙市、经济中等的衡阳市和经济欠发达的怀化市, 再从 3 个市中选取人口密度较大的公共场所随机偶遇、符合研究对象的人群进行调查。**结果** 在调查的 1 353 例可生育人群中, 期望生育二孩者占 64.7%; 期望子女性别为 1 男 1 女者占 61.0%; 期望生育时间间隔 3~5 年占 48.4%。被调查者的生育意愿与户口性质、家庭人均月收入的差异无统计学意义( $P>0.05$ ); 性别、年龄、职业、教育程度、婚姻状况、是否为独生子女、是否属于流动人口与可生育人群的生育意愿差异有统计学意义( $P<0.05$ )。将各个因素引入多因素 Logistic 逐步回归中, 以是否有二孩生育意愿为因变量, 最终有 3 个因素留存在逐步回归模型: 较大年龄、调查对象女性、非独生子女( $P$  均 $<0.05$ )。**结论** “全面二孩”政策下, 意愿生育二孩的人群占本次调查人群的 64.7%, 其中对可生育人群的生育意愿有影响的因素为性别、年龄、职业、教育程度、婚姻状况、是否为独生子女、是否属于流动人口。

**【关键词】** “全面二孩”政策; 可生育人群; 生育意愿

· 流行病学研究 ·

**Fertility desire and its influencing factors in Hunan Province under the policy of “comprehensive two children”** Wang Yujun, Ye Weijie, Mao Guangxu, Xie Hongwei

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**【Abstract】Objective** To understand the fertility willingness and its influencing factors of fertile population in Hunan Province, and to provide scientific basis and support for the population forecast and policy adjustment of Hunan Province after the policy of “comprehensive two children”. **Methods** According to the ladder distribution principle of Hunan Province, Hunan Province was divided into economically developed areas, economically middle areas and economically underdeveloped areas, and randomized from these three types of regions. The economic development of Changsha city, the economy of Hengyang city and the economically underdeveloped Huaihua city was selected, and then from the three cities in the selection of large population density of public places random encounter with the study of the crowd were investigated. **Results** Among the 1 353 fertile population surveyed, 64.7% were expected to have two children, and 61.0% were expected to have 1 male and 1 female child. The expectation of fertility was 3 to 5 years (48.4%) ( $P>0.05$ ). The difference of fertility intention of the population was statistically significant ( $P<0.05$ ). There was no difference in fertility willness according to sex, age, occupation, education level, marital status, whether the only child, whether it was a floating population and fertility ( $P>0.05$ ). All factors were introduced into the multivariate Logistic stepwise regression, and there were three factors that left the progressive regression model: the older age, the female, the non-only child ( $P<0.05$ ). **Conclusion** In the “two-child” policy, 64.7% of the population were willing to have two children, and the factors influencing the fertility expectation of the fertile population were gender, age, occupation, educational level, marital status, for the only child, and whether it belongs to the floating population.

**【Key words】** “Two children” policy; Fertile population; Fertility desire

## 体外受精/卵胞质内单精子显微注射双卵双胎减胎后妊娠结局的病例对照研究

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**【摘要】目的** 探讨双卵双胎妊娠早期减胎为单胎的妊娠结局。**方法** 2008年1月—2014年12月期间体外受精及卵胞质内单精子注射-胚胎移植(IVF/ICSI-ET)后双胎妊娠早期(孕45~75 d)减胎为单胎者102例(A组), 三胎妊娠早期减胎为双胎者73例(B组)以及双胎妊娠未减胎者4 638例(C组), 比较其中晚期流产率、早产率等进一步的妊娠结局。**结果** IVF/ICSI-ET后A组与B组和C组比较, 早产率(10.8%, 58.6%, 42.1%)、低出生体质量儿率(6.8%, 44.1%, 30.3%)明显降低, 孕周[(38.0 ± 2.0)周, (35.7 ± 2.3)周, (36.4 ± 2.1)周]、出生体质量[(3.17 ± 0.53) kg, (2.51 ± 0.59) kg, (2.69 ± 0.53) kg]明显增加, 差异有统计学意义( $P < 0.05$ ), 中晚期流产率差异无统计学意义( $P > 0.05$ )。**结论** IVF/ICSI后的双卵双胎妊娠, 于孕早期行减胎术安全, 具有更好的妊娠结局。

