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多囊卵巢综合征评估和管理国际循证指南推荐建议（2023 年版）

尹婧雯[1]　杨纨[1]　于多[1]　孙迪[1]主译　王洋[1]　黄佳[2]　江琳琳[2]　杨冬梓[2]　李蓉[1]审校

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【摘要】 研究问题　结合已有的最佳证据、临床经验和患者意愿，制定多囊卵巢综合征（polycystic ovarian syndrome，PCOS）女性的评估标准和管理建议。归纳总结　本次国际循证指南，包括 254 项推荐意见和实践要点，阐述了需优先解决的问题，以求统一诊疗流程，改善 PCOS 女性的个人感受和健康状态。已知事项　2018 年的国际 PCOS 指南综合了六大洲患者的资料及多学科的建议，现在被 196 个国家使用并广泛引用。它采用了强有力的方法学并强调了需要优先解决的问题。该指南的诊断标准从基于共识过渡到基于证据，提高了诊断的准确性，促进了治疗的一致性。然而，PCOS 患者的需求仍没有得到充分满足，证据质量偏低，证据和实践之间的差距仍然存在。研究设计、规模、持续时间　2023 年国际循证指南更新版重新召集了 2018 年的指南制定组织，涉及专业学会、多学科专家和各阶段 PCOS 患者的直接参与。遵循指南研究与评价（Appraisal of Guidelines for Research and Evaluation，AGREE）Ⅱ标准，完成了广泛的证据综合。在证据质量、可行性、可接受性、成本、实施、最终推荐强度、多样性和包容性方面，对推荐等级、评估、发展和评价（the Grading of Recommendations，Assessment，Development，and Evaluation，GRADE）框架进行了分级。参与者/材料、设置、方法　本摘要可以与完整的指南一起阅读。编写成员包括六大洲国际咨询和项目委员会，5 个指南制定小组以及儿科、患者和翻译委员会。大量的医学专业人员和患

者的参与提升了指南的范围和优先事项。国际上多个学科专家包括儿科、内分泌学、妇科、初级保健、生殖内分泌、产科、精神病学、心理学、营养学、运动生理学、肥胖干预、公共卫生等专家，以及患者群体、项目管理、证据分析和统计及翻译专家参与。71 个国家的 39 个协会和组织通过 12 个月的 20 场会议和 5 场面对面国际会议，提出了 58 项优先考虑的临床问题，涉及 52 项系统综述和 3 项叙事评论。5 个指南制定小组根据国际反馈和同行评议，独立审查方法学的严谨性，并由澳大利亚国家健康与医学研究委员会（Australian Government National Health and Medical Research Council，NHMRC）批准，经组内一致协商表决，对循证建议进行了修改。主要成果和改进　在过去的五年中，PCOS 评估和管理的证据总体上有所改善，但证据仍然是低到中等质量。该指南提供了 77 个循证建议，54 项临床共识建议和 123 项临床实践要点。本指南的主要更新包括：①进一步完善个体化诊断标准，简化诊断标准以及纳入抗苗勒管激素（anti-Müllerian hormone，AMH）作为超声的替代方案；②加强对 PCOS 更多方面特征的认识，包括代谢危险因素、心血管疾病、睡眠呼吸暂停、心理特征和妊娠期间不良结局的高风险因素；③强调了对疾病的认知不足、疾病负担的多样化、医疗保健专业继续教育的必要性，以及护理模式的改进和医患之间的共同决策，同时加强科研，以改善患者体验；④在意识到体质量问题的同时，强调健康的生活方式、情感健康和生活质量；⑤提出一个以循证医疗为前提，患者花费少、安全性高的生育管理方式。局限性　总体而言，证据和建议都得到了加强和改善，但证据仍然是低至中等质量，仍需要更深入的研究。同时需结合地方医疗系统的差异来提供医疗指导，翻译和普及指南。研究结果的广泛影响　在最佳循证证据、多学科专家建议和患者意愿的基础上，本指南为临床医师和患者提供了最佳的清晰的实践建议。该指南目前计划多方面发布和转载，以及多种语言的翻译、全球普及宣传。研究资助/竞争利益（S）　该指南主要由 NHMRC 资助，该委员会与美国生殖医学学会、内分泌学会、欧洲人类生殖与胚胎学会提供合作支持。指南制定小组成员未收取任何费用。差旅费用由赞助组织承担。根据 NHMRC 指导流程，利益冲突在整个指南制定过程、技术支持、同行评议中可以体现，相关细节可在 www.monash.edu/medicine/mchri/pcos 获取。

