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## 常规体外受精中国专家共识 (2024 年)

中国医师协会生殖医学专业委员会

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**【摘要】** 常规体外受精 (conventional *in vitro* fertilization, c-IVF) 是利用优化后的精子与卵母细胞自然结合完成 IVF 的一类辅助生殖技术, 主要应用于女性因素不孕、部分男性因素不育及不明原因不孕不育患者的助孕治疗。但目前尚缺乏 c-IVF 相关的操作标准或共识, 尤其对于如何选择最佳授精方式以避免受精率低或完全受精失败的发生, 始终是困扰辅助生殖临床医生与胚胎实验室人员的难题。因此, 由中国医师协会生殖医学专业委员会发起, 并联合全国多家生殖医学中心共同编撰了本共识, 旨在规范 c-IVF 的选择标准、精液优化处理及授精操作流程, 为辅助生殖临床医生和胚胎实验室人员提供实用性参考, 以期获得稳定且满意的辅助生殖助孕结局。

**【关键词】** 生殖技术, 辅助; 常规体外受精; 精液参数; 精液优化方式; 授精方式; 共识

### Chinese expert consensus on conventional *in vitro* fertilization (2024)

Chinese Association of Reproductive Medicine

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**【Abstract】** Conventional *in vitro* fertilization (c-IVF) is one of the most commonly used assisted reproductive technology (ART) approaches. In c-IVF, cumulus-intact oocytes are incubated with a defined range of spermatozoa, followed by a fertilization assessment a few hours later. c-IVF is primarily used for patients

with female factor infertility, some cases with male factor sterility, and unexplained infertility. Given the absence of standardized operating protocols or consensus regarding c-IVF, the selection of an optimal insemination method poses challenges for ART clinicians and embryologists when dealing with special cases involving critical semen parameters. Therefore, this consensus was initiated through collaboration with the Chinese Association of Reproductive Medicine and collaboratively compiled by numerous reproductive medicine centers in China. The objective of this consensus is to establish standardized protocols for semen preparation and fertilization procedures in c-IVF while providing selection criteria for insemination methods. This consensus serves as a practical reference for ART clinicians and embryologists aiming to achieve consistent and satisfactory outcomes in ART.

**【Key words】** Reproductive techniques, assisted; Conventional *in vitro* fertilization; Sperm parameters; Sperm preparation methods; Insemination methods; Consensus

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· 临床研究 ·

# 拮抗剂灵活方案添加拮抗剂后平均 LH 水平对 IVF/ICSI 鲜胚移植临床结 局及累积活产率的影响

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**【摘要】** 目的 探讨应用促性腺激素释放激素拮抗剂（gonadotropin-releasing hormone antagonis, GnRH-A）灵活方案促排卵添加 GnRH-A 后黄体生成素（luteinizing hormone, LH）水平对卵巢储备功能正常患者体外受精/卵胞质内单精子注射（*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI）鲜胚移植临床结局及累积活产率的影响。方法 回顾性队列研究分析 2016 年 1 月至 2021 年 6 月期间在郑州大学第三附属医院生殖医学中心采用拮抗剂灵活方案促排卵后行 IVF/ICSI 的卵巢储备功能正常的 685 例患者资料。采用四分位数法以添加拮抗剂后患者每次监测血清 LH 水平（根据卵泡生长速度及患者需要，通常为 2 次）直至扳机日血清 LH 水平的平均值进行分组，分为 A 组（小于纳入人群平均 LH 水平的第 25 百分位数， $LH < 1.25 \text{ U/L}$ ,  $n=166$ ）、B 组（处于纳入人群平均 LH 水平的第 25~50 百分位数， $1.25 \text{ U/L} \leq LH < 1.91 \text{ U/L}$ ,  $n=174$ ）、C 组（处于纳入人群平均 LH 水平的第 50~75 百分位数， $1.91 \text{ U/L} \leq LH < 2.85 \text{ U/L}$ ,  $n=171$ ）和 D 组（大于纳入人群平均 LH 水平的第 75 百分位数， $2.85 \text{ U/L} \leq LH \leq 7.55 \text{ U/L}$ ,  $n=174$ ）。比较 4 组患者的一般情况、临床资料、胚胎实验室指标、鲜胚移植周期临床结局指标及累积活产率。结果 经多因素线性回归校正混杂因素后，C 组患者的优质胚胎数、囊胚形成率显著高于 A 组，差异具有统计学意义（ $B=0.600$ , 95%  $CI$ : 0.086~1.114,  $P=0.022$ ;  $B=0.134$ , 95%  $CI$ : 0.052~0.216,  $P=0.001$ ）。D 组患者的优质胚胎数、可利用胚胎数、囊胚形成率显著高于 A 组，差异具有统计学意义（ $B=0.771$ , 95%  $CI$ : 0.259~1.284,  $P=0.003$ ;  $B=0.730$ , 95%  $CI$ : 0.205~1.255,  $P=0.007$ ;  $B=0.085$ , 95%  $CI$ : 0.003~0.167,  $P=0.042$ ）。经多因素 logistic 回归后，A 组患者与 B、C、D 组患者的活产率差异无统计学意义（ $P>0.05$ ）。D 组患者的累积活产率显著高于 A 组患者，差异具有统计学意义（ $aOR=2.439$ , 95%  $CI$ : 1.169~4.974,  $P=0.014$ ）。结论 在卵巢储备功能正常的患者中应用 GnRH-A 灵活方案促排卵，添加 GnRH-A 后平均 LH 水平对鲜胚移植周期临床结局无明显影响，但当平均 LH 水平  $< 1.25 \text{ U/L}$  时胚胎质量显著下降，并可能因此降低胚胎发育潜能进而降低累积活产率。

**【关键词】** 卵巢储备功能； 促性腺激素释放激素拮抗剂灵活方案； 黄体生成素； 临床结局

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# **Influence of mean LH levels after adding GnRH antagonists using a flexible GnRH antagonist protocol on clinical outcomes of IVF/ICSI fresh embryo transfer**

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**【Abstract】 Objective** To investigate the effect of luteinizing hormone (LH) levels on the clinical outcome and cumulative live birth rate of *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) fresh embryo transfer in patients with normal ovarian reserve function after application of a flexible protocol of gonadotropin-releasing hormone antagonist (GnRH-A) to promote ovulation with the addition of GnRH-A. **Methods** A retrospective cohort study was conducted to analyze the data of 685 patients with normal ovarian reserve function who underwent IVF/ICSI after ovulation induction with antagonist flexible regimen between January 2016 and June 2021 at the Reproductive Medicine Center of the Third Affiliated Hospital of Zhengzhou University. The quartile method was used to group patients after the addition of the antagonist by the mean value of serum LH each time they were monitored (usually twice, depending on the rate of follicular growth and patients' need) until the day of the trigger, and were divided into group A (smaller than the 25th percentile of the mean LH level of the included population,  $LH < 1.25$  U/L,  $n=166$ ), group B (in the 25th to 50th percentile of the mean LH level of the included population,  $1.25 \text{ U/L} \leq LH < 1.91 \text{ U/L}$ ,  $n=174$ ), group C (in the 50th to 75th percentile of the mean LH level of the included population,  $1.91 \text{ U/L} \leq LH < 2.85 \text{ U/L}$ ,  $n=171$ ), and group D (greater than the 75th percentile of the mean LH level of the included population,  $2.85 \text{ U/L} \leq LH \leq 7.55 \text{ U/L}$ ,  $n=174$ ). The general condition, clinical data, embryo laboratory indices, clinical outcome indices of fresh embryo transfer cycle and cumulative live birth rate were compared among the 4 groups. **Results** After correcting for confounding factors by multifactorial linear regression, the number of high-quality embryos and the rate of blastocyst formation of patients in group C were significantly higher than those in group A, and the differences were statistically significant ( $B=0.600$ , 95% *CI*: 0.086–1.114,  $P=0.022$ ;  $B=0.134$ , 95% *CI*: 0.052–0.216,  $P=0.001$ ). The number of high-quality embryos, the number of available embryos, and the rate of blastocyst formation of patients in group D were significantly higher than those in group A, and the differences were statistically significant ( $B=0.771$ , 95% *CI*: 0.259–1.284,  $P=0.003$ ;  $B=0.730$ , 95% *CI*: 0.205–1.255,  $P=0.007$ ;  $B=0.085$ , 95% *CI*: 0.003–0.167,  $P=0.042$ ). After multifactorial logistic regression, there was no statistically significant difference in live birth rate between group A and groups B, C and D ( $P>0.05$ ). The cumulative live birth rate of patients in group D was significantly higher than that in group A, and the difference was statistically significant ( $aOR=2.439$ , 95% *CI*: 1.169–4.974,  $P=0.014$ ). **Conclusion** In patients with normal ovarian reserve function, a flexible protocol of antagonists was applied to promote ovulation, and the addition of antagonists had no significant effect on the clinical outcome of the fresh embryo transfer cycle in terms of mean LH levels, but the quality of the embryos was significantly reduced when the mean LH level was  $<1.25$  U/L, and this may consequently reduce the developmental potential of the embryos and the cumulative live birth rate.