**【关键词】** 多胎妊娠; 双胎妊娠; 减胎; 妊娠结局

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· 临床报道 ·

**A case-control study on pregnancy outcome of fetal reduction to single fetus from dizygotic twins after *in vitro* fertilization and intracytoplasmic sperm injections**

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**【Abstract】 Objective** To discuss the pregnancy outcomes of reduction of biovular twin pregnancy. **Methods** The pregnancy outcomes including late abortion rate and premature delivery rate were compared among 102 cases of twin pregnancy underwent fetal reduction to singleton (group A), 75 cases of triplet pregnancy underwent fetal reduction to twin pregnancy (group B) in the early trimester of pregnancy and 4 638 cases of twin pregnancy did not accept fetal reduction (group C) after *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) from January 2008 to December 2014. **Results** The rate of premature, delivery with low birth weight children were reduced significantly, gestational weeks were longer and birth weight was increased significantly in the group of early fetal reduction of biovular twin pregnancy, compared with that in the group of triplet pregnancy reduced to twin pregnancy and the group of twin pregnancy without fetal reduction, and the differences were statistically significant ( $P < 0.05$ ). The differences in the late abortion rate were not statistically significant. **Conclusion** For the biovular twin pregnancy, it was safe and got better pregnancy outcome to conduct fetal reduction in the early trimester.

**【Key words】** Multiple pregnancy; Twin pregnancy; Fetal reduction; Pregnancy outcome

**Fund program:** Research Fund of National Health and Family Planning Commission of China (201402004); the Jiangsu Province Special Program of Medical Science (FXK201221); National Natural Science Foundation for Young Scholars of China (81401267)

## 产后 HELLP 综合征合并多器官功能障碍综合征: 1 例病案报道

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**【摘要】**目的 探讨连续性肾脏替代治疗(continuous renal replacement therapy, CRRT)对 HELLP 综合征(hemolysis, elevated liver enzymes, and low platelets syndrome)的治疗作用。方法 对 1 名 40 岁, 第二次自然妊娠, 二胎, 剖宫产后大出血随后发展为 HELLP 综合征并出现多器官功能障碍综合征(MODS)的女性患者, 进行院内 ICU 救治并给予连续性肾脏替代治疗(CRRT)。结果 经治疗 36 d 后, 患者好转出院, 后电话随访, 未再出现相关不适症状。结论 肾上腺糖皮质激素及 CRRT 的应用提高了 HELLP 综合征患者的生存率及生活质量, 但应用的时机和剂量还需要大规模的研究。

**【关键词】** HELLP 综合征; 连续性肾脏替代治疗(CRRT); 多器官功能障碍综合征(MODS)

**基金项目:** 国家自然科学基金(81371983)

· 个案报道 ·

**Analysis of 1 case of HELLP syndrome combined with multiple organ dysfunction syndrome after delivery**

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**【Abstract】Objective** To investigate the effect of continuous renal replacement therapy (CRRT) of hemolysis elevated, liver enzymes, and low platelets syndrome (HELLP syndrome) treatment. **Methods** Hospital ICU treatment and CRRT were performed in the female patient of 40-year old, second natural twin pregnancy, cesarean section, postpartum hemorrhage and development for HELLP and the multiple organ dysfunction syndrome (MODS). **Results** After treatment for 36 d, the patient was discharged from the hospital, and after telephone follow-up, there was no related symptoms. **Conclusion** The application of adrenal glucocorticoid and CRRT improve the survival and living quality of patients with HELLP syndrome, but the timing and dose of the application also require a large-scale study.

**【Key words】** HELLP syndrome; Continuous renal replacement therapy (CRRT); Multiple organ dysfunction syndrome (MODS)

**Fund program:** The National Nature Science Foundation of China (81371983)



· 现场调查 ·

## 体外受精 - 胚胎移植助孕患者健康信息需求的质性研究

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**【摘要】**目的 了解体外受精 - 胚胎移植(IVF-ET)助孕患者疾病信息需求及生活体验。**方法** 选取南阳市医专一附院、南阳市第一人民医院、南阳市中心医院 20 例接受 IVF-ET 助孕治疗的患者进行半结构访谈, 采用现象学分析法分析资料。**结果** IVF-ET 助孕患者的健康信息需求分为 4 个阶段: 建立病历阶段、控制性促排卵监测阶段、取卵阶段、移植阶段。**结论** IVF-ET 助孕患者疾病信息需求问题显著, 基于患者真实需求构建信息支持策略亟待解决。

