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• ART 子代安全性专栏 •

# PGT 活检技术对妊娠围产结局及子代健康影响的分析研究

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**【摘要】** 目的 探讨胚胎植入前遗传学检测(preimplantation genetic testing, PGT)技术对妊娠围产结局及子代健康的影响。方法 回顾性病例对照研究分析 2015 年 1 月至 2021 年 8 月期间在海军军医大学第二附属医院生殖医学中心进行 PGT 和卵胞质内单精子注射(intracytoplasmic sperm injection, ICSI)助孕、冷冻复苏周期单囊胚移植的患者资料, 纳入 882 例患者, 共行 1 081 个冻融胚胎移植(frozen-thawed embryo transfer, FET)周期。其中 PGT 组 399 例患者, 行 527 个周期, ICSI 组 483 例患者, 行 554 个周期。根据 PGT 技术指征不同, 将 PGT 组又分为染色体结构异常检测/单基因遗传学检测(PGT for structural rearrangements/monogenic defects/single gene defects monogenic, PGT-SR/M)亚组和胚胎染色体非整倍体检测(PGT for aneuploidies, PGT-A)亚组, 分别与 ICSI 组比较临床妊娠率、流产率、活产率。对移植后临床妊娠者进行分析, 以活产作为观察终点, 其中 PGT-SR/M 亚组共 102 例行 189 个周期, PGT-A 亚组共 184 例行 338 个周期, ICSI 组 268 例, 分别比较围产结局以及子代安全性。结果 PGT-SR/M 亚组的临床妊娠率[71.96%(136/189)]高于 ICSI 组[61.73%(342/554),  $P=0.011$ ], 而 PGT-A 亚组的临床妊娠率[64.50%(218/338)]与 ICSI 组差异无统计学意义( $P>0.05$ )。PGT-SR/M 亚组与 PGT-A 亚组的活产率高于 ICSI 组, 但差异均无统计学意义(均  $P>0.05$ )。各组间流产率、早产率、妊娠并发症发生率差异均无统计学意义(均  $P>0.05$ )。另外, PGT-SR/M 亚组与 PGT-A 亚组在新生儿低出生体重率、巨大儿出生率、出生缺陷发生率等方面差异也均无统计学意义(均  $P>0.05$ )。PGT 组儿童 2 岁内的生长发育曲线正常, 与 ICSI 组相比, PGT 组的身高和体质量差异均无统计学意义(均  $P>0.05$ )。结论 相同授精方式下, 侵入性的胚胎活检操作并未增加妊娠围产相关并发症的发生, 而且, 暂未发现 PGT 对子代的生长发育有不利影响。

【关键词】 胚胎植入前遗传学检测； 精子注射，细胞质内； 早产； 低出生体质量； 出生缺陷

基金项目：国家自然科学基金面上项目（82271662）

### Effect of PGT biopsy on perinatal outcome and offspring health

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**【Abstract】 Objective** To explore the effect of preimplantation genetic testing (PGT) on perinatal outcome and offspring health. **Methods** Retrospective case-control analysis was made on the data of patients undergoing PGT and intracytoplasmic sperm injection (ICSI) assisted pregnancy and single blastocyst transplantation in Reproductive Medicine Center of the Second Affiliated Hospital of Naval Medical University from January 2015 to August 2021. A total of 882 patients were included and 1 081 cycles of frozen-thawed embryo transfer (FET) were performed. Among them, 399 patients in the PGT group underwent 527 cycles, and 483 patients in the ICSI group underwent 554 cycles. According to the different indications of PGT technology, they were divided into PGT for structural rearrangements/monogenic defects/single gene defects monogenic (PGT-SR/M) subgroup and PGT for aneuploidies (PGT-A) subgroup. The clinical pregnancy rate, the abortion rate and the live birth rate were compared with those in the ICSI group. The clinical pregnancy after transplantation was analyzed, and the live birth was taken as the observation end point. There were 102 cases in the PGT-SR/M subgroup, 184 cases in the PGT-A subgroup, and 268 cases in the ICSI group. The perinatal outcome and the safety of offspring were compared respectively. **Results** The clinical pregnancy rate in the PGT-SR/M subgroup [71.96% (136/189)] was higher than that in the ICSI group [61.73% (342/554),  $P=0.011$ ], while there was no statistically significant difference between the PGT-A subgroup [64.50% (218/338)] and the ICSI group ( $P>0.05$ ). The live birth rate of both PGT-SR/M subgroup and PGT-A subgroup was higher than that of the ICSI group, but the differences were not statistically significant (all  $P>0.05$ ). There were no statistically significant differences in the rates of miscarriage, premature birth, and pregnancy complications among the groups (all  $P>0.05$ ). In addition, there were no statistically significant differences between the PGT-SR/M subgroup and the PGT-A subgroup in terms of low birth weight rate, macrosomia birth rate, and the incidence of birth defect (all  $P>0.05$ ). The growth and development curve of children in the PGT group was normal within 2 years of age, and there were no statistically significant differences in height and weight between the PGT group and the ICSI group (all  $P>0.05$ ). **Conclusion** Under the same fertilization method, invasive embryo biopsy procedures did not increase the incidence of perinatal complications during pregnancy, and no adverse effects of PGT on the growth and development of offspring have been found.

【 Key words 】 Preimplantation genetic testing; Sperm injection, intracytoplasmic; Preterm birth; Low birth weight; Birth defect

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• ART 子代安全性专栏 •

# 人类辅助生殖技术单胎活产的围产期结局: 一项回顾性倾向性评分匹配队列研究

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【摘要】 目的 比较人类辅助生殖技术(assisted reproductive technology, ART)助孕与自然妊娠(spontaneously conceived, SC)孕产妇单胎活产的围产期结局。方法 本研究为回顾性队列研究,收集了2008年至2019年期间于郑州大学第三附属医院产科分娩且获得单胎活产的孕产妇住院病案资料,纳入了1727例行ART助孕的产妇,并按照1:3的比例匹配同一天分娩的5181例SC产妇。按分娩时间匹配后再采用1:1倾向性评分匹配法(propensity score matching, PSM)对两组人群的基线数据进行匹配,最终ART组和SC组各纳入产妇1439例。主要结局指标为健康活产儿率,次要结局指标为妊娠期高血压疾病发生率、妊娠期糖尿病发生率、早产率等围产期结局。结果 进行PSM之后,ART组健康活产儿比例[70.67% (1017/1439)]较SC组[77.28% (1112/1439)]低( $P<0.001$ );两组间的妊娠并发症发生率,包括妊娠期糖尿病发生率、妊娠期肝内胆汁淤积综合征发生率、妊娠期甲状腺功能异常发生率、羊水过少发生率、前置胎盘发生率、剖宫产率和胎盘效率差异均存在统计学意义(均 $P<0.05$ );两组间的新生儿结局,包括孕周、早产率、极早产率、小于孕龄儿发生率以及新生儿重症监护病房(neonatal intensive care unit, NICU)住院率差异均存在统计学意义(均 $P<0.05$ )。多因素logistic回归分析的结果显示,ART助孕和妊娠并发症是健康活产儿的危险因素