**【Key words】** Ovarian reserve; Flexible gonadotropin-releasing hormone antagonist protocol; Luteinizing hormone; Clinical outcomes

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# 卵巢储备功能正常患者应用 PPOS 与激动剂长方案的每取卵周期累积活产率比较

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**【摘要】** 目的 比较激动剂长方案和高孕激素状态下促排卵 (progestin-primed ovarian stimulation, PPOS) 方案在卵巢储备功能正常患者中的每取卵周期累积活产率。方法 回顾性队列研究分析了 2017 年 1 月至 2019 年 12 月期间在同济大学附属上海市第一妇婴保健院生殖医学科接受体外受精/卵胞质内单精子注射 (*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI) 助

孕的年龄小于 40 岁且卵巢储备正常（月经周期正常、卵泡刺激素<10 U/L、窦卵泡计数>5）的女性。主要结局指标为促排卵之日起 18 个月内的累积活产率。结果共 995 例患者纳入分析，其中使用 PPOS 方案 509 例（PPOS 组），激动剂长方案 486 例（激动剂长方案组）。两组患者的基本特征以及临床和实验室指标基本相似，但 PPOS 组的不孕年限 [3（2，4）年] 较激动剂长方案组 [3（2，5）年] 更短（ $P=0.015$ ）。激动剂长方案组中有 372 例（77%）进行了鲜胚移植，获得临床妊娠 218 例、活产 197 例。新鲜胚胎每移植周期临床妊娠率、持续妊娠率和活产率分别为 58.6%（218/372）、54.0%（201/372）和 53.0%（197/372），而 PPOS 组没有进行鲜胚移植。在研究期间，PPOS 组共进行冻融胚胎移植（frozen-thawed embryo transfer, FET）662 个周期，在激动剂长方案组中共进行 257 个 FET 周期。激动剂长方案组 FET 周期移植周期活产率为 42.8%（110/257），显著高于 PPOS 组 [31.1%（206/662）， $OR=0.727$ ，95%  $CI$ : 0.607~0.871， $P<0.001$ ]。PPOS 组在所有 FET 周期中的胚胎种植率 [29.2%（293/1004）] 低于激动剂长方案组 [34.5%（157/455）， $OR=0.846$ ，95%  $CI$ : 0.721~0.992， $P=0.041$ ]。在一个完整的 IVF/ICSI 周期（包括新鲜胚胎及随后所有冷冻胚胎）后，PPOS 组在 18 个月随访期内的累积活产率 [40.5%（206/509）] 显著低于激动剂长方案组 [63.2%（307/486）， $OR=0.641$ ，95%  $CI$ : 0.565~0.726， $P<0.001$ ]。与 PPOS 组相比，激动剂长方案组从促排卵到妊娠和活产的平均时间均显著缩短（均  $P<0.001$ ）。在 Kaplan-Meier 分析中，激动剂长方案组累积持续妊娠达到活产率显著高于 PPOS 组（long rank 检验， $P<0.001$ ）。Cox 回归分析调整其他混杂因素后显示采用的刺激方案与累积活产率密切相关（ $OR=1.917$ ，95%  $CI$ : 1.152~3.190， $P=0.012$ ）。结论 在卵巢储备正常的女性中，采用 PPOS 方案相比传统的激动剂长方案而言累积活产率更低，达妊娠/活产时间更长。

【关键词】 受精，体外； 胚胎移植； 高孕激素状态下促排卵； 促性腺激素释放激素激动剂长方案； 累积活产率

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### Comparison of cumulative live birth rates per oocyte retrieval cycle in patients with normal ovarian reserve function treated with PPOS and GnRH agonist long protocol

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【Abstract】 **Objective** To compare the cumulative live birth rates per oocyte retrieval cycle in patients with normal ovarian response between the

gonadotropin-releasing hormone agonist (GnRH-a) long protocol and the progestin-primed ovarian stimulation (PPOS) protocol. **Methods** A retrospective cohort study was conducted in Centre of Assisted Reproduction, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine between January 2017 and December 2019. Women who underwent *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) treatment with normal ovarian reserve and <40 years of age were included. Other inclusion criteria included regular menstrual cycles, serum follicle-stimulating hormone level <10 U/L, and the antral follicle count >5. The primary outcome was the cumulative live birth rate (CLBR) within 18 months from the start of ovarian stimulation. **Results** A total of 995 patients were included in the study, with 509 patients in the PPOS group and 486 patients in the GnRH-a long group. Both groups had almost comparable demographic and cycle stimulation characteristics except for duration of infertility which was shorter in the PPOS group [3 (2,4) years] than in the GnRH-a long group [3 (2,5) years,  $P=0.015$ ]. In the GnRH-a long group, 372 patients (77%) underwent fresh embryo transfer, resulting in 218 clinical pregnancies and 197 live births. The clinical pregnancy rate, the ongoing pregnancy rate, and the live birth rate per embryo transfer cycle were 58.6% (218/372), 54.0% (201/372) and 53.0% (197/372), respectively. No fresh embryo transfer was performed in the PPOS group. During the study period, there were 662 frozen-thawed embryo transfer (FET) cycles in the PPOS group and 257 FET cycles in the GnRH-a long group. The PPOS group had a live birth rate of 31.1% (206/662) per FET cycle, which was notably lower than the GnRH-a long group [42.8% (110/257),  $OR=0.727$ ; 95%  $CI$ : 0.607–0.871;  $P<0.001$ ]. The implantation rate of all FET cycles in the PPOS group was also lower than that in the GnRH-a long group [29.2% (293/1 004) vs. 34.5% (157/455),  $OR=0.846$ , 95%  $CI$ : 0.721–0.992;  $P=0.041$ ]. CLBRs after one complete IVF/ICSI cycle including fresh and subsequent FET cycles within 18 months follow up were significantly lower in the PPOS group [40.5% (206/509)] than in the long agonist group [63.2% (307/486),  $OR=0.641$ , 95%  $CI$ : 0.565–0.726]. Compared with the PPOS group, the GnRH-a long group had a significantly shorter duration from the start of ovarian stimulation to pregnancy and live birth ( $P<0.001$ ). In Kaplan-Meier analysis, the CLBR was significantly higher in the GnRH-a long group than in the PPOS group (long rank test,  $P<0.001$ ). Adjusted Cox-regression analysis revealed stimulation protocol adopted was strongly associated with the CLBR ( $OR=1.917$ , 95%  $CI$ : 1.152–3.190,  $P=0.012$ ). **Conclusion** Progestin primed ovarian stimulation was associated with a lower cumulative live birth rates and a long time to pregnancy/live birth than the long agonist protocol in women with a normal ovarian reserve.

**【 Key words 】** Fertilization *in vitro*; Embryo transfer; Progestin-primed ovarian stimulation; Gonadotropin-releasing hormone agonist long protocol; Cumulative live birth rate

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# 新鲜周期第 4 天和第 5 天移植临床结局及母婴结局比较

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**【摘要】** 目的 探讨新鲜周期第 4 天 (day 4, D4) 胚胎移植对体外受精 (*in vitro* fertilization, IVF) 或卵胞质内单精子注射 (intracytoplasmic sperm injection, ICSI) 临床结局及母婴结局的影响。方法 回顾性队列研究分析了 2019 年 1 月至 2021 年 12 月期间就诊于邢台不孕不育专科医院生殖医学中心在受精后 D4 或第 5 天 (day 5, D5) 移植 1 枚最优质的胚胎行 IVF 或 ICSI 的患者临床资料。比较 D4 移植组 ( $n=273$ ) 和 D5 移植组 ( $n=88$ ) 的临床结局及母婴结局。结果 D5 移植组人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 注射日雌二醇水平 [ $3\ 516\ (2\ 273, 4\ 116)$  ng/L] 显著高于 D4 移植组 [ $2\ 940\ (1\ 935, 3\ 877)$  ng/L,  $P=0.023$ ], hCG 注射日黄体生成素 (luteinizing hormone, LH) 水平 [ $0.82\ (0.63, 1.11)$   $\mu$ g/L] 显著低于 D4 移植组 [ $0.94\ (0.69, 1.20)$   $\mu$ g/L,  $P=0.026$ ]。D5 移植组的双原核 (two pronuclei, 2PN) 受精率 [ $71.13\%\ (929/1\ 306)$ ] 和可用胚胎率 [ $51.73\%\ (509/984)$ ] 显著高于 D4 移植组 [ $67.26\%\ (2\ 539/3\ 775)$ ,  $P=0.010$ ;  $48.00\%\ (1\ 306/2\ 721)$ ,  $P=0.045$ ]。D4 移植组的临床妊娠率 [ $63.37\%\ (173/273)$ ] 和活产率 [ $53.11\%\ (145/273)$ ] 显著高于 D5 移植组 [ $46.59\%\ (41/88)$ ,  $P=0.005$ ;  $36.36\%\ (32/88)$ ,  $P=0.006$ ]。两组间的异位妊娠率、单卵双胎率、流产率、早产率、死产率、剖宫产率、分娩孕周、男/女比例及出生体质量等差异均无统计学意义 (均  $P>0.05$ )。logistic 回归分析结果显示胚胎移植天数对临床妊娠率和活产率的影响呈显著相关性