**【关键词】** 体外受精 - 胚胎移植(IVF-ET); 信息需求; 质性研究

· 现场调查 ·

**Qualitative research on disease information needs of patients undergoing *in vitro* fertilization and embryo transfer** Wang Bingjuan, Sun Hui, Sun Huixia

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**【Abstract】Objective** To explore the disease information needs and treatment experience of patients undergoing *in vitro* fertilization and embryo transfer (IVF-ET). **Methods** A semi-structured interview was conducted with 20 patients undergoing IVF-ET. Data were analyzed based on phenomenological research method. **Results** The disease information needs of patients undergoing IVF-ET were classified into four stages: establishing a medical record stage, ovulation monitoring stage, taking the egg stage, embryo transfer stage. **Conclusion** The problem of patients undergoing IVF-ET was significant, and their treatment experience was worthy of attention.

## 评估和改善子宫内膜容受性治疗反复种植失败的研究进展

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**【摘要】** 反复种植失败(RIF)是困扰辅助生殖技术(ART)发展的难题,子宫内膜容受性是体外受精-胚胎移植(IVF-ET)成功的关键因素。如何提高RIF患者的子宫内膜容受性日益受到生殖医学界的关注。本文从子宫内膜容受性评价常用临床方法到宫腔镜治疗宫腔结构异常、子宫内膜机械性损伤、调节母-胎免疫容受性、药物抑制子宫收缩、改善子宫内膜厚度、改善子宫内膜血流等方面,对RIF的治疗方法进行了阐述与总结,以期为未来的科学研究及临床治疗提供参考。

**【关键词】** 反复种植失败(RIF); 子宫内膜容受性; 体外受精-胚胎移植(IVF-ET)

### Progress of evaluating and improving endometrial receptivity to cure repeated implantation failure

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**【Abstract】** Repeated implantation failure (RIF) is a challenging problem for the development of assisted reproductive technology (ART). Endometrial receptivity is one of the key factors for the management of *in vitro* fertilization and embryo transfer (IVF-ET). How to improve the endometrial receptivity of patients with RIF has received considerable attentions by the reproductive medicine. This article reviewed evaluation indexes for endometrial receptivity and detailed treatments for improving the endometrial receptivity in order to provide the evidence-based reference for clinical researches. These treatments include the hysteroscopy treatment, endometrial mechanical injury, regulation of maternal-fetal immune tolerance, drug inhibition of uterine contraction, endometrial thickness improvement, and improvement of endometrial blood flow.

**【Key words】** Repeated implantation failure (RIF); Endometrial receptivity; *In vitro* fertilization-embryo transfer (IVF-ET)

## 溶血磷脂酸在卵母细胞体外成熟过程中作用的研究进展

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**【摘要】** 卵母细胞体外成熟(IVM)已成为一项热门的辅助生殖技术(ART), 有广泛的应用和发展前景。但其体外成熟率和受精后的发育能力还有待提高, 培养条件需要进一步优化。溶血磷脂酸(LPA)是磷脂激素家族的重要成员, 有生长因子和激素样活性, 可产生广泛的生物学效应。研究表明 LPA 存在于卵泡液中, 对卵泡发育、卵母细胞 IVM、受精、胚胎发育、种植等产生重要作用。本文就 LPA 特性及其在卵母细胞体外成熟过程中的作用做一简要的阐述。

**【关键词】** 溶血磷脂酸(LPA); 卵母细胞; 体外成熟(IVM)

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**Research progress on the roles of lysophosphatidic acid in *in vitro* maturation of oocytes** Xing Yaxin,  
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**【Abstract】** *In vitro* maturation (IVM) of oocytes has become a popular assisted reproductive technology (ART), which has broad application and development prospects. However, the maturation rate and developmental competence of those oocytes need to be improved. The most commonly used IVM culture conditions are still unsatisfied. Lysophosphatidic acid (LPA), which has growth factor-like and hormone-like activities, is an important member of the phospholipid autacoid family. LPA can produce a wide range of biological effects. Studies have shown that LPA exists in follicular fluid, which has an important effect on follicular development and oocytes maturation, subsequent fertilization, embryo development and implantation. This article briefly reviews the characteristics of LPA and its role in IVM of oocytes.