【关键词】　多囊卵巢综合征；　指南；　循证；　评估；　管理；　证据分级

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·国际指南与解读·

《2023 多囊卵巢综合征评估和管理国际循证指南》更新要点解读

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【摘要】 多囊卵巢综合征（polycystic ovary syndrome，PCOS）是一种常见的妇科内分泌疾病，导致女性无排卵性不孕及月经失调的主要原因，且远期代谢、心血管疾病、生殖系肿瘤及情绪心理障碍风险增加，影响女性青春期到绝经后整个生命健康。为协助全球医务人员制定临床决策，提供更优“PCOS 生命全周期管理”方针，欧洲人类与生殖胚胎学会、美国生殖医学会于 2018 年共同发布了 PCOS 评估和管理国际循证指南。2023 年 8 月，指南制定小组整合新的循证证据，并联合美国内分泌学会和欧洲内分泌学会对指南进行了更新，本文就指南更新要点进行介绍和解读。

【关键词】 多囊卵巢综合征； 指南； 抗苗勒管激素； 解读； 更新

基金项目：湖南省科技创新计划（2021SK50605）

Interpretation to the Update Key Points of *International Evidence-based Guideline for the Assessment and Management of Polycystic Ovary Syndrome 2023*

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【Abstract】 Polycystic ovary syndrome (PCOS) is a common endocrinopathy affecting reproductive aged women, leading to infertility and menstrual disorders, and increasing the risk of cardiometabolic diseases, reproductive tumors, and emotional and psychological disorders in later life. In order to aid healthcare professionals and consumers in decisions about appropriate and effective care, and to provide a better approach to the "full life cycle management of PCOS", the European Society of Human Reproduction and Embryology and American Society for Reproductive Medicine published international evidence-based guidelines in 2018, and the guidelines were updated in August 2023 by integrating new evidence-based evidence, in collaboration with the Endocrine Society and European Society of Endocrinology. This article introduces and explains the key points of the new guideline update.

【 Key words 】 Polycystic ovary syndrome; Guideline; Anti-Müllerian hormone; Interpretation; Update

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·临床研究·

分析高孕酮状态下促排卵方案温和刺激和常规刺激对波塞冬第 4 组人群累积活产率的影响

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【摘要】 目的　评估高孕酮状态下促排卵方案（progestin-primed ovarian stimulation protocols，PPOS）中，温和刺激和常规刺激在波塞冬 4 组人群中的累积活产率（cumulative live birth rate，CLBR）。方法　本研究属于单中心、回顾性队列研究。研究纳入 2017 年 1 月至 2020 年 3 月期间在郑州大学第三附属医院生殖中心首次行体外受精/卵胞质内单精子注射（*in vitro* fertilization/intracytoplasmic sperm injection，IVF/ICSI） 助孕的周期，纳入符合波塞冬标准第 4 组患者，所有患者均行 PPOS。根据促性腺激素（gonadotropin，Gn）启动剂量不同，分为温和刺激和常规刺激两组。温和刺激组 Gn 启动剂量为 150 U；常规刺激组 Gn 启动剂量为 300 U。主要观察指标为 CLBR。次要观察指标为获卵数、双原核（two pronuclei，2PN）数、可利用胚胎数、优质胚胎数和累积妊娠率。结果　共有 1 334 个周期符合纳入排除标准，经倾向性评分匹配（propensity score matching，PSM）模型 1∶3 匹配后，共纳入温和刺激 116 个周期，常规刺激 348 个周期进行统计描述和分析。常规刺激组的 Gn 用量［2 700.00（2 400.00，3 300.00） U］显著高于温和刺激组［1 500.00（918.75，2 456.25） U，*P*<0.001］。常规刺激组的获卵数［3.00（2.00，4.00）个］、2PN 数［2.00（1.00，3.00 个）］、可利用胚胎数［1.00（1.00，2.00）个］和优质胚胎数［1.00（0.00，1.00）个］显著高于温和刺激组［2.00（1.00，3.00）个，*P*<0.001；1.00（1.00，2.00）个，*P*=0.002；1.00（0.00，2.00）个，*P*=0.002；0.00（0.00，1.00）个，*P*=0.025］。温和刺激和常规刺激的累积妊娠率差异无统计学意义［分别为 15.52%（18/116），19.54%（68/348），*P*=0.334］。温和刺激组的 CLBR 为 11.21%（13/116），常规刺激组的 CLBR 为 14.08%（49/348），两组间

