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# 不同年龄卵巢低反应患者早卵泡期长效长方案与拮抗剂促排卵方案临床效果比较

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**【摘要】目的** 探讨适合不同年龄卵巢低反应(POR)患者的临床促排卵方案。**方法** 回顾性分析了2015年1月—2017年12月期间在河南省人民医院接受体外受精-胚胎移植(IVF-ET)助孕的POR患者654个周期。根据方案及年龄不同分为A组(拮抗剂方案, 年龄<35岁, 134例)、B组(早卵泡期长效长方案, 年龄<35岁, 150例)、C组(拮抗剂方案, 年龄≥35岁, 172例)和D组(早卵泡期长效长方案, 年龄≥35岁, 198例), 比较A组与B组, C组与D组的基础情况、临床及实验室指标、临床结局等。**结果** A组与B组、C组与D组相比, 基本情况差异均无统计学意义( $P>0.05$ ); A组的促性腺激素(Gn)使用总量 $[(1\ 963.4\pm\ 613.3)\ \text{IU}]$ 、Gn使用时间 $[(7.77\pm\ 1.83)\ \text{d}]$ 、人绒毛膜促性腺激素(hCG)注射日内膜厚度 $[(9.15\pm\ 2.32)\ \text{mm}]$ 低于B组 $[(3\ 010.2\pm\ 936.9)\ \text{IU}$ 、 $(10.91\pm\ 2.63)\ \text{d}$ 、 $(10.20\pm\ 2.97)\ \text{mm}]$ ( $P<0.001$ 、 $P<0.001$ 、 $P=0.001$ ), 而A组的Gn启动日雌二醇 $[(36.55\pm\ 16.02)\ \text{ng/L}]$ 、卵泡刺激素(FSH) $[(8.64\pm\ 2.90)\ \text{IU/L}]$ 、促黄体生成素(LH) $[(4.39\pm\ 2.33)\ \text{IU/L}]$ 、hCG注射日LH水平 $[(3.08\pm\ 2.97)\ \text{IU/L}]$ 高于B组 $[(10.55\pm\ 7.29)\ \text{ng/L}$ 、 $(3.53\pm\ 1.93)\ \text{IU/L}$ 、 $(1.01\pm\ 0.84)\ \text{IU/L}$ 、 $(1.36\pm\ 1.10)\ \text{IU/L}]$ , 差异均有统计学意义( $P$ 均 $<0.001$ ); 同一年龄组2种促排卵方案之间的周期取消率、胚胎种植率、临床妊娠率及活产率比较, 差异均无统计学意义( $P>0.05$ )。**结论** 在POR患者中早卵泡期长效长方案和拮抗剂方案的临床结局相似, 但是拮抗剂方案性价比更高。

**【关键词】** 受精, 体外; 胚胎移植; 高育龄; 卵巢低反应; 拮抗剂方案; 长方案; 活产率

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**Comparison of clinical outcomes between gonadotropin-releasing hormone agonist long protocol in early follicular phase and gonadotropin-releasing hormone antagonist protocol in patients with poor ovarian response at different ages**

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**【Abstract】 Objective** To explore the suitable protocol for poor ovarian response (POR) patients in young and advanced ages. **Methods** The data of 654 *in vitro* fertilization (IVF) cycles in POR women between January 2015 and December 2017 in Henan Provincial People's Hospital were collected retrospectively. The cycles were divided into four groups according to protocol and the age: group A [gonadotropin-releasing hormone antagonist (GnRH-A) protocol, <35 years old, 134 cycles], group B [gonadotropin-releasing hormone agonist (GnRH-a) long protocol in early follicular phase, <35 years old, 150 cycles], group C (GnRH-A protocol,  $\geq 35$  years old, 172 cycles) and group D (GnRH-a long protocol in early follicular phase,  $\geq 35$  years old, 198 cycles). The general characteristics, clinical and laboratory data and clinical outcomes were compared among the four groups. **Results** The general characteristics had no significant difference between group A and group B, group C and group D ( $P>0.05$ ). Total dosage of gonadotropin (Gn) used, duration of Gn used, endometrial thickness on human chorionic gonadotropin (hCG) injection day were significantly lower ( $P<0.001$ ,  $P<0.001$ ,  $P=0.001$ ) in group A [(1 963.4 $\pm$ 613.3) IU, (7.77 $\pm$ 1.83) d, (9.15 $\pm$ 2.32) mm] than in group B [(3 010.2 $\pm$ 936.9) IU, (10.91 $\pm$ 2.63) d, (10.20 $\pm$ 2.97) mm]. Compared with group B [(10.55 $\pm$ 7.29) ng/L, (3.53 $\pm$ 1.93) IU/L, (1.01 $\pm$ 0.84) IU/L, (1.36 $\pm$ 1.10) IU/L], the levels of estradiol, follicle stimulating hormone (FSH), luteinizing hormone (LH) on Gn used day, and the levels of LH on hCG injection day of group A [(36.55 $\pm$ 16.02) ng/L, (8.64 $\pm$ 2.90) IU/L, (4.39 $\pm$ 2.33) IU/L, (3.08 $\pm$ 2.97) IU/L] were higher (all  $P<0.001$ ). There were no significant differences in cycle cancellation rate, embryo implantation rate, clinical pregnancy rate and live birth rate between the two clinical protocol in the same age group ( $P>0.05$ ). **Conclusion** The clinical outcomes of the GnRH-a long protocol in early follicular phase and the GnRH-A protocol in POR patients are comparable, but the GnRH-A protocol is more cost-effective.