( $OR=0.81$ , 95%  $CI$ : 0.67~0.97,  $P=0.020$ ), 胎盘效率是健康活产儿的保护因素 ( $OR=1.73$ , 95%  $CI$ : 1.59~1.88,  $P<0.001$ )。结论 SC 产妇的围产期结局较 ART 助孕更安全。

【关键词】 生殖技术, 辅助; 自然妊娠; 单胎活产; 围产期结局

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## Perinatal outcomes of singleton live birth resulting from human assisted reproductive technology: a retrospective propensity score matching cohort study

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**【Abstract】 Objective** To compare perinatal outcomes of singleton live births between human assisted reproductive technology (ART) and spontaneously conceived (SC). **Methods** This study was a retrospective cohort study, collecting data on patients who delivered and obtained singleton live birth in the Obstetrics Department of the Third Affiliated Hospital of Zhengzhou University between 2008 and 2019. A total of 1 727 ART patients were included in this study, and 5 181 SC patients who delivered during the same day were matched at a ratio of 1 : 3. After matching according to delivery time, the baseline data of the two groups were matched using 1 : 1 propensity score matching (PSM), and finally 1 439 patients were included in the ART and SC groups, respectively. The primary outcome measure was the healthy baby rate, and the secondary outcome measures were perinatal outcomes such as the incidences of hypertensive disorders of pregnancy, gestational diabetes and preterm delivery rate. **Results** After PSM, healthy baby rate was lower in the ART group compared with the SC group [77.28% (1 112/1 439) vs. 70.67% (1 017/1 439),  $P<0.001$ ]. Pregnancy complications, including the incidence of gestational diabetes, intrahepatic cholestasis syndrome during pregnancy, abnormal thyroid function during pregnancy, oligohydramnios, placenta previa, cesarean delivery, and placental efficiency, were statistically different between the two groups (all  $P<0.05$ ). The neonatal outcomes, including gestational age, preterm delivery rate, very preterm delivery rate, incidence of small for gestation age and neonatal intensive care unit admission rate were statistically different between the two groups (all  $P<0.05$ ). The results of multivariate logistic regression analysis showed that ART and pregnancy complications were risk factors for healthy baby ( $OR=0.81$ , 95%  $CI$ : 0.67~0.97,  $P=0.020$ ), however, placental efficiency was a protective factor for healthy baby ( $OR=1.73$ , 95%  $CI$ : 1.59~1.88,  $P<0.001$ ). **Conclusion** Perinatal outcomes were safer in the SC group than in the ART group.



**【Keywords】** Reproductive techniques, assisted; Spontaneously conceived; Singleton live births; Perinatal outcomes

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## • ART 子代安全性专栏 •

# 整倍体囊胚发育天数对母婴结局的影响

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**【摘要】** 目的 探究整倍体囊胚的发育天数是否对孕产期并发症及新生儿结局存在影响。方法 回顾性队列研究分析 2017 年 10 月至 2021 年 6 月期间在上海交通大学医学院附属仁济医院生殖医学中心进行胚胎植入前非整倍体遗传学检测 (preimplantation genetic testing for aneuploidies, PGT-A), 移植整倍体单囊胚并获得单胎活产的 893 例患者的临床资料。按照移植囊胚的发育天数, 将患者分为第 5 天 (day 5, D5) 组 ( $n=768$ ) 及第 6 天 (day 6, D6) 组 ( $n=125$ )。采用 2:1 倾向性评分匹配 (propensity score matching, PSM) 方法对两组的女方年龄、体质指数 (body mass index, BMI)、不孕年限进行匹配, 匹配后纳入 D5 组 250 例, D6 组 125 例。比较两组患者的基线特征、取卵和移植周期特征、孕产期并发症及新生儿结局。同时, 根据女方年龄将患者进一步分为 <35 岁组和  $\geq 35$  岁组进行分层分析。结果 PSM 后 D5 组与 D6 组女方年龄、BMI、不孕年限、助孕指征等基线特征差异均无统计学意义 (均  $P>0.05$ )。两组获卵数和双原核 (two pronuclei, 2PN) 数差异均无统计学意义 (均  $P>0.05$ ), 但 D5 组冷冻胚胎数 [5.00 (3.00, 7.00) 个] 较 D6 组多 [3.00 (2.00, 5.00) 个,  $P<0.001$ ]。D5 组移植优质胚胎的周期占比 [81.6% (204/250)] 较 D6 组高 [40.0% (50/125),  $P<0.001$ ]。两组的妊娠期糖尿病、妊娠期高血压疾病、妊娠期甲状腺疾病、早产、未足月胎膜早破、胎盘相关疾病及产后出血的发生率差异均无统计学意义 (均  $P>0.05$ )。两组的新生儿出生体质量、胎龄、性别、低出生体质量、巨大儿、小于胎龄儿、大于胎龄儿及出生缺陷发生率等差异均无统计学意义 (均  $P>0.05$ )。根据年龄的分层分析

显示,不同年龄层中 D5 组和 D6 组母婴结局差异均无统计学意义(均  $P>0.05$ )。  
结论 整体倍体囊胚的发育天数对孕产期并发症及新生儿结局无显著影响。

【关键词】 囊胚移植; 孕产期并发症; 新生儿结局; 胚胎植入前非整倍体遗传学检测; 囊胚发育天数

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## Effect of blastulation time on maternal and neonatal outcomes following single euploid blastocyst transfer

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【Abstract】 **Objective** To investigate whether blastulation time would impact maternal and neonatal outcomes following single euploid blastocyst transfer.

**Methods** A retrospective cohort study was conducted at the Centre for Reproductive Medicine of Renji Hospital, Shanghai Jiao Tong University School of Medicine between October 2017 and June 2021. Totally 893 patients who received preimplantation genetic testing for aneuploidies (PGT-A) and delivered singleton live birth after frozen single euploid blastocyst transfer were included. Patients were divided into day 5 (D5) group ( $n=768$ ) and day 6 (D6) group ( $n=125$ ) according to timing of blastulation. Propensity score matching (PSM) with a ratio of 2 : 1 was conducted to balance potential confounding factors including female age, body mass index (BMI) and infertility duration. After PSM, there were 250 patients in D5 group and 125 patients in D6 group. Basic characteristics, ovarian stimulation and embryo transfer cycle characteristics, pregnancy complications and neonatal outcomes of the two groups were compared. Furthermore, patients were divided into <35 years old group and  $\geq 35$  years old group by maternal age to conduct stratified analysis.