差异无统计学意义（*P*=0.431）。结论　常规卵巢刺激的 Gn 用量增加，获卵数和可利用胚胎数多于温和刺激，但两种刺激方案的 CLBR 是相似的。因此，对于使用 PPOS 方案的卵巢低预后患者，温和刺激也是一种重要的临床选择。

【关键词】　累积活产率；　获卵数；　控制性卵巢刺激；　高孕酮状态下促排卵

基金项目：2021 年度河南省医学科技攻关联合共建项目（LHGJ20210451）

Analysis of the cumulative live birth rate of Poseidon 4 group by mild stimulation and conventional stimulation with progestin-primed ovarian stimulation protocols

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【**Abstract**】　**Objective**　To evaluate the cumulative live birth rate (CLBR) of mild stimulation and conventional stimulation in Poseidon 4 group for progestin-primed ovarian stimulation protocols (PPOS). **Methods**　It was a single-center, retrospective cohort study. The study included the first *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) cycles in the Reproductive Center of the Third Affiliated Hospital of Zhengzhou University from January 2017 to March 2020, and included patients met the criteria of Poseidon 4 group and accepted PPOS. According to the different starting dosage of gonadotropin (Gn), it was divided into mild stimulation group and conventional stimulation group. In mild stimulation group, Gn starting dosage was 150 U, and in conventional stimulation group Gn starting dosage was 300 U. The primary outcome measure was CLBR. Secondary observation indicators were No. of oocytes retrieved, No. of two pronuclei (2PN), No. of available embryos, No. of high-quality embryos and cumulative pregnancy rate. **Results**　A total of 1 334 cycles met the inclusion and exclusion criteria. After 1∶3 propensity score matching (PSM) model, 116 cycles of mild stimulation and 348 cycles of conventional stimulation were included for analysis. The total dosage of Gn used in the conventional ovarian stimulation group was significantly higher than that in the mild stimulation group [2 700.00 (2 400.00, 3 300.00) U *vs*. 1 500.00 (918.75, 2 456.25) U, *P*<0.001]. The number of oocytes retrieved [3.00 (2.00, 4.00)], 2PN [2.00 (1.00, 3.00)], available embryos [1.00 (1.00, 2.00)] and high-quality embryos [1.00 (0.00, 1.00)] in the conventional stimulation group were significantly higher than those in the mild stimulation group [2.00 (1.00, 3.00), *P*<0.001; 1.00 (1.00, 2.00), *P*=0.002; 1.00 (0.00,2.00),*P*=0.002; 0.00 (0.00, 1.00), *P*=0.025]. There was no statistical difference in the cumulative pregnancy rate between mild stimulation and conventional stimulation [15.52% (18/116) *vs*. 19.54% (68/348), *P*=0.334]. The CLBR of the mild stimulation group was 11.21% (13/116), and the CLBR of the conventional stimulation group was 14.08% (49/348), with no significant difference between the two groups (*P*=0.431). **Conclusion** Conventional stimulation increased the dosage of Gn used, and the number of

oocytes retrieved and available embryos were more than those in mild stimulation, but the CLBR was similar between the two protocols. Therefore, mild stimulation is also an important clinical option for patients with low ovarian prognosis.

【Key words】 Cumulative live birth rate; Number of oocytes retrieved; Controlled ovarian stimulation; Progestin-primed ovarian stimulation protocols