**【Key words】** Fertilization *in vitro*; Embryo transfer; Advanced maternal age; Poor ovarian response; Gonadotropin-releasing hormone antagonist protocol; Long protocol; Live birth rate

DOI: 10.3760/cma.j.issn.2096-2916.2019.07.001

## CD163<sup>+</sup> 和 CD86<sup>+</sup> 巨噬细胞在反复种植失败患者 子宫内膜中的表达

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**【摘要】** 目的 探究子宫内膜中 M1/M2 极化型巨噬细胞的平衡与反复种植失败 (RIF) 发生机制的关系。方法 选取 2015 年 6 月—2016 年 6 月期间在常德市第一人民医院生殖医学中心 1 次移植成功的 29 例患者作为对照组; 选取 25 例 RIF 患者作为 RIF 组, 用免疫组织化学的方法检验患者子宫内膜中 CD86、CD163、CD68 阳性细胞的表达情况。结果 RIF 患者子宫内膜中 CD163<sup>+</sup>/CD68<sup>+</sup> 细胞的比值 ( $60.66 \pm 2.41$ ) 较对照组 ( $79.79 \pm 1.45$ ) 明显下降, 差异有统计学意义 ( $P < 0.000 1$ )。结论 RIF 患者子宫内膜中 M1 极化型巨噬细胞比例增加, M2 极化型巨噬细胞比例下降, 可能是导致患者胚胎种植失败的原因之一。

**【关键词】** 反复种植失败; CD163; CD86; 巨噬细胞; 冻融胚胎移植; 子宫内膜容受性

DOI: 10.3760/cma.j.issn.2096-2916.2019.07.002

### Expression of CD163<sup>+</sup> and CD86<sup>+</sup> macrophages in endometrium of recurrent implantation failure patients

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**【Abstract】 Objective** To explore the endometrium of macrophages in the M1/M2 polarization balance relations with recurrent implantation failure (RIF) mechanism. **Methods** We collected 29 patients with successful transplantation from June 2015 to June 2016 in Reproductive Medicine Center of Changde First People's Hospital as control group, 25 patients with RIF as RIF group. The expressions of CD86<sup>+</sup>, CD163<sup>+</sup> and CD68<sup>+</sup> cells in endometrium of the two groups were examined by immunohistochemistry. **Results** The ratio of CD163<sup>+</sup>/CD68<sup>+</sup> ( $60.66 \pm 2.41$ ) in the endometrium of RIF patients was significantly lower than that in control group ( $79.79 \pm 1.45$ ,  $P < 0.000 1$ ). **Conclusion** The imbalance of M1/M2 macrophages in the endometrium which lead to the decline of immune tolerance may be one of the reasons for the failure of embryo transplantation.

**【Key words】** Recurrent implantation failure; CD163; CD86; Macrophage; Frozen-thawed embryo transfer; Endometrial receptivity

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## 贵阳市汉族与布依族育龄女性叶酸代谢关键酶基因位点多态性研究

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**【摘要】** 目的 调查贵州省贵阳市汉族、布依族育龄女性叶酸代谢关键酶 *MTHFR*(C677T、A1298C)、*MTRR*(A66G) 基因多态性, 为叶酸营养增补方案提供分子医学理论依据。方法 选取 2017 年 2 月—2018 年 6 月期间在贵州中医药大学第一附属医院进行备孕及孕期检查的女性为研究对象, 共计 4143 人(其中汉族 3942 人、布依族 201 人)。采集并提取研究对象口腔黏膜上皮脱落细胞, 抽提 DNA, 利用荧光定量 PCR 方法检测并分析受检者 *MTHFR*(C677T、A1298C) 和 *MTRR*(A66G) 基因分型情况, 并与已报道的其他地区其他民族进行比较。结果 贵阳市汉族女性 *MTHFR*(C677T、A128C) 位点基因型频率和等位基因频率与郑州、乌鲁木齐、珠海、长春、廊坊等地汉族女性及本地布依族女性相比差异均有统计学意义 ( $P < 0.05$ ), 其中贵阳市汉族女性 *MTHFR* C677T 高风险基因型 TT 型 (14.05%) 明显低于郑州 (40.7%)、乌鲁木齐 (26.05%)、长春 (31.75%)、廊坊 (33.94%) 汉族女性, 高于珠海汉族女性 (5.71%) 及当地布依族女性 (8.46%); 贵阳布依族女性 *MTHFR* 677TT 型 (8.46%) 明显低于延边朝鲜族 (18.77%)、银川回族 (16.53%)、思南苗族 (12.93%)、大理白族 (14.54%)、辽源满族 (26.00%), 高于三亚黎族 (3.38%), *MTRR* 66GG 型 (6.97%) 低于新疆维吾尔族 (16.48%)、三亚黎族 (13.04%), 差异均具有统计学意义 ( $P < 0.05$ )。结论 贵阳市汉族与布依族育龄女性叶酸代谢关键酶基因位点多态性不同于其他地区, 其中关键基因位点 *MTHFR* C677T 的高风险比例明显低于其他地区人群(郑州汉族、乌鲁木齐汉族、长春汉族、廊坊汉族、延边朝鲜族、银川回族、思南苗族、思南土家族、大理白族、辽源满族), 叶酸利用能力高于以上地区人群, 具有地域特异性, 可以有针对性地制定符合当地民族特征的个性化叶酸补服方案。

**【关键词】** 贵阳; 汉族; 布依族; 5,10-亚甲基四氢叶酸还原酶; 甲硫氨酸合成酶还原酶

**基金项目:** 中国疾病预防控制中心妇幼保健中心妇幼保健分子遗传医学研究专项计划 (FY-ZX-ZD-334)

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### Study on single nucleotide polymorphism polymorphism of key enzymes in folic acid metabolism in Han and Buyi women in Guiyang City

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**【Abstract】 Objective** To study the characteristics of the key enzyme folic acid metabolism *MTHFR* (C677T, A1298C) and *MTRR* (A66G) in the women of the Buyi and Han ethnic groups in Guiyang City, Guizhou Province, and to provide reference for guiding the local folic acid health during pregnancy. **Methods** Totally 4143 fertile women including 201 Buyi women and 3942 Han women were selected from February 2017 to June 2018 in the First Affiliated Hospital of Guizhou University of Traditional Chinese Medicine. Genomic DNAs were obtained from oral mucosa cells. Detections of *MTHFR* and *MTRR* gene polymorphisms were conducted with Taqman-MGB technology. Genotype and allele frequency were compared with other ethnic minorities women that have been reported before. **Results** The genotype frequencies and allele frequencies of *MTHFR* (C677T, A128C) sites in Han women of Guiyang City were significantly different from those of Han women and local Buyi women in Zhengzhou, Urumqi, Zhuhai, Changchun and Langfang ( $P < 0.05$ ). Among them, the high-risk genotype TT (14.05%) of *MTHFR* C677T in Han women in Guiyang was significantly lower than that in Zhengzhou (40.7%), and was higher than that in Zhuhai Han women (5.71%) and local Buyi women (8.46%); *MTHFR* 677TT type in Guiyang Buyi women (8.46%) was significantly lower than that in Yanbian Korean (18.77%), Yinchuan Hui (16.53%), Sinan Miao (12.93%), Dali Bai (14.54%), Liaoyuan Man (26.00%), and was higher than that in Sanya Li (3.38%), there were statistical differences ( $P < 0.05$ ). *MTRR* 66GG type in Guiyang Buyi women (6.97%) was lower than that in Xinjiang Uygur (16.48%) and Sanya Yi (13.04%) with significant differences ( $P < 0.05$ ). **Conclusion** *MTHFR* (C677T, A1298C) and *MTRR* (A66G) genotype frequency in Guiyang Han and Guiyang Buyi women were different from others minorities, which could guide for a more individualized folic acid supplement program for different ethnic women.