**Results** There were no statistically significant differences in the baseline characteristics including female age, BMI, infertility duration and indication for infertility treatment between the two groups after PSM (all  $P>0.05$ ). The number of oocytes retrieved and the number of two pronuclei (2PN) did not differ between the two groups (all  $P>0.05$ ), while the number of embryos cryopreserved was significantly increased in D5 group than in D6 group [5.00 (3.00, 7.00) vs. 3.00 (2.00, 5.00),  $P<0.001$ ]. The proportion of cycles transferring good-quality embryos was significantly higher in D5 group than in D6 group [81.6% (204/250) vs. 40.0% (50/125),  $P<0.001$ ]. No significant differences were observed in the incidences of gestational diabetes, hypertensive disorders of pregnancy, thyroid diseases during pregnancy, premature preterm rupture of membranes, preterm delivery, placenta disorder and postpartum hemorrhage between the two groups (all  $P>0.05$ ). The birth weight, gestational age, neonate sex, the incidences of low birth weight,

macrosomia, small for gestational age, large for gestational age and birth defects did not differ as well (all  $P>0.05$ ). In stratified analysis, there were no significant differences in maternal and neonatal outcomes between D5 group and D6 group for women who aged  $<35$  years or  $\geq 35$  years (all  $P>0.05$ ). **Conclusion** Timing of blastulation in euploid blastocysts does not impact maternal and neonatal outcomes.

**【Key words】** Blastocyst transfer; Pregnancy complications; Neonatal outcomes; Preimplantation genetic testing for aneuploidies; Timing of blastulation

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## 剖宫产史对体外受精-胚胎移植妊娠结局影响的 meta 分析

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**【摘要】** 目的 系统评价剖宫产史对体外受精-胚胎移植 (*in vitro* fertilization and embryo transfer, IVF-ET) 妊娠结局的影响。方法 计算机检索 PubMed、Web of Science、Cochrane Library、Embase、Ovid 数据库、万方数据库、中国期刊全文数据库、维普中文科技期刊数据库及中国生物医学文献数据库, 搜索关于剖宫产史患者进行 IVF-ET 助孕的文献, 检索时间为建库至 2022 年 8 月。经文献筛选及资料提取后, 采用 Stata16.0 软件进行 meta 分析。结果 纳入符合标准的文献共 20 篇, 患者 24 753 例。剖宫产组患者 IVF-ET 的种植率、临床妊娠率及活产率显著低于顺产组降低 ( $OR=0.79$ , 95%  $CI$ : 0.66~0.95,  $P=0.013$ ;  $OR=0.72$ , 95%  $CI$ : 0.63~0.83,  $P<0.001$ ;  $OR=0.73$ , 95%  $CI$ : 0.64~0.83,  $P<0.001$ ), 而早期流产率高于顺产组, 差异均有统计学意义 ( $OR=1.18$ , 95%  $CI$ : 1.07~1.30,  $P=0.001$ )。亚组分析结果显

示,剖宫产后切口憩室(previous cesarean scar defect, PCSD)患者的种植率、临床妊娠率及活产率比顺产组显著降低( $OR=0.47$ , 95%  $CI$ : 0.31~0.73,  $P=0.001$ ;  $OR=0.47$ , 95%  $CI$ : 0.30~0.72,  $P=0.001$ ;  $OR=0.41$ , 95%  $CI$ : 0.26~0.65,  $P<0.001$ ),而早期流产率显著增加( $OR=2.38$ , 95%  $CI$ : 1.12~5.09,  $P=0.023$ )。结论 剖宫产史显著降低 IVF-ET 的种植率、临床妊娠率及活产率,增加早期流产率,且可能与 PCSD 相关。受纳入研究的质量和数量的限制,上述结论还需要更多大样本、高质量的研究予以验证。

【关键词】 剖宫产; 受精,体外; 胚胎移植; 妊娠结局; 剖宫产后切口憩室

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### **Influence of previous caesarean section on reproductive outcomes of *in vitro* fertilization and embryo transfer: a meta-analysis**

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【Abstract】 **Objective** To systematically evaluate the effect of previous cesarean section (CS) on pregnancy outcome of *in vitro* fertilization and embryo transfer (IVF-ET). **Methods** PubMed, Web of Science, Cochrane Library, Embase, Ovid, Wanfang database, CNKI, VIP database and CBM were searched from inception to August 2022 to collect studies about the effect of CS on pregnancy outcome of IVF-ET. Meta-analysis was performed by Stata16.0 software after information extraction. **Results** A total of 20 studies involving 24 753 patients were included. Meta-analysis displayed that the implantation rate, the clinical pregnancy rate and the live birth rate of CS group were significantly lower than those of vaginal delivery (VD) group ( $OR=0.79$ , 95%  $CI$ : 0.66–0.95,  $P=0.013$ ;  $OR=0.72$ , 95%  $CI$ : 0.63–0.83,  $P<0.001$ ;  $OR=0.73$ , 95%  $CI$ : 0.64–0.83,  $P<0.001$ ), accompanied by increased early abortion rate ( $OR=1.18$ , 95%  $CI$ : 1.07–1.30). The results of subgroup analysis showed that compared with VD group, the implantation rate, the clinical pregnancy rate and the premature birth rate of patients with previous cesarean scar defect (PCSD) were significantly reduced ( $OR=0.47$ , 95%  $CI$ : 0.31–0.73,  $P=0.001$ ;  $OR=0.47$ , 95%  $CI$ : 0.30–0.72,  $P=0.001$ ;  $OR=0.41$ , 95%  $CI$ : 0.26–0.65,  $P<0.001$ ), while the early abortion rate was significantly increased ( $OR=2.38$ , 95%  $CI$ : 1.12–5.09,  $P=0.023$ ). **Conclusion** CS significantly reduced the implantation rate, the clinical pregnancy rate and the live birth rate of IVF-ET, and increased the early abortion rate, which might be associated with PCSD. However, due to the quantity and quality of the included studies, the above conclusion needs to be verified by more large-sample and high-quality studies.

【Key words】 Cesarean section; Fertilization *in vitro*; Embryo transfer; Pregnancy outcome; Previous cesarean scar defect

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# 2010—2019 年北京市辅助生殖技术助孕后子代出生缺陷发生情况分析

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**【摘要】** 目的 调研 2010—2019 年北京市辅助生殖技术 (assisted reproductive technology, ART) 子代出生缺陷的发生情况及变化趋势。方法 对北京市开展人类 ART 的机构进行回顾性观察研究, 共收集到 8 家机构 2010 年 1 月 1 日至 2019 年 12 月 31 日共 389 978 个 ART 治疗周期的随访结果及出生缺陷的发生情况。结果 共有 1 367 个 ART 周期存在出生缺陷, 出生缺陷发生率为 120.87/万; 其中循环系统畸形最常见。流产周期发生出生缺陷的年均增速 (108.36%) 略高于分娩周期 (103.77%)。人工授精的出生缺陷发生率 (123.15/万) 与体外受精技术 (105.23/万) 的差异无统计学意义 ( $P=0.097$ )。结论 近 10 年, 北京市 8 家生殖中心 ART 助孕后子代出生缺陷发生率呈逐年上升趋势。应进一步加强落实出生缺陷三级预防策略, 减少出生缺陷儿的分娩。

**【关键词】** 生殖技术, 辅助; 出生缺陷; 发生率; 趋势

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## Analysis on birth defects in offspring after assisted reproductive technology in Beijing from 2010 to 2019

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**【Abstract】 Objective** To investigate the incidence rate and development trend of birth defects in offspring after assisted reproductive technology (ART) in Beijing from 2010 to 2019. **Methods** The institutions that carry out ART in Beijing were retrospectively investigated. The follow-up outcomes and the incidence of birth defects in a total of 389 978 ART treatment cycles were collected from 8 ART institutions between January 1, 2010 to December 31, 2019. **Results** There were 1 367 ART pregnancies with birth defects, and the overall incidence rate was 120.87/10 000. The most common anomalies were malformations of circulatory system. The annual increase in birth defects was slightly higher during the pregnancy loss cycles (108.36%) than during the delivery cycles (103.77%). There was no significant difference in the prevalence of birth defects between artificial insemination (123.15‰) and *in vitro* fertilization technology (105.23‰,  $P=0.097$ ). **Conclusion** In recent 10 years, the incidence rate of birth defects in offspring conceived by ART at 8 reproductive centers in Beijing showed an increasing trend. The implementation of the tertiary prevention strategy of birth defects should be further strengthened to reduce the number of newborns with birth defects.