( $OR=0.468$ , 95%  $CI$ : 0.266~0.824,  $P=0.009$ ;  $OR=0.481$ , 95%  $CI$ : 0.273~0.847,  $P=0.011$ )。结论 IVF/ICSI 中新鲜周期 D4 移植临床妊娠率及活产率均优于 D5 移植, 母婴结局相当, 在临床工作中可考虑优先选择 D4 胚胎移植。

【关键词】 移植, 第 4 天; 移植, 第 5 天; 妊娠结局; 母婴结局

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## Comparison of clinical outcomes and maternal and fetal outcomes between day 4 and day 5 embryo transfer in fresh cycle

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**【Abstract】 Objective** To investigate the effects of day 4 (D4) embryo transfer on clinical outcomes and maternal and infant outcomes *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI) in fresh cycles. **Methods** We retrospectively analyzed the clinical data of 361 IVF and ICSI cycles from January 2019 to December 2021 in the Reproductive Medicine Center of Xingtai Infertility Specialist Hospitals in a cohort study. In all cycles, one of the best quality embryo was transferred at D4 or D5 after fertilization. The clinical outcomes and maternal and fetal outcomes of D4 transfer group and D5 transfer group were compared. **Results** Compared with D4 transfer group, the estradiol value on human chorionic gonadotropin (hCG) injection day significantly increased in D5 transfer group [3 516 (2 273, 4 116) ng/L vs. 2 940 (1 935, 3 877) ng/L,  $P=0.023$ ], and the luteinizing hormone (LH) value on hCG injection day significantly decreased [0.82 (0.63, 1.11)  $\mu$ g/L vs. 0.94 (0.69, 1.20)  $\mu$ g/L,  $P=0.026$ ], two pronuclei (2PN) fertilization rate [71.13% (929/1 306)] and the available embryo rate [51.73% (509/984)] in D5 transfer group were significantly higher than those in D4 transfer group [67.26% (2 539/3 775),  $P=0.010$ ; 48.00% (1 306/2 721),  $P=0.045$ ]. The clinical pregnancy rate [63.37% (173/273)] and the live birth rate [53.11% (145/273)] in D4 transfer group were significantly higher than those in D5 transfer group [46.59% (41/88),  $P=0.005$ ; 36.36% (32/88),  $P=0.006$ ]. There were no significant differences in ectopic pregnancy rate, monozygotic twins rate, abortion rate, preterm birth rate, stillbirth rate, caesarean section rate, delivery gestation, male/female ratio and birth weight (all  $P>0.05$ ). The results of logistic regression analysis showed that the days of embryo transfer had a significant correlation with the pregnancy rate and the live birth rate ( $OR=0.468$ , 95%  $CI$ : 0.266–0.824,  $P=0.009$ ;  $OR=0.481$ , 95%  $CI$ : 0.273–0.847,  $P=0.011$ ). **Conclusion** In IVF/ICSI of fresh cycles, the clinical pregnancy rate and the live birth rate of D4 transplantation are better than that of D5 transplantation, and the maternal and fetal outcomes are similar. Therefore, D4 embryo transplantation can be preferred in clinical work.

**【Key words】** Embryo transfer, day 4; Embryo transfer, day 5; Pregnancy outcome; Maternal and fetal outcomes

**Fund program:** Medical Science Research Project of Hebei Province (20221862, 20221863, 20221865)

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# PGT-SR 后囊胚形态学评分与冻融单囊胚移植活产的相关性分析

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**【摘要】** 目的 探讨胚胎植入前染色体结构重排检测 (preimplantation genetic testing for chromosome structural rearrangements, PGT-SR) 后囊胚形态学评分对冻融单囊胚移植活产的影响。方法 回顾性病例对照研究分析 2015 年 3 月至 2021 年 1 月期间于郑州大学第一附属医院生殖医学中心行 PGT-SR 助孕后冻融单囊胚移植患者的临床资料, 共 1 412 个移植周期。依据是否获得活产分为活产组 ( $n=634$ ) 和未活产组 ( $n=778$ ), 根据囊胚扩张度、内细胞团和滋养层细胞形态对囊胚进行评分, 比较各形态学参数的活产率差异。通过二元 logistic 回归评估每个形态学参数对单囊胚移植活产的预测价值。再依据囊胚发育天数分为第 5 天囊胚 ( $n=977$ ) 和第 6 天囊胚 ( $n=435$ ), 进一步探究第 5 天和第 6 天囊胚的不同扩张度分期的活产。结果 活产组的不孕年限 [ $2.88 \pm 2.41$ ] 年] 比未活产组 [ $3.18 \pm 2.67$ ] 年,  $P=0.028$ ] 短。活产组的移植日内膜厚度 [ $10.12 \pm 2.03$ ] mm] 和第 5 天囊胚移植周期比例 [75.6% ( $479/634$ )] 比未活产组 [ $9.78 \pm 1.76$ ] mm,  $P=0.003$ ; 64.0% ( $498/778$ ),  $P<0.001$ ] 高; 两组间内膜准备方案、囊胚扩张度和滋养层细胞等级构成比比较差异均有统计学意义 ( $P=0.008$ 、 $P=0.002$ 、 $P=0.015$ )。两组间内细胞团等级构成比差异无统计学意义 ( $P=0.236$ )。调整相关混杂因素后, 二元 logistic 回归分析结果显示, 与 1~2 期相比, 3 期、4 期的活产率显著升高 ( $aOR=1.894$ , 95%  $CI$ : 1.056~3.394,  $P=0.032$ ;  $aOR=1.970$ , 95%  $CI$ : 1.046~3.709,  $P=0.036$ ), 内细胞团和滋

养层细胞等级并不是活产的独立影响因素( $aOR=1.480$ , 95%  $CI$ : 0.790~2.772,  $P=0.221$ ;  $aOR=1.242$ , 95%  $CI$ : 0.952~1.621,  $P=0.111$ )。内膜准备方案、囊胚发育天数和内膜厚度同样是活产的独立影响因素,与激素替代方案相比,自然周期方案的活产率显著升高( $aOR=1.425$ , 95%  $CI$ : 1.028~1.975,  $P=0.033$ );与第 6 天囊胚相比,第 5 天囊胚的活产率显著升高( $aOR=1.448$ , 95%  $CI$ : 1.068~1.963,  $P=0.017$ )。进一步分析相同囊胚发育天数的不同扩张度分期的活产,结果显示,第 5 天囊胚的不同扩张度分期间的活产率差异有统计学意义( $P=0.002$ ),3 期、4 期和 6 期的活产率[51.1% (360/704)、50.3% (87/173)、58.3% (7/12)] 均高于 1~2 期 [28.1% (16/57)], 均  $P<0.0125$ 。结论行 PGT-SR 助孕后冻融周期单囊胚移植时,建议优先选择扩张度为 3~4 期的第 5 天囊胚移植,选择自然周期内膜准备方案可获得更高的活产率。

【关键词】 冻融胚胎移植; 单囊胚移植; 形态学评分; 活产率; 胚胎植入前结构重排遗传学检测

### Analysis of the correlation between the morphological score of blastocyst and the live birth of frozen-thawed single blastocyst transfer after PGT-SR

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【Abstract】 **Objective** To explore the effect of morphological score of blastocyst on the live birth of frozen-thawed single blastocyst transfer after preimplantation genetic testing for chromosome structural rearrangements (PGT-SR). **Methods** In this retrospective case-control study, the clinical data of 1 412 patients who underwent frozen-thawed single blastocyst transfer after PGT-SR assisted pregnancy in Center for Reproductive Medicine, the First Affiliated Hospital of Zhengzhou University from March 2015 to January 2021 were analyzed. According to whether the live birth was obtained, it was divided into two groups: live birth group ( $n=634$ ) and non-live birth group ( $n=778$ ). Blastocysts were graded according to degree of blastocyst expansion, inner cell mass and trophoctoderm morphology, and the differences of live birth rate of each morphological parameter were compared. The predictive value of each morphologic parameter to live birth after single blastocyst transfer was evaluated by binary logistic regression. Then it was divided into day 5 (D5) blastocyst ( $n=977$ ) and day 6 (D6) blastocyst ( $n=435$ ) according to the blastocyst development days, and the live birth rate among different blastocyst expansions in D5 and D6 blastocysts was further explored. **Results** The live birth group had shorter infertility duration [(2.88±2.41) years], higher endometrial thickness [(10.12±2.03) mm] and higher proportion of D5 blastocyst transfer cycle [75.6% (479/634)] compared with the non-live birth group [(3.18±2.67) years,  $P=0.028$ ; (9.78±1.76) mm,  $P=0.003$ ; 64.0% (498/778),  $P<0.001$ ]. There were significant differences in endometrial preparation protocols, blastocyst expansion and trophoblast cell grade between the two groups ( $P=0.008$ ,  $P=0.002$ ,  $P=0.015$ ). There was no significant difference in the grade of inner cell mass between