**【Key words】** Guiyang; Han; Buyi; 5,10-Methylenetetrahydrofolate reductase; Methionine synthase reductase

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## 广东地区育龄期女性游离睾酮指数正常参考值建立

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**【摘要】** 目的 探讨广东地区育龄期女性中高雄激素血症 (HA) 的游离睾酮指数 (FAI) 诊断界值。方法 通过多级系统整群随机抽样方法, 在 2 个城区和 2 个郊区的 16 个群体中抽出 3009 名在 20~45 岁间的女性, 再通过随机方法, 在抽出的样本抽取约一半的对象 ( $n=1526$ )。对再抽取的对象在剔除可能影响雄激素水平的因素后作为参照组 ( $n=444$ ) 进行临床和实验室的检查。收集研究对象的临床资料, 计算 FAI 值。用 *K-means* 聚类分析方法 ( $K=2$ ) 和第 5 位及第 95 位百分位数确定 FAI 的界值。结果 在参照组人群中, FAI 的参考范围按第 5 位及第 95 位百分位数计算, 为 0.7~6.4。在总体人群中, 聚类分析方法将 6.1 作为划分 HA 的界值。通过聚类分析和百分位数法观察到, FAI 的诊断界值随年龄增加而下降。FAI 值与年龄负相关 ( $r=-0.185$ ,  $P<0.000 1$ ), 与调整年龄后的体质量指数 (BMI) 呈正相关 ( $r=0.250$ ,  $P<0.000 1$ )。结论 FAI 的参考范围为 0.7~6.4, HA 的 FAI 诊断界值为 6.1。按照该界值诊断 HA, 伴 HA 的女性发生合并代谢紊乱的发病率明显增加。

**【关键词】** 高雄激素血症; 游离睾酮指数; 总睾酮; 性激素结合球蛋白; *K-means* 聚类分析

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### Determining the cutoff value of free androgen index for the diagnosis of hyperandrogenemia

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**【Abstract】 Objective** To determine the normative cutoff value of free androgen index (FAI) among reproductive-age women in China. **Methods** A multistage systematic cluster random sampling was conducted by which a total sample of 3009 women aged 20–45 years were randomly selected from 16 communities in two urban and two rural regions, and about half of them ( $n=1526$ ) were selected by random sampling. Among these women, 444 subjects without known factors affecting androgen levels were selected as the reference group to undergo clinical and laboratory tests. Clinical data of subjects were collected and the FAI was calculated according to the following equation. The normative cutoff value of the FAI was computed based on the 5th–95th percentiles and  $K$ -means cluster analysis ( $K=2$ ). **Results** A reference range of 0.7–6.4 of FAI was recommended by the 5th and 95th percentiles for the reference group.  $K$ -means cluster analysis identified 6.1 as the cutoff value of FAI for the total population. The means of FAI decreased with age increasing among the total population, either evaluated by  $K$ -means or percentile analysis. The FAI value was negatively correlated with age ( $r=-0.185$ ,  $P<0.000 1$ ), and positively correlated with BMI ( $r=0.250$ ,  $P<0.000 1$ ), after the adjustment of age. **Conclusion** A reference range of FAI was 0.7–6.4, and the cutoff value of FAI for HA was 6.1. According to this cutoff value, the hyperandrogenic women present with higher risks for metabolic disorders.

**【Key words】** Hyperandrogenemia; Free androgen index; Total testosterone; Sex hormone binding globulin;  $K$ -means cluster analysis

**Fund program:** Surface Program of National Natural Science Foundation of China (81771545, 81471425); Key Program of Guangdong Provincial Bureau of Traditional Chinese Medicine (No. [2017] 19); 5010 Program of Sun Yat-sen University (2014005)

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# 体外受精 - 胚胎移植对小鼠胎盘和胎鼠早期生长的影响

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**【摘要】** 目的 探讨辅助生殖技术 (ART) 对小鼠胎盘和胎鼠早期生长的影响。方法 利用 CD1 小鼠建立自然受孕组 (SC 组)、受精卵体外培养 (IVC) 组与体外受精 (IVF) 组。胚胎发育的第 10.5 日、第 14.5 日以及第 18.5 日 (即妊娠的早、中、晚孕期), 收集胎盘和胎鼠, 比较 3 组小鼠的妊娠率、流产率, 观察小鼠胎盘发育及胎鼠宫内生长。结果 妊娠早期 [孕 10.5 d(E10.5)], IVC 组与 IVF 组小鼠妊娠率 (32.5%, 38.2%) 低于 SC 组 (56.5%) ( $P=0.012$ ;  $P=0.014$ ), 流产率 (34.5%, 45.2%) 高于 SC 组 (12.1%) ( $P<0.001$ ;  $P<0.001$ ), 而 IVC 与 IVF 组间比较差异无统计学意义 ( $P>0.05$ ); 妊娠中期 (E14.5), IVC 组与 IVF 组胎鼠重量 [(195.4±26.2) g, (221.5±32.6) g] 低于 SC 组 [(322.2±26.9) g] ( $P<0.001$ ;  $P<0.001$ ), 胎盘效率 (1.4±0.2, 1.6±0.4) 低于 SC 组 (2.5±0.3) ( $P<0.001$ ;  $P<0.001$ ), IVC 组胎鼠重低于 IVF 组 ( $P=0.006$ ), 胎盘效率差异无统计学意义 ( $P>0.05$ ); 妊娠晚期 (E18.5), IVC 组与 IVF 组胎鼠重 [(743.1±35.6) g, (617.7±29.8) g] 低于 SC 组 [(883.1±53.2) g] ( $P<0.001$ ;  $P<0.001$ ), 胎盘效率 (3.0±0.4, 2.0±0.1) 低于 SC 组 (4.9±0.5) ( $P<0.001$ ;  $P<0.001$ ), IVC 组胎鼠重、胎盘效率均高于 IVF 组 ( $P<0.001$ ;  $P<0.001$ )。结论 与自然妊娠相比, ART 小鼠妊娠率降低、流产率增加; ART 影响孕期小鼠胎盘发育, 改变孕期体质量, 降低胎盘效率。