**【Key words】** Reproductive techniques, assisted; Birth defects; Incidence rate; Trend

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## 卵胞质内单精子注射技术有效性及其对子代安全性影响的研究进展

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**【摘要】** 卵胞质内单精子注射 (intracytoplasmic sperm injection, ICSI) 技术是目前主要的人类辅助生殖技术 (assisted reproductive technology, ART) 之一。该项技术通过显微操作系统将单个精子注入卵子, 有效地解决了少弱畸形精子症等男性因素相关的不育问题, 在全世界产出数百万儿童。目前, 越来越多非男性因素不孕症也采用 ICSI 技术。然而, 不同于常规体外受精 (*in vitro* fertilization, IVF) 更自然的精卵结合, ICSI 技术具有有创性, 其安全性受到了人们的关注。本文旨在对 ICSI 的临床结局及其对子代的影响进行系统综述, 从而为 ICSI 技术的有效性及其对子代安全性问题提供线索和依据。

**【关键词】** 生殖技术, 辅助; 精子注射, 细胞质内; 受精; 治疗结果

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## Research progress on the effectiveness and offspring safety of intracytoplasmic sperm injection technology

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**【Abstract】** Intracytoplasmic sperm injection (ICSI) is one of the main techniques in assisted reproductive technology (ART) currently. By injecting a single sperm into the egg through microscopy system, ICSI can solve the problem of infertility due to male factors effectively, such as oligoasthenoterazoospermia, producing millions of children around the world. Nowadays, more and more couples with non-male factor infertility use ICSI as well. However, unlike conventional *in vitro* fertilization (IVF), ICSI technology is invasive and its safety has attracted attention. We systematically reviewed the clinical outcomes of ICSI and its effects on offspring, so as to provide clues and bases for the effectiveness and offspring safety of ICSI.

**【Key words】** Reproductive techniques, assisted; Sperm injections, intracytoplasmic; Fertilization; Treatment outcome

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## • ART 子代安全性专栏 •

# 辅助生殖技术对后代神经精神健康影响的研究进展

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**【摘要】** 辅助生殖技术 (assisted reproductive technology, ART) 在治疗不孕症、支持人口发展方面作出了巨大的贡献。尽管它通常被认为是安全的, 但越来越多的研究提示, 因其非生理性的体外操作, 非自然的发育环境、施于配子与胚胎发育的关键时期等背景, ART 可能会给后代带来各种近远期的健康风险。研究认为, ART 可能影响后代神经精神健康, 包括增加脑瘫、癫痫、自闭症等神经、精神疾病的患病风险, 影响认知发展、学业表现等。本文综述了 ART 对后代神经发育障碍、神经疾病、精神疾病的影响, 为防治精神和神经疾病、提升辅助生殖后代安全性提供新方向。

**【关键词】** 生殖技术, 辅助; 神经发育障碍; 神经认知障碍

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**Research progress on the risk of neurological and psychiatric disorders in offspring born from assisted reproductive technology**

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**【Abstract】** Assisted reproductive technology (ART) has made a great contribution to treat infertility and support population development. However, more and more studies have found that ART may bring various short-term and long-term health risks to the offspring due to its non-physiological *in vitro* operation, unnatural reproductive characteristics, and application in the critical period of gametes and embryonic development. Studies have found that the key operations of ART may affect the neurological and psychiatric health of offspring, including disease risk and academic performance, through affecting the gamete, the epigenetic regulatory program of the embryo, and the hormonal environment. This article reviewed the effects of ART on neurodevelopmental disorders, neurological diseases, and mental diseases in offspring, providing new ideas for the prevention and treatment of mental and neurological diseases and improving the safety of assisted reproduction.

**【Key words】** Reproductive techniques, assisted; Neurodevelopmental disorders; Neurocognitive disorders

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• ART 子代安全性专栏 •

## 辅助生殖技术对子代发育源性糖脂代谢病发生 风险影响的研究进展

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**【摘要】** 近年来, 辅助生殖技术 (assisted reproductive technology, ART) 已经成为支撑人口发展的重要技术。虽然 ART 解决了部分不孕不育患者“生不出”的问题, 但因其非生理性的体外操作, ART 对子代近远期健康的影响仍存在争议。

已有研究显示, ART 各关键操作可能通过影响配子、胚胎的表观遗传调控程序增加子代出生后糖脂代谢病的发生。本文将系统阐述控制性超促排卵、胚胎体外培养、卵子体外成熟培养、卵胞质内单精子注射、胚胎冷冻和胚胎植入前遗传学检测等 ART 关键操作环节对子代发育源性糖脂代谢病发生风险的影响, 为改良 ART 诊疗策略、提升 ART 子代安全性提供新思路。

【关键词】 生殖技术, 辅助; 肥胖; 糖脂代谢病; 发育源性疾病; 表观遗传

基金项目: 国家重点研发计划 (2022YFC2703500); 浙江省重点研发计划 (2021C03098)

## Research progress on the effects of assisted reproductive technology on the risk of offspring developmental glycolipid metabolic disease

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【Abstract】 In recent years, assisted reproductive technology (ART) has become an integral part of modern medicine and now plays a key role in population growth. Although ART has solved the problem of "no child" among some infertile couples, the short-term and long-term health outcomes of offspring conceived by ART is still controversial due to its non-physiological operating conditions. It has been found that the key procedures of ART may increase offspring's risk of developmental glycolipid metabolic disease by resetting epigenetic memory in gamete and embryo early development. This article systematically described the effects of controlled ovulation hyperstimulation, *in vitro* embryo culture, *in vitro* oocyte maturation, intracytoplasmic sperm injection, embryo cryopreservation and preimplantation genetic testing on offspring's risk of developmental glycolipid metabolic diseases, to provide new ideas for confirming offspring safety and improving the therapeutic strategy of assisted reproduction

【Key words】 Reproductive techniques, assisted; Obesity; Glycolipid metabolic diseases; Developmental origins of diseases; Epigenetic inheritance