the two groups ( $P=0.236$ ). After adjusting the related confounding factors, the results of binary logistic regression showed that the live birth rate in expansion 3 and expansion 4 was significantly higher than that in expansion 1-2 ( $aOR=1.894$ , 95%  $CI$ : 1.056-3.394,  $P=0.032$ ;  $aOR=1.970$ , 95%  $CI$ : 1.046-3.709,  $P=0.036$ ), and the inner cell mass and trophoctoderm were not independent influencing factors of live birth ( $aOR=1.480$ , 95%  $CI$ : 0.790-2.772,  $P=0.221$ ;  $aOR=1.242$ , 95%  $CI$ : 0.952-1.621,  $P=0.111$ ). Endometrial preparation regimens, blastocyst development days and endometrial thickness were also independent influencing factors of live birth. Compared with hormone replacement therapy regimen, the live birth rate of natural cycle regimen was significantly higher ( $aOR=1.425$ , 95%  $CI$ : 1.028-1.975,  $P=0.033$ ). Compared with D6 blastocyst, the live birth rate of D5 blastocyst was also significantly higher ( $aOR=1.448$ , 95%  $CI$ : 1.068-1.963,  $P=0.017$ ). There was a significant difference in the live birth rate among the different expansion of D5 blastocyst ( $P=0.002$ ). Compared with the degree of blastocyst expansion 1-2 [28.1% (16/57)], the live birth rate in expansion 3, expansion 4 and expansion 6 was significantly higher [51.1% (360/704), 50.3% (87/173), 58.3% (7/12); all  $P<0.012$  5]. **Conclusion** Higher live birth rate can be obtained by preferentially selecting D5 blastocyst transfer with the degree of expansion 3 and expansion 4 stages and choosing the natural cycle endometrial preparation regimen after PGT-SR assisted pregnancy.

**【Key words】** Frozen-thawed embryo transfer; Single blastocyst transfer; Morphological grading; Live birth rate; Preimplantation genetic testing for chromosome structural rearrangements

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• 实验研究 •

## 血清外泌体 miR-17-5p 对早发性

## 卵巢功能不全患者 Treg 细胞的作

## 用及机制研究

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**【摘要】** 目的 探索早发性卵巢功能不全 (premature ovarian insufficiency, POI) 患者血清外泌体 miR-17-5p 与调节性 T (regulatory T, Treg) 细胞的关系及其在 POI 发生中的机制。方法 采用病例对照研究, 收集 2019 年 1 月至 2020 年 12 月期间于南京医科大学第一附属医院妇科内分泌门诊确诊的 32 例中国汉族特发性 POI 患者为 POI 组, 32 例同期行健康体检且月经规律的中国汉族女性作为正常组。应用实时定量 PCR 验证血清外泌体 miR-17-5p 相对表达量。收集健康成年女性外周血单个核细胞 (peripheral blood mononuclear cell, PBMC) 与提取的 POI 患者或正常组女性血清外泌体共培养 72 h 及转染 miR-17-5p 模拟物 72 h (记为 miR-17-5p 模拟物组), 同时以 PBS 为阴性对照, 应用流式细胞术检测 PBMC 中 Th1、Th17 和 Treg 细胞比例。通过 miR-17-5p 模拟物/抑制剂转染体外诱导型 Treg (induced Treg, iTreg) 细胞, 应用流式细胞仪检测细胞增殖/凋亡情况, 生物信息分析 miR-17-5p 的靶基因。结果 与正常组相比, POI 组血清外泌体 miR-17-5p 的相对表达量明显升高 ( $P<0.001$ )。POI 外泌体与 PBMC 共培养后 Treg 细胞比例 [ $(0.93\pm0.40)\%$ ] 低于阴性对照组 [ $(3.77\pm0.89)\%$ ,  $P=0.005$ ]。miR-17-5p 模拟物组 PBMC 中的 Treg 细胞比例 [ $(4.30\pm1.91)\%$ ] 显著低于阴性对照组 [ $(11.97\pm1.82)\%$ ,  $P=0.007$ ], 而 Th1 细胞及 Th17 细胞比例变化均无统计学意义 (均  $P>0.05$ )。过表达/抑制 miR-17-5p 均不影响 iTreg 细胞的诱导效率 (均  $P>0.05$ )。过表达 miR-17-5p 后 iTreg 细胞凋亡比例 [ $(16.31\pm1.27)\%$ ] 显著高于阴性对照组 [ $(13.01\pm1.80)\%$ ,  $P=0.035$ ]。与 miR-17-5p 抑制物阴性对照组 [ $(11.42\pm0.23)\%$ 、 $(87.60\pm0.70)\%$ ] 相比, miR-17-5p 抑制物组 iTreg 细胞凋亡比例 [ $(7.97\pm0.71)\%$ ,  $P=0.001$ ] 显著降低, iTreg 细胞增殖比例 [ $(88.83\pm0.25)\%$ ,  $P=0.045$ ] 显著增加。生物信息分析提示转换生长因子受体 2 基因可能是 miR-17-5p 的靶基因。结论 POI 的血清外泌体 miR-17-5p 表达明显上调, 其可能通过抑制 iTreg 细胞增殖、促进 iTreg 细胞凋亡导致外周血中 Treg 细胞比例下降, 参与 POI 的发生。

**【关键词】** 外泌体; 早发性卵巢功能不全; 调节性 T 细胞; miR-17-5p

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## Mechanism of serum exosomal miR-17-5p on regulation of Treg cells in premature ovarian insufficiency

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**【Abstract】 Objective** To explore the involvement of serum exosomal miR-17-5p in the pathogenesis of regulatory T (Treg) cells deficiency in premature ovarian insufficiency (POI) patients. **Methods** In a case-control study, 32 Chinese Han women with POI and 32 Chinese Han women with regular menstrual cycles (healthy control, HC) attending the Department of Gynecological Endocrinology, the First Affiliated Hospital of Nanjing Medical University from January 2019 to December 2020 were recruited. The relative expressional level of serum exosomal miR-17-5p was confirmed by reverse transcription quantitative polymerase chain reaction (RT-qPCR). To understand how POI-exosome affects Treg cells, peripheral blood mononuclear cells (PBMC) of healthy volunteer were transfected with miR-17-5p, and cultured with PBS as the control or with exosomes derived from POI women or HC for 72 h. Subsequently, to evaluate the functionality of the miR-17-5p upregulated in POI-exosome, native CD4<sup>+</sup> T cells from healthy donors were sorted by magnetic beads and induced into induced Treg (iTreg) cells *in vitro*, and the induction efficiency, the proliferation and apoptosis rates of iTreg cells were detected after transfection with miR-17-5p mimic/inhibitor. TargetScan, miRDB, miRTarBase and miRWalk were used to predict targets gene of miR-17-5p. **Results** The expression level of serum exosomal miR-17-5p was markedly up-regulated in POI compared with HC ( $P<0.001$ ). Furthermore, after culture with POI-exosome [(0.93±0.40)%], the frequency of Treg cells was significantly reduced as compared with that culture with PBS [(3.77±0.89)%,  $P=0.005$ ]. Subsequently, the frequency of Treg cells in miR-17-5p mimic group [(4.30±1.91)%] was significantly lower than that in negative control group [(11.97±1.82)%,  $P=0.007$ ]. In contrast, both Th1 and Th17 did not be affected (both  $P>0.05$ ). The induction efficiency of iTreg cells did not be influenced by transfection with miR-17-5p (both  $P>0.05$ ), however, the iTreg cells apoptosis rate in miR-17-5p mimic group [(16.31±1.27)%] was significantly higher than that in negative control group [(13.01±1.80)%,  $P=0.035$ ], while apoptosis rate was significantly lower [(7.97±0.71)%] and proliferation rate was higher [(88.83±0.25)%] in miR-17-5p inhibitor group than those in negative control group [(11.42±0.23)%,  $P=0.001$ ; (87.60±0.70)%,  $P=0.045$ ]. Transforming growth factor beta receptor 2 was most likely targets gene of miR-17-5p. **Conclusion** The exosomal miRNA profile of patients with POI differed from that of HC, and miR-17-5p, which is markedly increased in POI patients, decreased the frequency of Treg cells by inhibiting iTreg cell proliferation and promoting iTreg cells apoptosis. Thus, our study suggested that exosomal miR-17-5p promoted iTreg cells apoptosis and resulted in Treg cells deficiency in POI pathogenesis.