**【关键词】** 生殖技术, 辅助; 小鼠; 胎鼠重; 胎盘效率

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**Effects of *in vitro* fertilization and embryo transfer on the early growth of mouse placenta and fetal mice**

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**【Abstract】 Objective** To investigate the effect of assisted reproductive technology (ART) on the early growth of placenta and fetus in mice. **Methods** Experimental mice were divided into three groups: female mice mate naturally with male mice (SC group); female mice and male mice were fertilized *in vitro*, zygotes were *in vitro* cultured (IVC group); female mice and male mice were fertilized and cultured *in vitro* (IVF group). Placentas and fetal rats of three groups were collected on day 10.5, day 14.5 and day 18.5 (early, middle and late gestation in pregnancy, respectively), and the pregnancy rate and the abortion rate of the three groups were calculated respectively. **Results** In early pregnancy (E10.5), the pregnancy rate in IVC group and IVF group (32.5%, 38.2%) was lower than that in SC group (56.5%) ( $P=0.012$ ;  $P=0.014$ ), the abortion rate (34.5%, 45.2%) was higher than that in SC group (12.1%) ( $P<0.001$ ;  $P<0.001$ ), but there was no statistical difference between IVC group and IVF group ( $P>0.05$ ). During middle pregnancy (E14.5), fetus weight in IVC group and IVF group [(195.4±26.2) g, (221.5±32.6) g] was lower than that in SC group [(322.2±26.9) g] ( $P<0.001$ ;  $P<0.001$ ), placental efficiency (1.4±0.2, 1.6±0.4) was lower than that in SC group (2.5±0.3) ( $P<0.001$ ;  $P<0.001$ ), the fetus weight of IVC group was lower than that of IVF group ( $P=0.006$ ), and there was no statistical difference in placental efficiency ( $P>0.05$ ). During late pregnancy (E18.5), the fetus weight in IVC group and IVF group [(743.1±35.6) g, (617.7±29.8) g] was lower than that in SC group [(883.1±53.2) g] ( $P<0.001$ ;  $P<0.001$ ), placental efficiency (3.0±0.4, 2.0±0.1) was lower than that in SC group (4.9±0.5) (all  $P<0.001$ ), the fetus weight of IVC group was lower than that of IVF group ( $P=0.006$ ), and there was no statistical difference in placental efficiency ( $P>0.05$ ). **Conclusion** Compared with natural pregnancy, ART can reduce the pregnancy rate and increase the abortion rate, and affect the development of mouse placenta during pregnancy, change the growth weight during pregnancy and reduce the placental efficiency.

**【Key words】** Reproductive technology, assisted; Mouse; Fetal rat weight; Placental efficiency

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# 第 5 日和第 6 日冻融囊胚移植的临床结局 Meta 分析

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**【摘要】** 目的 系统性评价冻融第 5 日 (D5) 和第 6 日 (D6) 囊胚移植的临床结局。方法 采用电子检索方式进行文献初检, 计算机检索 Medline、Cochrane Library、VIN、PubMed、中国知网和万方数据库。检索冻融后 D5 和 D6 囊胚移植结局对比的研究文献, 评价指标包括活产率、临床妊娠率、囊胚复苏率、着床率、流产率等。由评价者按照纳入与排除标准选择试验, 提取资料和评价质量, 并采用 RevMan5.3 软件进行 Meta 分析。结果 共纳入 16 项研究, 包括 13 484 个周期。Meta 分析结果显示: D5 冻融囊胚组的活产率 ( $RR=1.25$ , 95%  $CI=1.18\sim 1.33$ )、临床妊娠率 ( $RR=1.25$ , 95%  $CI=1.14\sim 1.37$ )、着床率 ( $RR=1.38$ , 95%  $CI=1.24\sim 1.53$ ) 均高于 D6 冻融囊胚组 ( $P$  均  $<0.05$ ); 组间囊胚复苏率相似 ( $RR=1.04$ , 95%  $CI=0.99\sim 1.09$ ,  $P=0.12$ ); 但 D5 冻融囊胚组的流产率较低 ( $RR=0.65$ , 95%  $CI=0.48\sim 0.87$ ,  $P=0.004$ )。结论 D5 冻融囊胚组在活产率、临床妊娠率、着床率方面优于 D6 冻融囊胚组, 但 D5 冻融囊胚组流产率低于 D6 冻融囊胚组。受纳入研究样本量及质量的限制, D5 和 D6 冻融囊胚移植对临床结局的影响还需开展多样本、高质量的研究。

**【关键词】** 冻融囊胚移植; 临床妊娠率; 活产率; Meta 分析

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### A Meta-analysis of clinical efficacy of day 5 and day 6 frozen-thawed blastocyst transfers

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**【Abstract】 Objective** To systematically evaluate the clinical outcomes of day 5 (D5) and day 6 (D6) frozen-thawed blastocyst transfers. **Methods** The literatures were searched electronically from the database, including Medline, Cochrane Library, VIN, PubMed, CNKI, Wanfang database. Literatures concerning trials in relation to the comparison of the outcomes of D5 and D6 frozen-thawed blastocyst transfers were searched. The evaluation indicators included live birth rate, clinical pregnancy rate, blastocyst recovery rate, implantation rate and abortion rate. Two evaluators selected the trials according to the inclusion and exclusion criteria, extracted the data and the quality evaluation, then Meta-analysis was conducted by using RevMan5.3 software. **Results** A total of 16 randomized controlled trials were included, involving 13 484 cycles. The results showed that D5 frozen-thawed blastocyst group's live birth rate ( $RR=1.25$ , 95%  $CI=1.18-1.33$ ), clinical pregnancy rate ( $RR=1.25$ , 95%  $CI=1.14-1.37$ ), and implantation rate ( $RR=1.38$ , 95%  $CI=1.24-1.53$ ) were higher than those in D6 frozen-thawed blastocyst group ( $P<0.05$ ); the recovery rate of blastocyst was similar in the two groups ( $RR=1.04$ , 95%  $CI=0.99-1.09$ ,  $P=0.12$ ), while the abortion rate of the D5 frozen-thawed blastocyst group was lower ( $RR=0.65$ , 95%  $CI=0.48-0.87$ ,  $P=0.004$ ). **Conclusion** It is suggested that the D5 frozen-thawed blastocyst group is superior to the D6 frozen-thawed blastocyst group in terms of live birth rate, clinical pregnancy rate and implantation rate, while the abortion rate is lower. However, the result is limited by the small sample size and quality of the included studies, so more samples and high-quality trials are needed to increase the credibility of the evidence.