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• 临床研究 •

# 高雄激素血症对 PCOS 患者新鲜周期胚胎移植妊娠结局的影响

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**【摘要】** 目的 探究高雄激素血症对多囊卵巢综合征 (polycystic ovarian syndrome, PCOS) 患者进行新鲜周期移植后妊娠结局的影响。方法 回顾性队列研究分析 2015 年 1 月至 2019 年 12 月期间在北京大学第三医院妇产科生殖医学中心进行新鲜胚胎移植助孕的 876 例 PCOS 患者的临床资料, 根据助孕治疗前血清雄激素水平是否升高 (血清睾酮 $\geq 2.53$  nmol/L 或/和雄烯二酮 $\geq 11.5$  nmol/L) 分为高雄激素组 ( $n=274$ ) 及非高雄激素组 ( $n=602$ ), 比较两组患者妊娠结局, 观察高雄激素血症对早期流产及早产妊娠结局的影响。结果 高雄激素组患者年龄 [ $30.23\pm 3.63$ ] 岁、体质量指数 [ $25.66\pm 4.16$ ] kg/m<sup>2</sup>、黄体生成素/卵泡刺激素水平 ( $1.38\pm 0.95$ ) 与非高雄激素组患者 [ $31.22\pm 3.76$ ] 岁,  $P<0.001$ ; ( $24.45\pm 4.06$ ) kg/m<sup>2</sup>,  $P<0.001$ ;  $0.99\pm 2.06$ ,  $P=0.004$ ] 相比, 差异均有统计学意义。高雄激素组早期流产率 [ $28.8\%$  ( $79/274$ )]、早产率  $19.6\%$  ( $32/163$ ) 与非高雄激素组 [ $18.8\%$  ( $113/602$ ),  $P=0.001$ ;  $8.9\%$  ( $41/459$ ),  $P<0.001$ ] 相比明显升高, 活产率  $59.5\%$  ( $163/274$ ) 比非高雄激素组 [ $76.2\%$  ( $459/602$ ),  $P<0.001$ ] 明显下降。多因素分析调整混杂因素后结果仍具有统计学意义, 高雄激素组患者活产率明显下降 (aOR=2.248, 95% CI: 1.641~3.080), 早期流产风险 (aOR=1.869, 95% CI: 1.329~2.630)、早产风险 (aOR=0.403, 95% CI: 0.240~0.675) 明显增加。高雄激素是早期流产、活产和早产的独立影响因素。结论 高雄激素血症增加 PCOS 患者辅助生殖助孕后早期流产及早产风险, 降低活产率。

**【关键词】** 高雄激素血症; 多囊卵巢综合征; 胚胎移植; 早期流产; 早产; 活产

基金项目: 北京市科技计划 (Z191100006619085)

## Effect of hyperandrogenism on pregnancy outcomes of fresh cycle embryo transfer in patients with polycystic ovary syndrome

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**【Abstract】 Objective** To explore the effect of hyperandrogenism on the reproductive outcomes of patients with polycystic ovarian syndrome (PCOS). **Methods** This retrospective cohort study enrolled 876 patients with PCOS who underwent fresh *in vitro* fertilization/intracytoplasmic sperm injection at the

Reproductive Medicine Center of Department of Obstetrics and Gynecology, Peking University Third Hospital. The patients were divided into hyperandrogenism group ( $n=274$ ) and non-hyperandrogenism group ( $n=602$ ) according to the androgen serum androgen levels (serum testosterone  $\geq 2.53$  nmol/L or/and androstenedione  $\geq 11.5$  nmol/L). The pregnancy outcomes of women with and without hyperandrogenism were compared. Multiple logistic regression models were used to eliminate essential impacts on early miscarriage and preterm birth outcomes. **Results** There were significant differences in the age [ $(30.23 \pm 3.63)$  years vs.  $(31.22 \pm 3.76)$  years,  $P < 0.001$ ], body mass index [ $(25.66 \pm 4.16)$  kg/m<sup>2</sup> vs.  $(24.45 \pm 4.06)$  kg/m<sup>2</sup>,  $P < 0.001$ ], luteinizing hormone/follicle-stimulating hormone ( $1.38 \pm 0.95$  vs.  $0.99 \pm 2.06$ ,  $P = 0.004$ ) of patients between hyperandrogenism group and non-hyperandrogenism group (all  $P < 0.05$ ). Patients in hyperandrogenism group had higher rates of early miscarriage [28.8% (79/274) vs. 18.8% (113/602),  $P = 0.001$ ], preterm birth [19.6% (32/163) vs. 8.9% (41/459),  $P < 0.001$ ] and lower rate of live birth [59.5% (163/274) vs. 76.2% (459/602),  $P < 0.001$ ] than those of non-hyperandrogenism group. After multivariate analysis adjusted for confounding factors including age, the conclusion remained unchanged. Compared with non-hyperandrogenism group, the live birth rate in hyperandrogenism group was significantly decreased (aOR=2.248, 95% CI: 1.641-3.080), while the risks of early miscarriage (aOR=1.869, 95% CI: 1.329-2.630) and preterm birth (aOR=0.403, 95% CI: 0.240-0.675) in hyperandrogenism group were significantly increased. Hyperandrogenism was an independent factor for the above pregnancy outcomes. **Conclusion** PCOS patients with hyperandrogenism may have higher rates of early miscarriage and preterm birth than those without hyperandrogenism, with decreases in the rate of live birth.

**【 Key words 】** Hyperandrogenism; Polycystic ovary syndrome; Embryo transfer; Miscarriage; Preterm birth; Live birth

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• 临床研究 •

## 人工周期冻融单囊胚移植前口服雌激素时间不影响单胎子代出生结局

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**【摘要】** 目的 探讨人工周期冻融胚胎移植(frozen-thawed embryo transfer, FET)中, 孕酮应用前口服雌激素时间对单胎子代出生结局的影响。方法 采用回顾性队列研究, 分析 2015 年 1 月至 2019 年 12 月期间在郑州大学第三附属医院生殖医学科行体外受精(*in vitro* fertilization, IVF)或卵胞质内单精子注射(intracytoplasmic sperm injection, ICSI)助孕, 全胚冷冻第一次行 FET 周期的患者临床资料。患者均采用人工周期准备子宫内膜, 分析单囊胚移植且分娩单胎子代周期。根据孕酮转化子宫内膜前口服雌激素时间, 将所有 FET 周期分为四组:  $\leq 12$  d ( $n=306$ )、13~15 d ( $n=620$ )、16~18 d ( $n=471$ )和 $\geq 19$  d ( $n=275$ )。主要观察指标为小于胎龄儿(small for gestational age, SGA)发生率, 次要观察指标为早产、低出生体质量、巨大儿和大于胎龄儿(large for gestational age, LGA)发生率。结果 共纳入 1 672 个单囊胚移植且单胎分娩 FET 周期。四组间 SGA 的发生率分别为 7.8% (24/306)、4.8% (30/620)、5.7% (27/471)和 7.6% (21/275), 差异无统计学意义( $P=0.204$ )。多元逻辑回归分析结果显示孕酮应用前雌激素使用时间不影响单胎子代 SGA 的发生率(以 $\leq 12$  d 为参照, 13~15 d: aOR=1.37, 95% CI: 0.70~2.70,  $P=0.361$ ; 16~18 d: aOR=0.74, 95% CI: 0.40~1.36,  $P=0.336$ ;  $\geq 19$  d: aOR=0.81, 95% CI: 0.44~1.49,  $P=0.501$ )。四组间新生儿早产率( $P=0.204$ )、低出生体质量( $P=0.582$ )、巨大儿( $P=0.201$ )和 LGA ( $P=0.335$ )的发生率差异均无统计学意义。结论 在人工周期 FET 中, 孕酮应用前口服雌激素时间不影响单囊胚移植单胎子代出生结局。