**【Key words】** Exosomes; Premature ovarian insufficiency; Regulatory T cells; miR-17-5p

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• 临床报道 •

## 不同食盐摄入水平对辅助生殖技术女性首次移植周期助孕结局的影响

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**【摘要】** 目的 研究不同食盐摄入水平对行辅助生殖技术助孕女性首次移植周期妊娠结局的影响。方法 回顾性队列研究分析 2021 年 1 月至 2021 年 7 月期间于河南省人民医院生殖医学中心接受体外受精/卵胞质内单精子注射-胚胎移植助孕首次移植周期的 163 例患者的资料。点尿法近似估算患者的 24 h 钠盐摄入量, 并以其第 25 和第 75 百分位数将所有患者分为 3 组: 低盐组( $\leq 9.21$  g,  $n=41$ )、中盐组( $9.22\sim 13.31$  g,  $n=81$ ) 和高盐组( $\geq 13.32$  g,  $n=41$ )。分析比较各组间控制性促排卵指标及移植后临床结局。通过多因素 logistic 回归分析调整混杂因素后分析 3 组患者的临床结局。结果 高盐组患者的 MII 卵率[72.7%(410/564)]、优质胚胎率[42.1%(109/259)] 低于低盐组患者[82.5%(461/559), 52.4%(154/294), 均  $P<0.05$ ], 3 组间比较差异均有统计学意义( $P<0.001$ ,  $P=0.048$ )。中盐组患者其双原核卵裂率[99.1%(568/573)] 高于低盐组患者[96.1%(294/306),  $P<0.05$ ], 3 组间比较差异有统计学意义( $P=0.003$ )。胚胎种植率、临床妊娠率、早期流产率、活产率, 各组间差异均无统计学意义(均  $P>0.05$ )。调整可能的混杂因素后, 中盐组的临床妊娠率( $OR=0.520$ , 95%  $CI$ : 0.221~1.221,  $P=0.133$ )、早期流产率( $OR=1.226$ , 95%  $CI$ : 0.219~6.851,  $P=0.817$ )、活产率( $OR=0.730$ , 95%  $CI$ : 0.323~1.647,  $P=0.448$ ) 及高盐组的临床妊娠率( $OR=0.659$ , 95%  $CI$ : 0.246~1.762,  $P=0.406$ )、早期流产率( $OR=1.080$ , 95%  $CI$ : 0.162~7.180,  $P=0.937$ )、活产率( $OR=1.012$ , 95%  $CI$ : 0.396~2.588,  $P=0.980$ ) 与低盐组相比, 其差异均无统计学意义。结论 高食盐摄入水平并不影响首次助孕移植周期的临床妊娠结局, 但对卵子成熟、正常卵裂及优质胚胎形成有不利影响。

**【关键词】** 受精, 体外; 胚胎移植; 盐摄入; 点尿法

**Effect of the salt intake levels on clinical outcomes of the first transfer cycle in women undergoing assisted reproductive technology**

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**【Abstract】 Objective** To explore the effect of different salt intake levels on clinical outcomes after the first embryo transfer in women undergoing assisted reproductive technology. **Methods** This was a retrospective cohort study. A total of 163 patients with the first *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer from January 2021 to July 2021 in Reproductive Medical Center, Henan Provincial People's Hospital were recruited. The spot urine method was used to estimate the 24 h salt intake of patients, and all patients were divided into three groups based on their 25th and 75th percentiles: low-salt group ( $\leq 9.21$  g,  $n=41$ ), medium-salt group (9.22–13.31 g,  $n=81$ ), and high-salt group ( $\geq 13.32$  g,  $n=41$ ). Baseline data and clinical outcomes were analyzed and compared among the three groups. **Results** The rate of MII oocyte [72.7% (410/564)], and the rate of high-quality embryos [42.1% (109/259)] in the high-salt group were lower than those in the low-salt group [82.5% (461/559),  $P<0.05$ ; 52.4% (154/294),  $P<0.05$ ], the differences among the three groups were statistically significant ( $P<0.001$ ,  $P=0.048$ ). The rate of normal cleavage [99.1% (568/573)] in the medium-salt group was higher than that in the low-salt group [96.1% (294/306),  $P<0.05$ ], and the difference among the three groups was statistically significant ( $P=0.003$ ). After adjusting for potential confounding factors by using multivariate logistic regression, the clinical pregnancy rate ( $OR=0.520$ , 95%  $CI$ : 0.221–1.221,  $P=0.133$ ), the early miscarriage rate ( $OR=1.226$ , 95%  $CI$ : 0.219–6.851,  $P=0.817$ ), and the live birth rate ( $OR=0.730$ , 95%  $CI$ : 0.323–1.647,  $P=0.448$ ) in the medium-salt group, the clinical pregnancy rate ( $OR=0.659$ , 95%  $CI$ : 0.246–1.762,  $P=0.406$ ), the early miscarriage rate ( $OR=1.080$ , 95%  $CI$ : 0.162–7.180,  $P=0.937$ ), and the live birth rate ( $OR=1.012$ , 95%  $CI$ : 0.396–2.588,  $P=0.980$ ) in the high-salt group were comparable with the low-salt group (all  $P>0.05$ ). **Conclusion** High level of salt intake does not affect the clinical pregnancy outcomes of infertile women in their first transplantation cycle. However, it has an adverse effect on oocyte maturation, normal cleavage, and high-quality embryo formation.

**【Key words】** Fertilization *in vitro*; Embryo transfer; Salt intake; Spot urine method

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• 临床报道 •

# 女性性功能障碍与性激素相关性的多中心横断面研究

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**【摘要】** 目的 探讨内源性性激素与女性性功能的相关性。方法 本研究是一项队列研究的基线数据, 纳入 2020 年 4 月至 2021 年 3 月期间在首都医科大学附属北京妇产医院、北京市朝阳区妇幼保健院、北京市朝阳区太阳宫社区卫生服务中心就诊符合标准的 711 例女性, 收集社会人口学资料(根据学历分为高中及以上、高中以下; 根据婚姻关系分为满意、一般、不满意)和检测血清性激素水平。采用女性性功能指数(female sexual function index, FSFI)量表评估女性性功能。根据生殖衰老研讨会+10(Stages of Reproductive Aging Workshop+10, STRAW+10)分期系统标准将研究对象分为生育期(R)组、绝经过渡期(T)组, 绝经后期(P)组。Spearman 秩相关分析和多元线性回归分析确定 FSFI 及其各维度分数与血清性激素水平之间的相关性。结果 多元线性回归分析显示, FSFI 总分与绝经后期、高中以下学历、婚姻关系一般、婚姻关系不满意呈显著负相关(均  $P<0.01$ )。除疼痛评分外, 高中以下学历、婚姻关系一般或不满意与 FSFI 中其他 5 个维度得分均呈负相关(均  $P<0.05$ ); 绝经后期与阴道润滑、性满意度和性交疼痛呈负相关(均  $P<0.05$ )。内源性性激素中的卵泡刺激素与所有 FSFI 得分均呈负相关(均  $P<0.05$ ); 除性高潮和性满意意外, 雌二醇与 FSFI 中其他 4 个维度得分呈正相关(均  $P<0.05$ ); 总睾酮与 FSFI 总分和性欲得分呈正相关(均  $P<0.05$ ); 游离睾酮与性高潮得分呈正相关( $P<0.05$ )。结论 雌二醇和总睾酮是女性性功能的保护因素。

**【关键词】** 绝经; 性激素; 女性性功能障碍; 性功能指数; 生殖衰老分期

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## **A multicentre cross-sectional study on the correlation of female sexual dysfunction with sex hormones**

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**【Abstract】 Objective** To explore the correlation between endogenous sex hormone factors and sexual function in Chinese women. **Methods** A total of 711 women who met the criteria were investigated in the Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing Chaoyang District Maternal and Child Health Care Hospital, Beijing Chaoyang District Taiyanggong Community Health Service Centre from April 2020 to March 2021. Sociodemographic data (data split into two groups according to educational background: high school or above and lower high school; and three categories based on marital relationship: satisfied, average, and dissatisfied) and serum levels of sex hormones were collected. Female sexual dysfunction (FSD) was evaluated using the female sexual function index (FSFI). Participants were divided into three groups according to the Stages of Reproductive Aging Workshop (STRAW+10): reproductive stage group, menopausal transition stage group and postmenopausal stage group. Spearman rank correlation analysis and multiple linear regression analyses were performed to determine the correlation between characteristics and scores of FSFI. **Results** The multivariate logistic regression analysis revealed that postmenopausal stage, secondary education level, neutral and dissatisfied marital relations were significantly negatively correlated with total FSFI score (all  $P < 0.01$ ). Secondary education level, neutral and dissatisfied marital relations were negatively associated with nearly all FSFI domains apart from pain score (all  $P < 0.05$ ); postmenopausal stage was negatively associated with lubrication, satisfaction and pain (all  $P < 0.05$ ). FSH was negatively associated with all FSFI domain scores (all  $P < 0.05$ ). There was a significantly positive correlation between estradiol and scores of FSFI dimensions other than orgasm and satisfaction (all  $P < 0.05$ ). Total testosterone positively

affected the score of total FSFI and desire (all  $P<0.05$ ); free testosterone was positively related to orgasm ( $P<0.05$ ). **Conclusion** Estradiol and total testosterone serve as protective factors for female sexual function.