**【Key words】** Frozen-thawed blastocyst transfers; Pregnancy rate; Live birth rate; Meta analysis

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## 经皮穴位电刺激技术在体外受精 - 胚胎移植取卵术中镇痛的疗效与安全性观察

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**【摘要】** 目的 观察经皮穴位电刺激 (TEAS) 技术在体外受精 - 胚胎移植 (IVF-ET) 取卵术中镇痛的有効性与安全性。方法 选取 2018 年 1—8 月期间在武汉大学人民医院生殖中心行取卵手术的患者 (直径  $\geq 14$  mm 的卵泡数量为 5~15 个), 共 108 例, 根据医生和患者的意愿分为试验组 ( $n=43$ )、安慰组 ( $n=20$ ) 和药物对照组 ( $n=45$ ), 术前 30 min 分别给予不同的干预措施。试验组给予 TEAS 2/100 Hz, 10~20 mA 电刺激, 安慰组给予 TEAS 2 Hz, 2 mA 电刺激, 药物对照组给予双氯芬酸钠栓 100 mg 直肠给药。分别观察 3 组患者的获卵率、疼痛评估指数 (PRI)、视觉模拟评分 (VAS)、现存疼痛强度 (PPI)、恶心评分、呕吐评分、双原核 (2PN) 受精率、2PN 卵裂率及优质胚胎率。结果 试验组 VAS 评分较安慰组和药物对照组低, 差异有统计学意义 (分别为  $P=0.033$ ,  $P<0.001$ ); 试验组恶心评分较安慰组低, PRI 评分和 PPI 评分均较药物对照组低, 差异有统计学意义 ( $P=0.028$ ,  $P=0.014$ ); 3 组间获卵率, 2PN 受精率, 2PN 卵裂率以及优质胚胎率差异无统计学意义 ( $P>0.05$ )。结论 在 IVF-ET 取卵术中, 经皮穴位电刺激镇痛效果优于安慰剂与双氯芬酸钠止痛栓, 且对 IVF-ET 结局无影响。

**【关键词】** 受精, 体外; 胚胎移植; 经皮穴位电刺激; 取卵术

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**Efficacy and safety of transcutaneous electrical acupoint stimulation anesthesia in the oocyte retrieval of *in vitro* fertilization-embryo transfer**

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**【Abstract】 Objective** To observe the efficacy and safety of transcutaneous electrical acupoint stimulation (TEAS) in the oocyte retrieval of *in vitro* fertilization-embryo transfer (IVF-ET). **Methods** Totally 108 patients who undergoing oocyte retrieval were selected (the number of follicles with diameter greater than or equal to 14 mm was 5–15) in this study and were divided into three groups (experimental group, placebo group and drug control group) guided by the wishes of doctors and patients. The experimental group was treated with TEAS treatment (2/100 Hz, 10–20 mA), the placebo group was treated with TEAS treatment (2 Hz, 2 mA), and the control group was treated with diclofenac sodium suppository (100 mg). The oocyte-obtained rate, pain regarded index (PRI), visual analogue score (VAS), present pain index (PPI), nausea score, vomiting score, two pronucleus (2PN) fertilization rate, 2PN cleavage rate, and high-quality embryo rate were observed in the three groups. **Results** VAS score in experimental group was lower than that in placebo group and drug control group, and the differences were statistically significant ( $P=0.033$ ,  $P<0.001$ , respectively). The nausea score of experimental group was lower than that of placebo group, and both PRI and PPI scores were lower than those of drug control group, with statistically significant differences ( $P=0.028$ ,  $P=0.014$ ). There was no statistically significant difference among the three groups in oocyte-obtained rate, 2PN fertilization rate, 2PN cleavage rate and high-quality embryo rate ( $P>0.05$ ). **Conclusion** In the oocyte retrieval of IVF-ET, the effect of transcutaneous electric acupoint stimulation on analgesia was better than placebo and diclofenac sodium suppository.

**【Key words】** Fertilization *in vitro*; Embryo transfer; Transcutaneous electrical acupoint stimulation; Oocyte retrieval

**Fund program:** National Natural Science Foundation of China (81771618); National Natural Science Foundation of China (81571513)

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## 宫腔镜子宫纵隔切除术对合并自然流产子宫纵隔患者生殖预后的影响

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**【摘要】** 目的 探讨自然流产合并子宫纵隔患者行宫腔镜子宫纵隔切除术 (transcervical resection of septa, TCRS) 后生殖预后。方法 回顾性分析 2016 年 1 月—2017 年 12 月期间于重庆市妇幼保健院就诊的 88 例有自然流产史的子宫纵隔患者的临床资料, 根据孕产史分为复发性流产组 ( $\geq 2$  次自然流产, 40 例) 和偶发性流产组 (1 次自然流产, 48 例), 比较两组患者 TCRS 术后治疗效果、妊娠结局和妊娠并发症。结果 复发性流产组术后早期流产率由术前 86.0% 下降为 13.3%, 足月活产率由术前的 2.8% 上升到 66.7%, 差异均有统计学意义 ( $P$  均  $<0.001$ )。偶发性流产组术后早期流产率由术前 81.1% 下降为 6.9%, 足月活产率由术前的 3.8% 上升到 75.9%, 差异均有统计学意义 ( $P$  均  $<0.001$ )。复发性流产组宫腔粘连发生率 (20.0%) 高于偶发性流产组 (4.2%,  $P=0.039$ ), 剖宫产率也更高 (85.0% 比 54.5%,  $P=0.047$ ), 差异均有统计学意义。结论 TCRS 可明显改善有自然流产史的子宫纵隔患者的生殖预后, 建议子宫纵隔患者在一次自然流产后尽早进行 TCRS, 可避免再次流产操作, 减少宫腔粘连的发生及降低剖宫产率。