**【关键词】** 婴儿, 小于胎龄; 冻融胚胎移植; 人工周期

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## Duration of oral administration of estrogen does not affect the outcome of singleton offspring outcomes in single frozen blastocyst transfer cycles

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**【Abstract】 Objective** To explore whether the duration of oral estrogen treatment before progesterone application affects neonatal outcome in single frozen-thawed embryo transfer (FET) with artificial cycles. **Methods** It was a retrospective cohort study. Patients who underwent *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI), receiving single frozen blastocyst transfer with artificial cycle and delivering a single live birth in the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University between January 2015 and December 2019 were included. All FET cycles were divided into four groups according to the estrogen treatment duration before progesterone application,  $\leq 12$

d ( $n=306$ ), 13–15 d ( $n=620$ ), 16–18 d ( $n=471$ ), and  $\geq 19$  d ( $n=275$ ). Primary outcome was the incidence of small for gestational age (SGA). Secondary outcomes were the incidence of preterm birth, low birth weight, macrosomia and large for gestational age (LGA). **Results** A total of 1 672 single blastocyst transfer cycles were included. The incidence of SGA among the four groups was 7.8% (24/306), 4.8% (30/620), 5.7% (27/471), and 7.6% (21/275), respectively, with no statistically significant difference ( $P=0.204$ ). The results of multiple logistic regression analysis showed that the duration of estrogen used before progesterone application did not affect the incidence of SGA in singleton offspring (with  $\leq 12$  d as the reference, 13–15 d: aOR=1.37, 95% CI: 0.70–2.70,  $P=0.361$ ; 16–18 d: aOR=0.74, 95% CI: 0.40–1.36,  $P=0.336$ ;  $\geq 19$  d: aOR=0.81, 95% CI: 0.44–1.49,  $P=0.501$ ). There were no significant differences in neonatal preterm birth rate ( $P=0.204$ ), low birth weight ( $P=0.582$ ), incidences of macrosomia ( $P=0.201$ ) and LGA infants ( $P=0.335$ ) among the four groups. **Conclusion** In artificial FET cycle, the duration of oral estrogen treatment before progesterone application does not affect the outcome of singleton offspring after single blastocyst transfer.

**【Key words】** Infant, small for gestational age; Frozen-thawed embryo transfer; Artificial cycle

**Fund program:** 2021 Henan Province Medical Science and Technology Research and Joint Construction Project (LHGJ20210441, LHGJ20210451)

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• 流行病学研究 •

## 孕前女性邻苯二甲酸酯暴露水平与生育力关联的巢式病例对照研究

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**【摘要】** 目的 探究孕前女性 7 种典型的邻苯二甲酸酯代谢物暴露水平与生育力的关联。方法 基于孕前队列, 开展巢式病例对照研究, 选取 2016 年至 2020 年在上海市嘉定区妇幼保健院招募计划备孕的孕前夫妇, 其中 100 例妊娠等待时间 (time to pregnancy, TTP) >12 个月即不孕症作为病例组, 随机抽取 TTP≤12 个月的 151 名女性作为对照组, 比较两组邻苯二甲酸酯各类代谢物的分布特征, 使用多因素二分类 logistic 回归模型和加权组合分位数回归模型分别评估典型的邻苯二甲酸酯 7 种代谢物对生育力的单独和联合影响。结果 病例组和对照组在孕前邻苯二甲酸单 (2-乙基己基) 酯 (mono- (2-ethylhexyl) phthalate, MEHP)、邻苯二甲酸单 (2-羧甲基) 己基酯 (mono- (2-carboxymethyl) -hexyl phthalate, MCMHP)、 $\Sigma$ DEHP [为 MEHP、MCMHP、邻苯二甲酸单 (2-乙基-5-氧己基) 酯、邻苯二甲酸单 (2-乙基-5-羟基己基) 酯和邻苯二甲酸单 (2-乙基-5-羧基己基) 酯检出浓度的和]、 $\Sigma$ PAE (7 种邻苯二甲酸酯代谢物检出浓度的和) 暴露水平方面差异均有统计学意义 ( $P=0.005$ ,  $P<0.001$ ,  $P=0.001$ ,  $P=0.007$ )。多因素二分类 logistic 回归模型显示与处于最低四分位数水平的女性相比, MEHP、MCMHP、 $\Sigma$ DEHP、 $\Sigma$ PAE 处于最高四分位数水平的女性不孕的风险增加 (aOR=2.40, 95% CI: 1.12~5.15,  $P=0.025$ ; aOR=7.74, 95% CI: 3.14~19.08,  $P<0.001$ ; aOR=4.35, 95% CI: 1.93~9.79,  $P<0.001$ ; aOR=2.04, 95% CI: 0.96~4.34,  $P=0.044$ )。加权组合分位数回归模型确定孕前 7 种邻苯二甲酸酯代谢物复合暴露是不孕的危险因素 ( $P<0.05$ ), 其中 MCMHP 贡献权重较大 (为 61.7%)。结论 育龄女性在备孕时应当重视环境中邻苯二甲酸酯的接触, 减少食用高度加工的食物以及使用塑料/聚氯乙烯材料包装的食品, 以提高人群生育力。

**【关键词】** 生育力; 孕前队列; 邻苯二甲酸酯; 巢式病例对照

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## Association between phthalate exposures and fecundity in preconception women: a nested case-control study

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**【Abstract】 Objective** To investigate the association between exposures of seven classic phthalate metabolites and fertility among preconception women before pregnancy. **Methods** Based on the preconception cohort, a nested case-control study was carried out. Preconception couples who were recruited from Shanghai Jiading District Maternal and Child Health Hospital from 2016 to 2020 with intention to conception were selected. A total of 100 women whose time to pregnancy (TTP) >12 months were selected as the case group, and 151 women with the TTP ≤12 months were randomly selected as control group. The single and joint effects on fertility of phthalate metabolites were analyzed by the comparison between the two groups via the multivariate binary logistic regression model, and the weighted quantile sum regression model. **Results** There were significant differences in mono-(2-ethylhexyl) phthalate (MEHP), mono-(2-carboxymethyl)-hexyl phthalate (MCMHP), the sum of the detected concentrations of MEHP, MCMHP, mono-(2-ethyl-5-oxohexyl) phthalate, mono-(2-ethyl-5-hydroxyhexyl) phthalate and mono-(2-ethyl-5-carboxypentyl) phthalate ( $\Sigma$ DEHP), and the sum of the detected concentrations of the seven phthalate metabolites ( $\Sigma$ PAE) exposure levels between the case group and control group ( $P=0.005$ ,  $P<0.001$ ,  $P=0.001$ ,  $P=0.007$ ). As shown by the multivariate binary logistic regression model, women with MEHP, MCMHP,  $\Sigma$ DEHP,  $\Sigma$ PAE at the highest quartile level were found to have significantly increased risk of infertility compared with women at the lowest quartile level (aOR=2.40, 95% CI: 1.12–5.15,  $P=0.025$ ; aOR=7.74, 95% CI: 3.14–19.08,  $P<0.001$ ; aOR=4.35, 95% CI: 1.93–9.79,  $P<0.001$ ; aOR=2.04, 95% CI: 0.96–4.34,  $P=0.044$ ). The weighted quantile sum regression model demonstrated that the exposure to seven phthalate metabolite mixtures in preconception was associated with an increased risk of infertility ( $P<0.05$ ). Among the seven phthalate metabolites, MCMHP had the largest contribution weight (61.7%). **Conclusion** Women of childbearing age should avoid the exposure to phthalates in the environment when preparing for conception, such as to reduce the consumption of highly processed foods and foods packaged with plastic/polyvinyl chloride materials to promote fertility.