**【Key words】** Menopause; Sex hormones; Female sexual dysfunction; Sexual function index; Staging of reproductive aging

**Fund program:** Beijing Municipal Administration of Hospitals' Ascent Plan (DFL20181401); China Health Promotion Foundation (CHPF-2018-OP-11); National Menopause Health Care Specialist Construction Unit of China [(2020)30]; The First Batch of Beijing Maternal and Child Health Specialist Demonstration Units "Menopausal Health Specialist" [(2017)35]

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• 临床报道 •

# 血清尿酸水平对冻融胚胎移植妊娠结局影响的研究

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李瑾然和相佳慧对本文有同等贡献

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**【摘要】** 目的 探讨冻融胚胎移植(frozen-thawed embryo transfer, FET)周期中血清尿酸水平对妊娠结局的影响。方法 采用回顾性队列研究, 分析 2017 年 1 月至 2022 年 6 月期间在南通大学附属医院生殖医学中心行 FET 的患者临床资料。尿酸 $>340\text{ }\mu\text{mol/L}$  定义为高尿酸组( $n=157$ ), 其余患者纳入对照组( $n=899$ )。利用倾向性评分匹配法(propensity score matching, PSM)及多因素 logistic 回归分析对导致不良妊娠结局的危险因素进行筛选。结果 高尿酸组患者超重比例 [60.5% (95/157)]、抗苗勒管激素水平 [4.59 (3.23, 6.32)  $\mu\text{g/L}$ ]、窦卵泡计数 [21 (15, 28)]、流产率 [43.7% (38/87)] 均高于对照组 [13.2% (119/899),  $P<0.001$ ; 4.46 (2.51, 5.27)  $\mu\text{g/L}$ ,  $P=0.024$ ; 19 (12, 25),  $P=0.003$ ; 23.6%

(120/509),  $P<0.001$ ], 基础卵泡刺激素 [(6.73±2.04) U/L]、转化日雌二醇水平 [232.97 (147.13, 358.40) pmol/L]、活产率 [31.2% (49/157)] 均低于对照组 [(7.42±2.29) U/L,  $P<0.001$ ; 285.80 (189.11, 393.52) pmol/L,  $P=0.001$ ; 43.3% (389/899),  $P=0.005$ ]。PSM 后, 高尿酸组患者流产率 [43.7% (38/87)] 仍显著高于对照组 [23.0% (17/74),  $P=0.006$ ], 且 PSM 前后高尿酸均导致 FET 患者流产的风险显著上升 (PSM 前:  $OR=2.193$ , 95%  $CI$ : 1.301~3.697,  $P=0.003$ ; PSM 后:  $OR=3.482$ , 95%  $CI$ : 1.620~7.483,  $P=0.001$ )。结论 孕前高尿酸可能是引起 FET 患者流产的重要原因之一, 在 FET 前控制患者尿酸水平或许可以减少流产的发生。

【关键词】 尿酸; 胚胎移植; 流产; 妊娠结局

基金项目: 江苏省卫生健康委员会资助 (F202051); 南通市社会民生面上项目 (MS22022119); 南通市卫生健康委员会资助 (MS2023019)

### **Influence of serum uric acid levels on pregnancy outcomes in patients with frozen-thawed embryo transfer**

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【Abstract】 **Objective** To investigate the influence of serum uric acid level on the pregnancy outcome of frozen-thawed embryo transfer (FET). **Methods** This study was a retrospective cohort study. Patients were recruited underwent the first FET cycles at the Reproductive Medicine Center of Affiliated Hospital of Nantong University from January 2017 to June 2022. According to uric acid  $>340 \mu\text{mol/L}$  or not, the patients were divided into high uric acid group ( $n=157$ ) and control group ( $n=899$ ). Propensity score matching (PSM) and multivariate logistic regression analysis were conducted to screen the risk factors for adverse pregnancy outcomes. **Results** Patients in high uric acid group had a higher proportion of overweight [60.5% (95/157)], higher level of anti-Müllerian hormone [4.59 (3.23, 6.32)  $\mu\text{g/L}$ ] and antral follicle count [21 (15, 28)] compared with control group [13.2% (119/899),  $P<0.001$ ; 4.46 (2.51, 5.27)  $\mu\text{g/L}$ ,  $P=0.024$ ; 19 (12, 25),  $P=0.003$ ], and lower levels of basic follicle-stimulating hormone [(6.73±2.04) U/L] and estradiol on transformation day [232.97 (147.13, 358.40) pmol/L] compared with control group [(7.42±2.29) U/L,  $P<0.001$ ; 285.80 (189.11, 393.52) pmol/L,  $P=0.001$ ]. The abortion rate was higher [43.7% (38/87)] and the live birth rate was lower [31.2% (49/157)] in high uric acid group than in control group [23.6% (120/509),  $P<0.001$ ; 43.3% (389/899),  $P=0.005$ ]. After PSM, the abortion rate was significantly higher in high uric acid group as far [43.7% (38/87)] than in control group [23.0% (17/74),  $P=0.006$ ], and high uric acid greatly increased the abortion rate in FET patients before and after PSM (before PSM:  $OR=2.193$ , 95%  $CI$ : 1.301~3.697,  $P=0.003$ ; after PSM:  $OR=3.482$ , 95%  $CI$ : 1.620~7.483,  $P=0.001$ ). **Conclusion** High level of uric acid



before the pregnancy is an important risk factor for abortion in FET cycles, and controlling uric acid levels prior to conducting FET may decrease the abortion rate.

**【Key words】** Uric acid; Embryo transfer; Abortion; Pregnancy outcome

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· 现场调查 ·

# 社会归属在不孕症女性抑郁状态与生育生活质量关联中的中介作用

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**【摘要】** 目的 探讨不孕女性抑郁状态、社会归属及生育生活质量之间的关系, 为有效改善不孕女性生活质量措施的制定提供理论依据。方法 2022 年 7 月至 2022 年 10 月期间随机抽样选取安徽医科大学附属第一医院的生殖辅助中心不孕症女性治疗患者 400 例, 采用一般基础问卷, 抑郁筛查自评量表 (PHQ-9)、社会归属测量问卷及生育生活质量量表进行调查。采用 Spearman 相关分析各变量间的关联, 通过 Bootstrap 程序和 PROCESS 软件检验中介效应。结果 400 例不孕女性抑郁得分中位数为 5 分, 达到亚临床轻度抑郁水平, 社会归属测量得分中位数为 12 分, 生育生活质量得分中位数 62.87 分。社会归属与抑郁状态呈负相关 ( $r=-0.206, P<0.001$ ); 社会归属与生育生活质量呈正相关 ( $r=0.267, P<0.001$ ); 抑郁状态与生育生活质量呈负相关 ( $r=-0.428, P<0.001$ )。中介分析显示, 在控制相关变量后, 不孕症女性抑郁状态对生育生活质量的间接效应为-0.069 0 (95% CI: -0.173 3~-0.008 3), 直接效应为-1.019 1 (95% CI: -1.436 3~-0.601 8), 通过社会归属对不孕症女性抑郁状态的生育生活质量中介效应占总效应的 6.34%。

结论 社会归属在不孕症女性抑郁状态和生育生活质量中起部分中介作用。应及时关注不孕症女性心理情况，给予她们更多的社会认可和支持以改善生育生活质量。

【关键词】 不孕症； 社会归属； 抑郁； 生育生活质量

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## Mediating role of social belonging in the association between depression and fertility quality of life in infertile women

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**【Abstract】 Objective** To explore the relationship among depression, social belonging and fertility quality of life of infertile women, and to provide a theoretical basis for the development of effective measures to improve the quality of life of infertile women. **Methods** From July 2022 to October 2022, a random sample of 400 patients treated for infertility in the Reproductive Assisting Centre of the First Hospital of Anhui Medical University were selected using a general basic questionnaire, the Depression Screening Self-Rating Scale (PHQ-9), the Social Attribution Measurement Questionnaire and the Fertility Quality of Life Scale quality of life questionnaire (FertiQoL) were administered. Spearman correlation was used to analyze the association between the variables, and mediating effects were examined by Bootstrap procedure and PROCESS software. **Results** The 400 infertile women had a median depression score of 5, reaching a subclinical mild level of depression, a median score of 12 on the social belonging measure, and a median score of 62.87 on the FertiQoL. Social belonging was negatively correlated with depression ( $r=-0.206$ ,  $P<0.001$ ); social belonging was positively correlated with FertiQoL ( $r=0.267$ ,  $P<0.001$ ); and depression was negatively correlated with FertiQoL ( $r=-0.428$ ,  $P<0.001$ ). Mediation analysis showed that after controlling for relevant variables, the indirect effect of depression on FertiQoL in infertile women was  $-0.069\ 0$  (95% CI:  $-0.173\ 3--0.008\ 3$ ), and the direct effect was  $-1.019\ 1$  (95% CI:  $-1.436\ 3--0.601\ 8$ ), the mediating effect of FertiQoL through social belonging on depression in infertile women accounted for 6.34% of the total effect. **Conclusion** Social belonging plays a partial mediating role in depression and FertiQoL among infertile women. Infertile women should be given timely attention to their psychological situation and given more social recognition and support to improve their FertiQoL.