**【关键词】** 子宫纵隔; 复发性流产; 子宫纵隔切除术; 妊娠结局

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### Effect of hysteroscopic transcervical resection of septa on prognosis of patients with uterine septum combined with spontaneous abortion

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**【Abstract】 Objective** To analyze the effect of hysteroscopic transcervical resection of septa (TCRS) on prognosis of patients with uterine septum combined with spontaneous abortion. **Methods** From January 2016 to December 2017, 88 patients with spontaneous abortion complicated with uterine septum were treated with TCRS in Chongqing Health Center for Women and Children. According to the history of pregnancy, the patients were divided into recurrent abortion group ( $\geq 2$  times abortion,  $n=40$ ) and incident abortion group (once abortion,  $n=48$ ). Pregnancy outcomes between preoperative and postoperative were compared between the two groups. Then pregnancy outcomes and pregnancy complications were compared between the recurrent spontaneous abortion group and the sporadic abortion group. **Results** The early abortion rate in the recurrent spontaneous abortion group decreased from 86.0% to 13.3% after surgery, and the live birth rate increased from 2.8% to 66.7% postoperation (all  $P<0.001$ ). The early abortion rate in the incident abortion group decreased from 81.1% to 6.9% after surgery, and the full-term live birth rate increased from 3.8% to 75.9% postoperation (all  $P<0.001$ ). The incidence of intrauterine adhesions and cesarean section in the recurrent abortion group (20.0%, 85.0%) was significantly higher than that in the incident abortion group (4.2%, 54.5%) ( $P=0.039$ ,  $P=0.047$ ). **Conclusion** TCRS can significantly improve the pregnancy outcome of patients with spontaneous abortion. It is recommended that patients with uterine septum undergo transcervical resection of septum as soon as possible after the first spontaneous abortion, which can avoid re-abortion, and reduce the occurrence of intrauterine adhesions and the rate of cesarean section.

**【Key words】** Uterine septum; Recurrent spontaneous abortion; Uterine septal resection; Pregnancy outcome

**Fund program:** Chongqing Basic Research and Frontier Exploration Project (Chongqing Natural Science Foundation) (cstc2018jcyjAX0648)

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## 手淫取精失败患者身心体验的质性研究

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**【摘要】**目的 了解男性不育患者手淫取精失败后的真实感受，为改善其就诊体验提供依据。方法 采用目的采样法，选取 2018 年 3—5 月期间在南京医科大学第二附属医院生殖医学科接受辅助生殖治疗而取精失败的男性患者 15 例，资料采用面对面、半结构式深入访谈的形式进行收集，然后运用 Colaizzi 内容分析法对资料进行整理和分析。结果 取精失败后患者普遍存在负性身心体验，归纳为 5 个主题：自卑与挫败感，愧疚感，焦虑与烦躁，固执与愤怒，身体极度疲惫。结论 手淫取精失败后患者的身心体验问题显著，应针对手淫取精各环节制定相应措施。

**【关键词】**手淫；取精失败；身心体验；质性研究

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**Experience of patients failing to ejaculate masturbation: a qualitative study**

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**【Abstract】 Objective** To explore the experience of patients failing to ejaculate masturbation, providing references for improving their experience of medical care. **Methods** Purposive sampling method was used to select 15 patients who had failed to ejaculate masturbation in Reproductive Medicine Department, the Second Affiliated Hospital of Nanjing Medical University from March to May 2018. Research data were collected in the form of face-to-face and semi-structured in-depth interview, and analyzed by Colaizzi content analysis. **Results** After the failure of ejaculate masturbation, negative physical and mental feelings were common in male patients. In the research, 5 topics were extracted: inferiority and frustration, sense of guilt, anxiety and irritability, stubbornness and anger, extreme exhaustion. **Conclusion** The problem of experience of patients failing to ejaculate masturbation was significant, and their treatment experience was worthy of attention.

**【Key words】** Masturbation; Failing to ejaculate; Patient experience; Qualitative study

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## 广东省人类精子库 13 705 例供精志愿者淘汰原因分析

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**【摘要】目的** 分析人类精子库志愿者淘汰原因, 促进人类精子库对志愿者进行规范筛选, 提高筛选质量。**方法** 回顾性分析广东省专科医院人类精子库自 2003 年成立以来至 2017 年累计 15 年招募的全部 13 705 例供精志愿者的筛选资料, 采用描述性统计学方法对志愿者的淘汰原因进行分析。**结果** 筛选期间 80.5% 志愿者进行了 1 次精液检查, 19.5% 进行了 2 次精液检查。共有 54.7%(7498/13 705) 的志愿者因精液质量没有达到捐精标准被淘汰; 45.3%(6207/13 705) 的志愿者筛选精液质量达到捐精标准后又进行了传染病、性传播性疾病和遗传病等相关检查。全部检查筛选合格的志愿者 4160 名, 占 30.3%。共有 2047 名志愿者因实验室检测项目结果异常被淘汰, 占 33.0%。淘汰原因如下: 4.14%(257/6207) 乙肝表面抗原阳性, 0.19%(12/6207) 丙肝抗体阳性, 0.11%(7/6207) 梅毒抗体阳性, 0.03%(2/6207) 人类免疫缺陷病毒 (HIV) 抗体阳性, 3.63%(225/6207) 优生四项抗体阳性, 0.14%(9/6207) 衣原体阳性, 6.61%(410/6207) 支原体阳性, 0.03%(2/6207) 淋菌阳性, 0.27%(17/6207) 细菌培养有致病菌生长, 11.64%(722/6207) 地中海贫血筛查异常, 4.29%(266/6207) G6PD 酶缺乏, 1.92%(118/6207) 染色体核型异常。**结论** 捐精志愿者病原体的筛查阳性率均低于普通人群, 人类精子库须严格把握志愿者淘汰原则, 加强志愿者招募时的宣传教育工作。