**【Key words】** Lysophosphatidic acid (LPA); Oocyte; *In vitro* maturation (IVM)

**Fund program:** Research and Innovation Program for Graduate Students of Nantong University (YKC16074); Ministry of Science and Technology of China (2017YFC1001601)

## 卵巢功能保护物质的研究进展

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**【摘要】** 由癌症导致的卵巢功能早衰(POF)现状越发严峻, 卵巢保护和卵巢冻融移植是目前有望恢复生殖和内分泌功能的最理想方法, 如何保护卵巢功能成为国内外学者的研究重点。这其中包括促性腺激素(GnRH)类似物、抗苗勒管激素(AMH)和血管生成素(Ang)等不同物质的探索。本文就如何保护卵巢功能进行综述。

**【关键词】** 卵巢功能保护; 卵巢早衰(POF); 卵巢移植; 卵泡丢失

**Research progress on the protective substances of ovarian function** Wang Dalin, Fan Dongqing,

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**【Abstract】** The situation of premature ovarian failure (POF) led by therapies of cancer is becoming increasingly severe. The domestic and international scholars focus on the study of ovary function preservation nowadays. Ovarian protection and cryopreservation are the most effective and ideal ways to recover reproductive and endocrine functions. These studies include the exploration with varies substances such as gonadotropin analogues, anti-Müllerian hormone, and angiogenin. The review emphasized on different methods of ovarian preservation.

**【Key words】** Ovary function preservation; Premature ovarian failure (POF); Ovarian tissue transplantation; Follicle lost



## 人类卵巢组织异种移植的影响因素及研究进展

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**【摘要】** 人类卵巢组织异种移植目前已广泛用于观察卵泡的发育和评估卵巢冷冻等其他相关保存女性生育能力措施的一种实验手段。有许多因素影响移植的效果, 如动物受体、卵巢组织的准备、移植后血管的形成、促性腺激素的使用等。虽然目前的研究表明, 卵巢组织异种移植技术能保护女性的生育能力、恢复卵巢内分泌和生殖功能, 但是, 由于安全和伦理的限制它目前只在实验条件下进行。本文对影响人卵巢组织异种移植的因素及近年来的研究进展作一综述。

**【关键词】** 异种移植; 人类; 卵巢组织

**Influencing factors and research progress of the human ovarian tissue xenotransplantation** Wang Lin,  
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**【Abstract】** Human ovarian tissue xenotransplantation emerges as widely used experimental animal model to investigate the various aspects of follicle development and the effect of other related interventions of fertility preservations such as cryopreservation. There are many factors influence the effect of xenotransplantation, such as animal recipient, ovarian tissue preparation, vascular supply after transplantation and the use of gonadotropins. Although there is some evidence that this procedure might be effective in preservation of future female fertility and restoring ovarian endocrine and reproductive function, it should only be performed under experimental conditions, until the technique is found to be safe and ethical. This article reviews the factors affecting the xenotransplantation of human ovarian tissue and the recent progress in this paper.

**【Key words】** Xenotransplantation; Humans; Ovarian tissue

## 母-胎肠道内微生物群落以及母-胎微生物传输的研究进展

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**【摘要】** 妊娠胎盘、羊水、足月及早产儿胎便中均存在小型、多样性较低的微生物群落。研究表明这些肠道微生物群落组成与母体肠道、口腔微生物群落最为相似, 而且母体肠道微生物群落发生改变会引起胎儿肠道微生物群落的改变, 猜测肠道微生物的定植很可能发生在妊娠期, 并且可能存在母-胎之间微生物的传输通路。本研究就胎儿肠道微生物群落的发现及其国内外研究进展作一综述。

**【关键词】** 人体微生物组; 肠道微生物组; 胎儿微生物群落; 母-胎微生物传输

**Research progress on the maternal-fetal intestinal microbiome and maternal-fetal microbial transmission**

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**【Abstract】** There might be small and less diverse microbial communities in the placenta, amniotic fluid and meconium. Researches showed that these microbial communities were most similar to those of the oral cavity and intestinal canal. What's more, the fetal microbiome alters along with the change of maternal gut microbiome, which induces an hypothesis that the colonization of initial microorganism occurs before birth and there is a microbial transmission channel between mother and offspring. This article reviewed current researches on the fetal intestinal microbiome and maternal microbial transmission.