**【Key words】** Infertility; Social belonging; Depression; FertiQoL

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· 个案报道 ·

## X 染色体微小结构异常 1 例患者的遗传学诊断及配偶妊娠结局

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**【摘要】** 目的 探讨多种细胞与分子遗传学技术的联合应用在诊断染色体微小结构异常病例中的临床应用价值。方法 先证者, 男, 30 岁。因未避孕未孕 7 年于 2021 年 7 月至深圳中山泌尿外科医院生殖医学中心就诊。通过常规 G 显带技术分析染色体核型, 发现 1 例疑似 X 染色体发生微小结构畸变。运用高分辨 G 显带技术、拷贝数变异测序 (copy number variation sequencing, CNV-seq)、C 显带技术分析 & 荧光原位杂交 (fluorescence *in situ* hybridization, FISH), 明确染色体结构畸变来源及结构特征。随访该病例妊娠结局。结果 外周血淋巴细胞常规 G 显带染色体核型最初诊断为 46, Y, ? inv(X) (p22.3p22.2)。经高分辨 G 显带染色体核型分析、CNV-seq、C 显带分析及 FISH 检测确诊最终核型为 46, Y, der(X) t(X; Y) (p22.3; q12) mat。先证者配偶通过体外受精-胚胎移植技术助孕, 单胎妊娠。产前诊断羊水核型为 46, X, der(X) t(X; Y) (p22.3; q12) pat, 宫内超声胎儿未见异常。婴儿出生后一个月随访表型正常。结论 多种细胞与分子遗传学技术的联合应用, 为确诊染色体微小结构畸变提供了可信的技术平台, 为评估该类患者的表型、预后及子代风险等提供重要的遗传学依据。

**【关键词】** 荧光原位杂交; 染色体核型分析; G 显带; C 显带; 拷贝数变异

## Genetic diagnosis of one patient with microstructural abnormalities of the X chromosome and the pregnancy outcome of his spouse

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**【 Abstract 】 Objective** To explore the clinical application value of multiple cytogenetic and molecular genetic techniques in the diagnosing of chromosomal microstructural abnormalities. **Methods** The proband was a 30-year-old man. He went to Reproductive Medicine Center of Shenzhen Zhongshan Urology Hospital in July 2021 because of a 7-year history of primary infertility. Chromosome karyotype was analyzed by conventional G-banding technique. One case was found to be suspected of microstructural aberration in X chromosome. The origin and structural characteristics of this X chromosome structural aberration was identified by high-resolution G-banding, copy number variation sequencing (CNV-seq), C-banding and fluorescence *in situ* hybridization (FISH). The pregnancy outcome of this case was followed up. **Results** Conventional G-banding karyotype of peripheral blood lymphocytes was initially diagnosed as 46, Y, ?inv(X)(p22.3p22.2). The final karyotype of proband was interpreted as 46, Y, der(X) t(X; Y)(p22.3; q12) mat by high-resolution G-banding karyotype analysis, CNV-seq, C-banding analysis and FISH detection. His spouse had conceived singleton pregnancy via *in vitro* fertilization and embryo transfer. Prenatal diagnosis had been performed. Karyotype of amniotic fluid was 46, X, der(X) t(X; Y)(p22.3; q12) pat. No structural malformation was detected prenatally by ultrasound. The neonate was phenotypically normal one month after birth. **Conclusion** The combined application of multiple cytogenetic and molecular genetic techniques can provide a reliable technical platform for characterizing the microscopic structural aberrations of chromosomes, and an important genetic basis for exploring the phenotype, prognosis and offspring risk of such patients.

**【 Key words 】** *In situ* hybridization, fluorescence; Chromosome karyotype; G-banding; C-banding; Copy number variation

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· 实验技术 ·

## 高效液相色谱法测定复方左炔诺孕酮缓释微球注射剂药物含量的研究

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曹星辰和郭伊霖对本文有同等贡献

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**【摘要】** 目的 建立测定复方左炔诺孕酮缓释微球注射剂中左炔诺孕酮 (levonorgestrel, LNG) 和炔雌醇 (ethinylestradiol, EE) 含量的高效液相色谱法 (high-performance liquid chromatography, HPLC)。方法 采用 C18 色谱柱 Inertsil ODS-3 (4.7 mm×250 mm, 5 μm), 流动相为乙腈-水 (50:50, V/V), 流速为 1.0 mL/min, 柱温为 35 °C, 检测波长为 265 nm, 进样量为 20 μL。HPLC 检测方法学验证后测定微球含量。结果 LNG 在 5.03~201.20 μg/mL, EE 在 1.55~61.92 μg/mL 范围内均呈良好的线性关系 ( $r^2=0.9998$ ), 专属性、精密度、回收率、重复性、稳定性等符合要求。复方 LNG 缓释微球注射剂中 LNG 的含量是 16.26%, EE 的含量是 2.58%。结论 该 HPLC 测定方法简单、稳定、重现性好, 可为测定复方缓释制剂中左炔诺孕酮和炔雌醇含量提供参考。

**【关键词】** 左炔诺孕酮; 炔雌醇; 高效液相色谱法; 复方缓释微球注射剂; 含量测定

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**Study on the determination of compound levonorgestrel sustained release microspheres injection by HPLC**

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**【 Abstract 】 Objective** To establish a high-performance liquid chromatography (HPLC) for determining the content of levonorgestrel (LNG) and ethinylestradiol (EE) in compound levonorgestrel sustained-release microsphere injection. **Methods** C18 column Inertsil ODS-3 (4.7 mm×250 mm, 5 μm) was used. The mobile phase was acetonitrile-water (50 : 50, V/V). The flow rate was 1.0 mL/min. The column temperature was 35 °C. The detection wavelength was 265 nm, and the injection amount was 20 μL. The content of microspheres was determined after validation of HPLC detection methodology. **Results** The linear relationship was good in the range of 5.03–201.20 μg/mL LNG, 1.55–61.92 μg/mL EE ( $r^2=0.9998$ ). The specificity, precision, recovery, repeatability, stability, etc, met the requirements. The content of LNG in the compound LNG sustained-release microspheres injection was 16.26%, and the content of EE was 2.58%. **Conclusion** This HPLC can determine the content of compound levonorgestrel sustained-release injection microspheres, and the method is simple, stable, and has good reproducibility, providing a reference for the determination of levonorgestrel and ethinylestradiol in compound sustained-release preparations.

**【 Key words 】** Levonorgestrel; Ethinyl estradiol; High-performance liquid chromatography; Compound sustained-release microspheres; Content determination

**Fund program:** National Key Research & Development Program of China (2016YFC1000902); Science and Technology Innovation Action Plan of Shanghai (22DX1900400)

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· 综述 ·

# 不同促排卵方案在波塞冬低预后患者 IVF/ICSI 治疗中的应用进展

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**【摘要】** 接受辅助生殖技术治疗中的低预后患者主要表现为卵巢对外源性促性腺激素刺激反应不良、临床妊娠率低于同龄正常反应者, 既往此类人群采用博洛尼亚标准定义和诊断。为了提高研究人群的同质性, 2016 年波塞冬小组提出了新的低预后人群细分标准即波塞冬标准, 概念上从“低反应”转向“低预后”, 为低预后患者提供了临床咨询和治疗建议的分类依据。现有多种控制性促排卵方案应用于不同亚组的波塞冬低预后人群, 在不同亚组人群中的临床应用各有利弊。本文将对波塞冬分组标准下的低预后患者接受不同控制性超促排卵方案及辅助用药的临床应用进展进行阐述及总结。

**【关键词】** 生殖技术, 辅助; 卵巢刺激; 控制性超促排卵方案; 波塞冬标准; 低预后; 卵巢低反应

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## Progress in the application of different controlled ovarian stimulation protocols in IVF/ICSI treatment for POSEIDON patients

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**【 Abstract 】** Patients with low-prognosis undergoing *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) treatment are mainly manifested as poor ovarian response to exogenous gonadotropin stimulation and a lower clinical pregnancy rate than normal responders of the same age. In the past, Bologna criteria was used to define and diagnose those patients. In 2016, the Patient Oriented Strategies Encompassing Individualized Oocyte Number (POSEIDON) group proposed a new subdivision standard for low prognosis population in order to improve the homogeneity of them, which conceptually moved from poor response to poor prognosis and provided a classification basis for clinical treatment guidance and clinical counselling for POSEIDON patients. There are various controlled ovarian hyperstimulation protocols applied to POSEIDON groups, which have different effects on clinical application among different subgroups. This article will describe and summarize the progress of different ovulation induction regimens and adjuvant treatment strategies for patients with low-prognoses based on the POSEIDON criteria.