**【关键词】** 精子库; 志愿者; 筛选; 淘汰; 实验室检查

**基金项目:** 广东省医学科研基金 (2018182); 中华医学会基金 (16020310647); 广州市科技项目 (201707010394); 广东省科技项目 (2017A020214001)

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## Analysis of reasons for elimination of 13 705 sperm donors in the Human Sperm Bank of Guangdong Province

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**【Abstract】 Objective** To analyze the reasons for the elimination of human sperm bank volunteers in order to promote the standardized screening of human sperm bank volunteers, and improve the quality of screening. **Methods** A retrospective analysis was done on the screening data of all 13 705 sperm donors recruited by Guangdong Human Sperm Bank from its establishment in 2003 to 2017. **Results** During the screening period, 80.5% of the volunteers had one semen test and 19.5% had two semen tests. A total of 54.7% (7498/13 705) of the volunteers were eliminated because the quality of semen did not meet the standard of sperm donation; 45.3% (6207/13 705) of the volunteers were screened for semen quality to meet the standard of sperm donation and then examined for infectious diseases, sexually transmitted diseases and genetic diseases. A total of 4160 eligible volunteers were screened and accounted for 30.3%. A total of 2047 volunteers were eliminated by laboratory test results, accounting for 33%. The reasons for elimination were as follows: 4.14% (257/6207) HBsAg positive, 0.19% (12/6207) hepatitis C antibody positive, 0.11% (7/6207) syphilis antibody positive, 0.03% (2/6207) HIV antibody positive, 3.63% (225/6207) eugenic four antibodies positive, 0.14% (9/6207) *Chlamydia* positive, 6.61% (410/6207) *Mycoplasma* positive, 0.03% (2/6207) were positive for gonorrhea, 0.27% (17/6207) for pathogenic bacteria, 11.64% (722/6207) for thalassemia screening, 4.29% (266/6207) for G6PD enzyme deficiency, and 1.92% (118/6207) for chromosomal abnormalities. **Conclusion** The positive rate of pathogen screening in sperm donation volunteers was lower than that in the general population, so human sperm bank must strictly grasp the principle of volunteer elimination, and strengthen the publicity and education of volunteer recruitment.

**【Key words】** Sperm bank; Volunteers; Screening; Elimination; Laboratory examination

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## 多囊卵巢综合征糖脂代谢异常对卵母细胞及胚胎发育影响的研究进展

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**【摘要】** 多囊卵巢综合征(polycystic ovary syndrome, PCOS)是育龄期妇女常见的内分泌紊乱性疾病,容易并发糖代谢异常、脂代谢异常、子宫内膜增生或癌症等。目前认为 PCOS 患者的血液或卵泡液中高浓度的葡萄糖会影响卵母细胞及胚胎的发育,而脂代谢物质的具体影响机制尚不明确。本文总结已发表文献来阐明 PCOS 患者的糖脂代谢异常对卵母细胞及胚胎发育的影响机制,以期为 PCOS 的诊断和治疗提供理论依据。

**【关键词】** 多囊卵巢综合征; 糖脂代谢异常; 卵母细胞; 胚胎

**基金项目:** 国家自然科学基金项目(81571407); 河南省科技创新杰出人才(164200510019); 河南省医学科技攻关计划(201702216)

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**Research progress on the influence of polycystic ovary syndrome glycolipid metabolism abnormality on oocyte and embryo development**

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**【Abstract】** Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of reproductive age. It is easy to be complicated by abnormal glucose metabolism, abnormal lipid metabolism, endometrial hyperplasia or cancer. At present, it is believed that the high concentration of glucose in the blood or follicular fluid of PCOS patients will affect the development of oocytes and embryos, while the specific mechanism of the influence of lipid metabolites is still unclear. This paper summarizes published literatures to elucidate the influence mechanism of abnormal glucose and lipid metabolism on oocyte and embryo development in PCOS patients, so as to provide theoretical basis for the diagnosis and treatment of PCOS.

**【Key words】** Polycystic ovary syndrome; Abnormal glycolipid metabolism; Oocyte; Embryo

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## 胰高血糖素样肽 -1 受体激动剂在多囊卵巢综合征中的临床应用

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**【摘要】** 多囊卵巢综合征 (PCOS) 是育龄期妇女常见的生殖内分泌疾病。近年来, 胰高血糖素样肽 -1 (GLP-1) 受体激动剂的问世是重要的医学进展, 此类药物可以促进胰岛素分泌及胰岛  $\beta$  细胞生长, 抑制食欲减缓胃排空, 进而降低体质量和改善胰岛素抵抗 (IR), 同时有调整月经周期、性激素紊乱及提高妊娠率的作用, 因此逐渐应用于 PCOS 的治疗。目前较常使用的药物包括利拉鲁肽 (Liraglutide) 和艾塞那肽 (Exenatide), 多项研究证实此类药物无论是单独使用还是和二甲双胍联合应用, 都有很好的治疗效果。本文就 GLP-1 受体激动剂在 PCOS 中的临床应用作一综述。

**【关键词】** 胰高血糖素样肽 -1; 胰高血糖素样肽 -1 受体激动剂; 多囊卵巢综合征; 胰岛素抵抗

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**Application of glucagon like peptide-1 receptor agonists in the treatment of polycystic ovary syndrome**

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**【Abstract】** Polycystic ovary syndrome (PCOS) is one of the most common reproductive endocrine diseases of women in reproductive age. In recent years, the advent of glucagon like peptide-1 (GLP-1) receptor agonists is an important medical progress. Such drugs can promote insulin secretion and islet beta cell growth, inhibit appetite, slow down gastric emptying, reduce weight and improve insulin resistance (IR). What's more, it can adjust menstrual cycles, sex hormone disorders and increase the pregnancy rate of PCOS patients. As a result, they are gradually applied to the treatment of PCOS. Currently, the most frequent used drugs include liraglutide and exenatide. A number of studies have confirmed there are positively curative effects, both the monotherapy and the combining way with metformin. This article reviews the clinical application of GLP-1 receptor agonists in PCOS.