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·临床研究·

生长激素在反复种植失败患者鲜胚移植中的作用：一项回顾性队列研究

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【摘要】 目的 探讨生长激素（growth hormone，GH）的辅助治疗是否可以改善反复移植失败患者新鲜周期胚胎移植的妊娠结局。方法 回顾性队列研究分析 2016 年 1 月至 2020 年 12 月期间就诊于北京大学第三医院妇产科生殖医学中心满足反复种植失败患者的体外受精/卵胞质内单精子注射（*in vitro* fertilization/intracytoplasmic sperm injection，IVF/ICSI）新鲜移植周期资料。通过 SPSS26.0，根据年龄、体质量指数、不孕因素以及窦卵泡计数进行 1∶1 倾向性评分匹配，设定卡钳值为 0.015，所得数据分为 GH 治疗组（*n*=552）和无 GH 治疗组（*n*=552），比较两组卵巢刺激结局、着床率、临床妊娠率以及活产率。结果 GH 治疗组和无 GH 治疗组反复种植失败患者的活产率、着床率和临床妊娠率差异均无统计学意义（均 *P*>0.05）。基于促排卵方案的各组分析同样提示两组间活产率、着床率和临床妊娠率差异也均无统计学意义（均 *P*>0.05）。logistic 回归同样表明，GH 辅助治疗对反复移植失败患者的活产率无影响（*OR*=1.035，95% *CI*: 0.720~1.487，*P*=0.854）。结论 GH 辅助治疗可能无法改善反复种植失败患者鲜胚移植的活产率。

【关键词】 生长激素； 反复种植失败； 活产率

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Effects of growth hormone in patients with repeated implantation failures undergoing fresh embryo transfer: a retrospective cohort study

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【Abstract】 **Objectives** To investigate whether adjuvant treatment with growth hormone (GH) can improve the pregnancy outcomes of patients with fresh embryo transfer after repeated implantation failures (RIF). **Methods** This retrospective cohort study was performed in patients who underwent *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) fresh transfer cycle and were expected RIF from January 2016 to December 2020 in Reproductive Medicine Center, Department of Obstetrics and Gynecology, Peking University Third Hospital. Using SPSS26.0, a 1∶1 propensity score matching was conducted based on age, body mass index (BMI), infertility factors, and antral follicle count with a caliper value of 0.015. The data obtained were then divided into GH treatment group (*n*=552) and non-GH treatment group (*n*=552). The controlled ovarian stimulation outcomes, implantation rate, clinical pregnancy rate, and live birth rate were compared between the two groups. **Results** The implantation rate, the clinical pregnancy rate and the live birth rate of RIF patients in GH treatment group and non-GH treatment group were not significantly different (all *P*>0.05). Furthermore, analysis of various groups based on ovulation induction protocols similarly indicated no statistically significant differences in live birth rate, implantation rate, and clinical pregnancy rate between the two groups (all *P*>0.05). Logistic regression also indicated that GH adjuvant therapy has no effect on the live birth rate in RIF patients (*OR*=1.035, 95% *CI*: 0.720–1.487, *P*=0.854). **Conclusion** Adjuvant GH treatment may not improve the live birth rate of fresh embryo transfer in RIF patients.

【Key words】 Growth hormone; Repeated implantation failures; Live birth rate

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SIRT1、*FSHR* 基因多态性在蒙古族及汉族辅助生殖技术助孕女性中的分布研究