**【Key words】** Fertility; Preconception cohort; Phthalates; Nested case-control study

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• 流行病学研究 •

# 1990—2019 年中国不孕不育患者的疾病负担研究

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**【摘要】** 目的 分析 1990—2019 年中国不育不孕的男性和女性的患病情况和疾病负担情况。方法 利用 2019 年全球疾病负担数据库, 分析 1990—2019 年我国总人群、不同年龄组间不育不孕男性和女性的患病情况和伤残调整寿命年(disability adjusted life year, DALY)。结果 2019 年中国男性不育患病数、患病率、DALY 和 DALY 率分别为 1 457.74 万、2 011.18/10 万、7.79 万人年、10.76/10 万, 女性不孕患病数、患病率、DALY 和 DALY 率分别为 3 788.43 万、5 431.22/10 万、19.70 万人年、28.25/10 万, 女性的不孕患病和疾病负担情况高于男性。男性患病率和 DALY 率最高的年龄组分别为 35~39 岁和 30~34 岁年龄组, 女性患病率和 DALY 率最高的年龄组分别为 40~44 岁和 35~39 岁年龄组, 女性患病率和 DALY 率最高的年龄组较男性晚 5 岁。1990—2019 年, 不育不孕男性和女性患病率和 DALY 率在前 20 年左右有升高趋势, 在后 10 年左右有降低趋势, 但中国不育不孕的男性和女性患病率和 DALY 率明显高于全球及不同的社会人口学指数(socio-demographic index, SDI)地区。结论 近年来中国不育不孕患病率和 DALY 率虽然呈降低趋势, 但中国人口基数大, 在全球范围不育不孕疾病负担占比仍然较大, 应采取积极的预防以及治疗措施减轻男女性不育不孕的疾病负担。

【关键词】 不育，男性； 不孕，女性； 疾病负担； 患病率； 伤残调整寿命年

## Study on the disease burden of male and female infertility in China from 1990 to 2019

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**【Abstract】 Objective** To analyze the prevalence and disease burden of male and female infertility in China from 1990 to 2019. **Methods** The global disease burden database of 2019 was used to analyze the prevalence of male and female infertility and disability adjusted life years (DALY) in China from 1990 to 2019 among the total Chinese male and female population and different age groups. **Results** In 2019, the number, prevalence, DALY and DALY rate of male infertility in China were 14 577 432, 2 011.18/100 000, 77 983 person years, 1 076/100 000, respectively. The number, prevalence, DALY and DALY rate of female infertility were 37 884 300, 5 431.22/100 000, 197 046 person years, 28.25/100 000, respectively. The prevalence and disease burden of female infertility were higher than those of male infertility. The age group with the highest male prevalence rate and DALY rate were 35–39 and 30–34 years old respectively, the age group with the highest female prevalence rate and DALY rate were 40–44 and 35–39 years old respectively, and the age group with the highest female prevalence rate and DALY rate was 5 years later than the male age group. From 1990 to 2019, the prevalence rate and DALY rate of male and female infertility increased in the first 20 years or so, and decreased in the last 10 years or so. The prevalence rate and DALY rate of male and female infertility in China were significantly higher than those in the whole world and different socio-demographic index (SDI) regions. **Conclusion** Although the prevalence rate and DALY rate of male and female infertility in China have decreased in recent years, the population base of China is large, and the disease burden of male and female infertility in the world is still large. Active prevention and treatment measures should be taken to reduce the disease burden of male and female infertility.

**【 Key words 】** Infertility, male; Infertility, female; Disease burden; Prevalence rate; Prevalence disability adjusted life year

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· 个案报道 ·

# Robert 子宫盲腔妊娠 1 例病例报告并文献复习

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**【摘要】** 目的 探讨 Robert 子宫的诊断与治疗方法, 提高对本病的认识。方法 回顾性分析 1 例 Robert 子宫盲腔妊娠患者的临床资料。结果 患者通过三维彩色超声、磁共振成像影像学检查, 结合宫腹腔镜联合探查, 确诊为 Robert 子宫, 后进行宫腹腔镜联合 Robert 子宫斜隔切除+宫腔内妊娠物清除+宫内节育器置入术, 手术顺利。结论 Robert 子宫是一种罕见的子宫畸形, 临床表现多样, 早期易漏诊, 宫腹腔镜联合斜隔切除是最佳的治疗方法。

**【关键词】** 妊娠; Robert 子宫; 子宫畸形

## A case analysis of Robert's blind pregnancy and literature review

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**【Abstract】 Objective** To explore the diagnosis and treatment of Robert's uterus and improve the understanding of the disease. **Methods** The clinical data of a case of Robert's blind pregnancy were analyzed retrospectively. **Results** The patient was diagnosed as Robert's uterus through three-dimensional color Doppler ultrasound, magnetic resonance imaging examination, combined with hysteroscopy and laparoscopy, and then underwent surgical treatment with good results. **Conclusion** Robert's uterine sign is a rare uterine malformation with various clinical manifestations. It is easy to miss diagnosis in the early stage. Hysteroscopy combined with oblique septectomy is the best treatment.

**【Key words】** Pregnancy; Robert's uterus; Uterine malformation

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· 个案报道 ·

# 反复卵母细胞胞质中央颗粒化并 ICSI 受精失败的 1 例病例报道并文献复习

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**【摘要】** 目的 探究辅助助孕过程中人卵母细胞发生胞质中央颗粒化（centrally located granular cytoplasm, CLGC）的原因及其对胚胎发育潜能的影响。方法 对本中心 1 例卵母细胞均表现为 CLGC 并且行卵胞质内单精子注射（intracytoplasmic sperm injection, ICSI）受精失败的病例进行报道，结合文献分析 CLGC 形成的原因及其对胚胎发育潜能的影响。结果 该患者使用不同的促排卵方案及自然周期方案后，取得的卵母细胞均为 CLGC，进行 ICSI 后均未完成正常受精。结论 CLGC 对胚胎质量及发育潜能评估有重要参考价值，患者全部卵母细胞均为 CLGC 的情况较少见，当发生 CLGC 时，询问是否有毒物接触暴露史，适当调整促排卵方案也许可以改善 CLGC 发生，但并非绝对，需对卵母细胞的形态评估加以重视。

**【关键词】** 卵母细胞； 受精，体外； 精子注射，细胞质内； 胚胎移植； 胞质中央颗粒化

## A case report and literature review of repeated centrally located granular cytoplasm and ICSI fertilization failure

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**【Abstract】 Objective** To explore the causes of centrally located granular cytoplasm (CLGC) in human oocytes during assisted fertilization and its effect on embryonic developmental potential. **Methods** A case report was made on a patient in our center whose oocytes showed CLGC in intracytoplasmic sperm injection (ICSI) cycles, and the causes of CLGC formation and its impact on embryonic developmental potential were analyzed in combination with literature. **Results** The oocytes obtained from this patient were all CLGC after using different ovulation induction programs and natural cycle programs, and normal fertilization was not completed after ICSI. **Conclusion** CLGC has an important reference value for the evaluation of embryo quality and developmental potential. It is rare that all the oocytes of the patient are CLGC. When CLGC occurs, it may be possible to improve the occurrence

of CLGC by asking whether there is a history of toxic exposure or adjusting the ovarian stimulation protocol, but it is not absolute. Attention should be paid to the evaluation of oocytes.