**【Key words】** Reproductive techniques, assisted; Ovulation induction; Controlled ovarian hyperstimulation; POSEIDON criteria; Low prognosis; Poor ovarian response

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· 综述 ·

## 菌群与早发性卵巢功能不全的研究进展

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**【摘要】** 早发性卵巢功能不全 (premature ovarian insufficiency, POI) 是指在女性 40 岁之前卵巢功能衰退或丧失, 导致女性不孕的常见原因, 其发病机制复杂。近期微生物群与生殖内分泌疾病的研究成为了热点, 本综述菌群通过免疫反应、炎症因子及代谢功能等途径参与 POI 的发生发展过程, 同时通过服用益生菌、粪便微生物群移植等方式能够改善菌群失调, 从而改善 POI 相关症状。未来有望通过菌群与 POI 机制的进一步研究, 为 POI 的诊治提供新的策略。

**【关键词】** 早发性卵巢功能不全; 肠道菌群; 阴道微生态; 发病机制; 治疗

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### Research progress of microbiota and premature ovarian insufficiency

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**【Abstract】** Premature ovarian insufficiency (POI) is characterized by the decline or loss of ovarian function before the age of 40 years and account for one major cause of female infertility. Its pathogenesis is complex. Recently, the research on microbiota and reproductive endocrine diseases has become a hot spot. This article reviews the involvement of microbiota in the occurrence and development of



POI through immune response, inflammatory factors and metabolic function. At the same time, taking probiotics and fecal microbiota transplantation can correct the dysbiosis of flora, so as to improve the symptoms associated with POI. In the future, it is expected to provide new strategies for the diagnosis and treatment of POI through further research on the relationship between microbiota and POI.

**【Key words】** Premature ovarian insufficiency; Gut microbiome; Vaginal microbiota; Pathogenic mechanism; Therapy

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· 综述 ·

# Sirtuins 家族与生殖衰老关系的研究进展

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**【摘要】** 伴随着人类生育时间的推迟, 研究如何干预生殖系统衰老成为具有全球性意义的课题。Sirtuins 是 NAD<sup>+</sup>依赖性组蛋白去乙酰化酶, 在基因调控、细胞凋亡、能量代谢、衰老相关疾病和生殖系统中发挥关键作用。目前研究表明, Sirtuins 基因的缺失会导致雄性和雌性生殖系统发育失调以及生殖衰老, 而且通过药物干预 Sirtuins 的表达可以影响衰老引起的生殖系统功能衰退。本篇综述全面回顾了 Sirtuins 对雄性和雌性生殖系统衰老方面的影响和作用机制, 并列举了一些可以调控 Sirtuins 活性的天然药物, 为进一步在分子水平研究生殖衰老调控提供思路。

**【关键词】** Sirtuins; 生殖衰老; 天然药物

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## Research advances on the relationship between Sirtuins family and reproductive aging

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**【Abstract】** With the postponement of human reproductive time, studying how to intervene in reproductive system aging has become a globally significant topic. Sirtuins are NAD<sup>+</sup>-dependent histone deacetylases that play key roles in gene regulation, apoptosis, energy metabolism, age-related diseases, and the reproductive system. Current evidence suggests that deletion of the *Sirtuins* gene leads to developmental disorders and reproductive aging in both males and females, and that pharmacological intervention in Sirtuins expression can affect aging-induced decline in reproductive function. This review provides a comprehensive review of the effects and mechanisms of Sirtuins on male and female reproductive aging, and lists some natural drugs that can modulate Sirtuins activity, providing ideas for further studies on the regulation of reproductive aging at the molecular level.

**【Key words】** Sirtuins; Reproductive aging; Natural medicine

**Fund program:** National Natural Science Foundation of China (82060829, 81760835); Foundation of Gansu Key Laboratory of Protection and Utilization for Biological Resources and Ecological Restoration (LDSWZY2002-3)

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· 综述 ·

## Telocytes 对妊娠的影响及可能机制

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【摘要】 妊娠的建立依赖于胚胎的胎盘绒毛膜外细胞滋养细胞合适的侵袭、母胎间的血管重铸及母胎免疫耐受。近年来，特洛细胞（telocytes, TCs）作为一种新型的间质细胞被广泛报道，它可与同种细胞或其他类型细胞相互连接，参与组织再生和修复过程、信号转导、肌肉收缩协调的起搏、分泌功能和局部微环境的免疫调节、免疫监测，从而形成复杂的三维网络，发挥重要的作用。其中它在妊娠及相关疾病中的研究也是热点之一。本文通过对 TCs 在妊娠中的作用及可能机制进行综述，为探究 TCs 在胚胎着床及妊娠维持中的作用提供更多依据。

【关键词】 特洛细胞； 妊娠； 滋养层细胞

**Effect of telocytes on pregnancy and its mechanism**

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【Abstract】 The success of pregnancy relies on moderate trophoblast invasion, sufficient vascular remodeling and maternal-fetal tolerance. Recently, telocytes (TCs) have been widely reported as a novel type of interstitial cells. Functionally, TCs form a three-dimensional interstitial network by homocellular and heterocellular communication and are involved in tissue repair and regeneration, signal transduction, muscle contraction, secretion and immune regulation. One of the hotspots is the study of TCs in pregnancy establishment and pathological pregnancy. This paper reviews the role and possible mechanism of TCs on pregnancy, so as to provide more basis for exploring the role of TCs in embryo implantation and pregnancy maintenance.

【Key words】 Telocytes; Pregnancy; Trophoblast

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· 综述 ·

人间充质干细胞在生殖医学领域中的基础研究进展

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**【摘要】** 生殖医学的快速发展为助力解决人口问题作出了突出贡献，但仍无法满足所有的夫妇成为遗传学层面的“完整父母”。随着再生医学研究的深入，研究者发现干细胞具有促进内源性修复、改善氧化应激水平、调节免疫微环境等特性。因此，干细胞移植被认为是恢复受损生殖功能的有效疗法。由于来源广泛、容易获得和低免疫原性的特点，间充质干细胞被认为是移植治疗的理想来源，并且在大量生殖领域的科学和临床研究中被证明是有效的。本文就国内外各类间充质干细胞在生殖医学领域中的基础研究进展进行综述。

**【关键词】** 间充质干细胞； 生殖医学； 不孕，不育

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## **Basic research progress of human mesenchymal stem cells in the field of reproductive medicine**

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**【Abstract】** The rapid development of reproductive medicine has made outstanding contribution to the solution of population problem, but it still cannot satisfy all couples to become "complete parents" at the genetic level. As research progressed of regenerative medicine, it is found that the stem cells have the characteristics of promoting endogenous repair, improving oxidative stress level, regulating immune microenvironment, and so on. Therefore, the transplantation of stem cells is considered to be a new and effective therapy to restore the damaged reproductive function. The mesenchymal stem cells are considered as an ideal source for transplantation therapy because of the characteristics of wide source, easy acquisition and low immunogenicity. Furthermore, it has been proven effective in a large number of scientific and clinical researches in the reproductive field. This paper reviews the basic research progress on all kinds of mesenchymal stem cells in the field of reproductive medicine at home and abroad.

**【Key words】** Mesenchymal stem cells; Reproductive medicine; Infertility

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· 综述 ·

## 人类胚胎干细胞 DNA 损伤修复机制的研究进展

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**【摘要】** 胚胎干细胞具有显著的增殖和分化发育能力, 因此在细胞治疗、疾病建模和药物研发方面具有巨大的潜力。但高效的全能性却导致其往往伴随基因组的不稳定性, 尤其在 DNA 损伤方面更加凸显。人类胚胎干细胞拥有特殊的修复机制, 用以避免这类损伤在细胞内的积累或向子代的传递, 进而保障自我复制和分化发育的准确性和安全性。本文对人类胚胎干细胞 DNA 损伤的修复机制进行了总结, 旨在为结合其修复机制, 进一步探索干细胞治疗的新思路提供依据。

**【关键词】** 基因组不稳定性; 人类胚胎干细胞; DNA 修复机制; 干细胞治疗

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### Research progress on the repair mechanisms of DNA damage in human embryonic stem cells

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**【Abstract】** Embryonic stem cells have remarkable proliferative and differentiation developmental capabilities and thus have great potential for cell therapy, disease modeling, and drug development. However, such totipotency has

resulted in genomic instability, especially in the case of DNA damage. Human embryonic stem cells possess particular repair mechanisms to avoid the accumulation of such damage within the cell or its transmission to the offspring, thus ensuring the accuracy and safety of self-replication and differentiation development. This paper summarized the repair mechanisms of DNA damage in human embryonic stem cells and intends to provide a basis for further exploration of new ideas of stem cell therapy in conjunction with their repair mechanisms.

**【Key words】** Genomic instability; Human embryonic stem cells; DNA repair mechanisms; Stem cell therapy

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