**【Key words】** Glucagon-like peptide-1; Glucagon like peptide-1 receptor agonists; Polycystic ovary syndrome; Insulin resistance

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## 女性癌症患者生育能力保存

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**【摘要】** 近年来, 随着癌症患者生存率的提高和辅助生殖技术的快速发展, 女性癌症患者生育力保存技术得到了卓有成效的发展。女性癌症生育力保护与保存的方法有: 注射促性腺激素释放激素类似物 (GnRH-a), 胚胎冷冻、成熟卵母细胞冷冻、卵巢组织冷冻与移植、未成熟卵母细胞体外成熟、卵泡体外培养以及人造卵巢等。这些方法使得女性癌症患者在完成抗癌治疗后能够进行生育, 有望在不久的将来能够改善她们的生活质量, 更好地保存她们成为母亲的希望。

**【关键词】** 生育能力保存; 卵巢早衰; 胚胎冷冻; 体外成熟; 卵巢组织冷冻

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### Fertility preservation for female cancer patients

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**【Abstract】** At present, an improvement in the survival rates of cancer patients and the recent advancements in assisted reproductive technologies have led to remarkable progress in fertility preservation treatments. The methods of fertility protection and preservation for female cancer patients include: gonadotropin releasing hormone analogue (GnRH-a) injection, embryos cryopreservation, mature oocytes cryopreservation, ovarian tissue cryopreservation and implantation, oocytes *in vitro* maturation, follicles *in vitro* maturation and artificial ovaries, et al. These methods enable female cancer patients to have children after anti-cancer treatment, improve their quality of life and preserve their hope of becoming mothers.

**【Key words】** Fertility preservation; Premature ovarian failure; Embryos cryopreservation; *In vitro* maturation; Ovarian tissue cryopreservation

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## 子宫内膜异位症性不孕的研究进展

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**【摘要】** 子宫内膜异位症 (endometriosis, EMS) 是一种常见的良性妇科疾病, 临床表现为痛经、慢性盆腔痛、性交痛和不孕症等。EMS 是导致女性不孕的主要原因之一。EMS 产生一系列的改变, 如盆腔解剖结构和微环境的变化、炎症因子表达异常、激素变化和胚胎着床受损等, 都可能影响卵泡发育和子宫内膜容受性, 从而影响卵母细胞生长和成熟、受精、胚胎着床等过程, 进而影响妊娠。

**【关键词】** 子宫内膜异位症; 不孕症; 炎症; 卵泡发育; 子宫内膜容受性

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### **Progress of endometriosis-associated infertility**

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**【Abstract】** Endometriosis (EMS) is a common benign gynecological disease. Its clinical manifestations include dysmenorrhea, chronic pelvic pain, dyspareunia and infertility. EMS is one of the main causes of female infertility. There are series changes in EMS, such as changes in pelvic anatomy and microenvironment, abnormal expression of inflammatory factors, hormonal changes, and embryo implantation damage. These may affect follicular development and endometrial receptivity. It will affect the process of oocyte growth and maturation, fertilization and embryo implantation, which will have adverse effects on pregnancy outcomes.

**【Key words】** Endometriosis; Infertility; Inflammatory; Follicular development; Endometrial receptivity

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## 长链非编码 RNA 在免疫系统以及妊娠过程中的功能

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**【摘要】**长链非编码 RNA(lncRNA) 在天然和获得性免疫反应中已经成为基因表达的关键调节分子。尽管已有文献报道 lncRNA 与某些疾病相关, 特别是炎症相关疾病, 但对在妊娠及流产状态下的表达及功能知之甚少。本文回顾 lncRNA 调控转录程序的不同分子机制, 以及在免疫应答过程中如何控制细胞群的功能和维持体内平衡。此外, 还讨论免疫相关疾病以及妊娠中 lncRNA 对免疫系统的影响和所面临的挑战。

**【关键词】**妊娠并发症; 流产; 免疫调节; 长链非编码 RNA

**基金项目:** 国家自然科学基金 (81771618)

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**Function of long noncoding RNA in immunity and pregnancy**

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**【Abstract】** Long noncoding RNA (lncRNA) has been a key regulator of gene expression in innate and adaptive immunity. Although lncRNA has been reported to be associated with some diseases, especially inflammatory related diseases, its expression and function in pregnancy and abortion is still known little. We reviewed how lncRNA regulated transcription, and controlled the function and balance of the cells in the immune response. In addition, we discussed the impacts and challenges of lncRNA on immune system in immune-related diseases and pregnancy.

**【Key words】** Pregnancy complications; Abortion; Immunomodulating; Long non-coding RNA

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## 大气污染细颗粒物对女(雌)性生殖健康影响的研究进展

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**【摘要】**近年来, 大气污染中的细颗粒物(PM<sub>2.5</sub>) 对人体的健康危害受到持续地广泛关注, 然而其对于女(雌)性生殖健康危害的研究尚较为缺乏。文献数据显示, 无论是人群调查资料还是动物实验研究, PM<sub>2.5</sub> 暴露可能引起雌性生育能力降低、生殖系统损伤以及多种不良妊娠结局, 包括流产、早产、低出生体质量儿和胎盘重量下降等。其作用机制迄今以炎症介质假说、氧化损伤假说和干扰下丘脑-垂体-性腺轴假说被多数人认可。本文基于近十年有关 PM<sub>2.5</sub> 对雌性生殖危害的文献, 对该领域的研究进展做一综述, 可为今后 PM<sub>2.5</sub> 雌性生殖毒性的深入研究提供参考。

**【关键词】** 大气污染细颗粒物; 雌性; 生殖健康

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### Impact of atmospheric fine particles on female reproductive health

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**【Abstract】** Research on the health hazards of atmospheric particulate (PM<sub>2.5</sub>) pollutants has become a hot topic in the public and science community. There are a lot of researches on the respiratory and cardiovascular impacts of PM<sub>2.5</sub>. However, the literature regarding PM<sub>2.5</sub> and female reproductive health are limited, and revealed that PM<sub>2.5</sub> exposure might cause female fertility decrease, reproductive system damage, and a variety of adverse pregnancy outcomes (including miscarriage, premature birth, low birth weight and placental weight) in the epidemiology studies and animal experiments. Its action mechanism hypothesis included the inflammatory mediators hypothesis, the oxidative injury hypothesis, and the hypothalamic-pituitary-gonadal axis hypothesis. Based on the literatures on the female reproductive hazards of PM<sub>2.5</sub> in recent ten years, the present article summarized the research progress in this field and provide references for further research on female reproductive toxicity of PM<sub>2.5</sub> in the future.

**【Key words】** Atmospheric particulate; Female; Reproductive health

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