**【 Key words 】** Oocyte; Fertilization *in vitro*; Sperm injections, intracytoplasmic; Embryo transfer; Centrally located granular cytoplasm

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· 综述 ·

## 人绒毛膜促性腺激素在冻融胚胎移植中的研究进展

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**【摘要】** 人绒毛膜促性腺激素(human chorionic gonadotropin, hCG)是胚胎种植前产生的一种信号因子。近年来 hCG 在辅助生殖领域的胚胎发育、种植及维持妊娠状态过程中的作用, 得到了深入的研究与应用。由于新鲜周期形成胚胎数增加、胚胎植入前遗传学检测(preimplantation genetic testing, PGT)的应用及生育力保存等技术的需求, 冻融胚胎移植(frozen-thawed embryo transfer, FET)已成为人类辅助生殖中重要组成部分。本文就当前 hCG 在 FET 中的应用作一综述, 包括 hCG 在不同 FET 方案中的应用时机、剂量、给药方式及妊娠结局, 还探讨了其在薄型子宫内膜及反复胚胎种植失败女性中的应用。不同给药途径、不同药物来源 hCG 的作用效果是否有区别, 本文一并予以阐述。

**【关键词】** 宫腔灌注; 人绒毛膜促性腺激素; 冻融胚胎移植

### Advances of human chorionic gonadotropin in frozen-thawed embryo transfer

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**【Abstract】** Human chorionic gonadotropin (hCG) is a signal factor produced before embryo implantation. In recent years, the effects of hCG in the process of embryo development and implantation and maintaining of pregnancy in the field of assisted reproduction have been deeply studied and applied. Due to the increase in the number of embryos formed in the fresh cycle, the application of preimplantation genetic testing (PGT), fertility preservation, and other technical demands, frozen-thawed embryo transfer (FET) has become an important part of assisted reproduction of humans. This paper reviews the current application of hCG in FET, including the application time, dosage, administration method, and pregnancy outcome of hCG in different FET protocols. Its application in women with thin endometrium and repeated failures of embryo implantation was also discussed. This paper also defines whether there are differences in the effects of hCG with different routes of administration and different sources of drugs.

**【Key words】** Uterine perfusion; Human chorionic gonadotropin; Frozen-thawed embryo transfer

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· 综述 ·

## 子宫内膜异位症微生态改变及其对生育力影响的研究进展

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**【摘要】** 子宫内膜异位症 (endometriosis, EMS) 是妇科常见疾病, 常发生于育龄期妇女, 主要表现为盆腔疼痛、不孕等, 严重困扰女性的身心健康。人体各部位存在着种类繁多、数量庞大的微生物群, 通过微生物群落本身或代谢产物在生殖的各个阶段发挥重要作用。近年研究显示, EMS 患者各部位微生物群组成发生改变, EMS 对女性生育力的影响与人体微生态环境失衡有着密不可分的关系。本文对女性微生物群落和 EMS 之间的相互作用, 及微生态环境改变与 EMS 患者不良妊娠结局的关系进行综述。

【关键词】 子宫内膜异位症； 微生物群； 生育力

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## Research progress of microecological changes in endometriosis and its effect on fertility

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**【Abstract】** Endometriosis (EMS) is a common gynecological disease, usually occurs in women of reproductive age. EMS is characterized by pelvic pain, infertility and sexual discomfort, which seriously affects women's physical and mental health. There are a large number of microorganisms in various parts of the human body, which play an important role in various stages of reproduction through the microbial community itself or metabolites. Recent studies have found changes in the composition of microbiota in patients with EMS, and the effect of EMS on female fertility is closely related to imbalances in the human microecological environment. This article reviews the interaction between female microbiome and EMS, and the relationship between changes in microecological environment and adverse pregnancy outcomes in EMS patients.

**【Key words】** Endometriosis; Microbiota; Fertility

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• 综述 •

## 膜控储库型缓释给药系统在生殖健康领域的研究进展

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**【摘要】** 当今中国人口老龄化问题日益严重, 而在国家提倡三孩政策下的女性生育力又不断下降, 不论是中老年女性还是育龄女性都面临着生殖健康问题。传统口服制剂作用时间短且有的品种还存在生物利用度低的问题, 长效缓释制剂具有使用方便、血药浓度稳定、安全性更高等优点, 其开发为更多的生殖避孕药具研发和应用提供了理论基础与技术支持。在数十年的研发过程中诞生了多种不同类型的递药系统, 其中以聚合物为基质的膜控储库型制剂作为一种常见的药物缓释系统, 多用于生殖健康, 且具有广阔的市场前景。本文就生殖健康领域中以聚合物为载体递送药物的膜控储库型制剂做简要综述, 重点探讨了基于该种系统的聚合物材料选择、体外释放模型、制剂类型及研究进展、面临的挑战共四个关键问题, 为今后开发相关药具提供借鉴。

**【关键词】** 避孕; 缓释给药系统; 膜控储库; 聚合物; 释放模型

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## Research progress of membrane-controlled reservoir sustained-release drug delivery systems for reproductive health

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**【 Abstract 】** Nowadays, the aging of China's population is becoming increasingly serious, and fertility of women under the national three-child policy is declining, both middle-aged and elderly women and women of childbearing age are facing reproductive health problems. Traditional oral preparations have a short acting time and some varieties have low bioavailability problems, while the long-



acting sustained-release preparations have the advantages of convenient use, stable blood drug concentration and higher safety. Their development provides theoretical basis and technical support for the development and application of reproductive contraceptives. In the decades of research, a variety of different drug delivery systems have been born. Among them, the polymer-based membrane-controlled reservoir preparations, as a common drug sustained-release system, is mostly used in reproductive health and has broad market prospects. In this paper, polymer-based membrane-controlled reservoir drug delivery systems in the field of reproductive health was briefly reviewed, and four key issues including polymer material selection, *in vitro* drug release model, preparation types and research progress, and challenges were discussed, which can provide reference for the development of related contraceptives in the future.

**【 Key words 】** Contraception; Sustained-release drug delivery systems; Membrane-controlled reservoir; Polymers; Drug release model

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