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【摘要】 目的　探究辅助生殖技术（assisted reproductive technology，ART）助孕女性 *SIRT1* 和卵泡刺激素受体（follicle-stimulating hormone receptor，FSHR）基因多态性与卵巢功能的关系及在蒙古族及汉族间的差异性，为 ART 助孕个体化治疗提供依据。方法　采用回顾性队列研究，收集 2019 年 9 月至 2021 年 9 月期间于内蒙古医科大学附属医院生殖中心就诊的 204 例 ART 助孕患者的临床资料，其中，蒙古族 53 例，汉族 151 例。MassARRAY SNP 分型技术检测 *SIRT1* 的 rs2236319 及 *FSHR* 的 rs6165、rs6166 共 3 个位点，*SIRT1* 分为 3 组：AA 组（野生型）、AG 组（杂合型）、GG 组（突变型）；*FSHR* rs6165 分为 TT 组（野生型）、AT 组（杂合型）、AA 组（突变型）；*FSHR* rs6166 分为 NN 组（野生型）、NS 组（杂合型）、SS 组（突变型）3 种基因型，对比各组基因型频率及 ART 助孕临床和实验室数据的差异性。结果　①*SIRT1* rs2236319、*FSHR* rs6165、rs6166 位点等位基因频率、基因型频率在蒙古族与汉族 ART 女性患者组间差异均无统计学意义（均 *P*>0.05）。蒙古族及汉族 ART 女性一般临床资料及基础性激素、卵巢储备功能方面差异均无统计学意义（均 *P*>0.05）。②*SIRT1* 基因 rs2236319 位点突变型 GG 组的获卵数为 18.5 （13.0， 32.8）个，AA 组为 13.0 （7.0， 20.0）个，AG 组为 10.0 （5.0，21.0）个，3 组间比较差异具有统计学意义（*P*=0.019）。③*FSHR* 基因 rs6165 位点 AA 组的基础 FSH 水平为（7.45±2.73） U/L，TT 组为（5.97±2.23） U/L，TA 组为（6.70±2.04） U/L，3 组间比较差异具有统计学意义（*P*=0.005）。AA 组发生卵巢低反应的比例为 29.6%（8/27），TT 组为 8.5%（8/94），TA 组为 13.3%（11/83），3 组间比较差异具有统计学意义（*P*=0.017）。④*FSHR* 基因 rs6166 位点 SS 组的基础 FSH 水平为（7.48±2.78）U/L，NN 组为（6.08±2.28）U/L，NS 组为（6.61±1.99）U/L，3 组间比较差异具有统计学意义（*P*=0.016）。SS 组发生卵巢低反应的比例为 37.0%（10/26），NN 组为 8.5%（8/99），NS 组为 10.8% （9/79），3 组间比较差异具有统计学意义（*P*=0.001）。结论　蒙古族与汉族女性一般临床资料、基础性激素、卵巢储备功能无差异性。*SIRT1* 基因 rs2236319 位点基因多态性与卵巢高反应性相关。*FSHR* rs6165、rs6166 位点基因多态性与卵巢低反应性相关。3 个位点多态性与 ART 临床妊娠率无明显相关性。

【关键词】 多态性，单核苷酸； SIRT1； 卵泡刺激素受体； 卵巢反应性； 控制性超促排卵

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Study on the distribution of *SIRT*1 and *FSHR* polymorphism in Mongolian and Han women undergoing assisted reproductive technology

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【 **Abstract** 】 **Objective** To explore the relationship between the polymorphisms of *SIRT*1 and follicle-stimulating hormone receptor (FSHR) gene and ovarian function in women who underwent assisted reproductive technology (ART) and the differences between Mongolian and Han nationalities, so as to provide basis for the individualized treatment of ART assisted pregnancy. **Methods** A retrospective cohort study was performed. The clinical data of 204 ART patients who visited the Reproductive Center of the Affiliated Hospital of Inner Mongolia Medical University from September 2019 to September 2021 were collected. There were 53 cases of Mongolian nationality and 151 cases of Han nationality. MassARRAY SNP genotyping technology was used to detect three sites, which were rs2236319 of *SIRT*1 and rs6165 and rs6166 of *FSHR*. *SIRT*1 was divided into three groups: AA group (wild type), AG group (heterozygous type) and GG group (mutant type); *FSHR* rs6165 was divided into TT group (wild type), AT group (heterozygous type), AA group (mutant type); *FSHR* rs6166 was divided into NN group (wild type), NS group (heterozygous type) and SS group (mutant type). The differences of genotype frequency and clinical and laboratory data were compared. **Results** 1) The allele frequencies and genotype frequencies of *SIRT*1 rs2236319, *FSHR* rs6165, and rs6166 loci were not statistically different in composition between Mongolian and Han ART female patient groups. There were no significant differences between Mongolian and Han ART women in terms of general clinical data and basal sex hormones and ovarian reserve function (all $P>0.05$). 2) There was a statistically significant difference in the number of eggs captured at the rs2236319 locus of the *SIRT*1 gene among the mutant GG group [18.5 (13.0, 32.8)], the AA group [13.0 (7.0, 20.0)] and the AG group [10.0 (5.0, 21.0), $P=0.019$]. 3) There was a statistically significant difference in the basal FSH levels at the rs6165 locus of the *FSHR* gene among the AA group [(7.45±2.73) U/L], the TT group [(5.97±2.23) U/L] and the TA group [(6.70±2.04) U/L, $P=0.005$]. The proportion of ovarian hyporesponsiveness among the AA group [29.6% (8/27)], the TT group [8.5% (8/94)] and the TA group [13.3% (11/83)] was statistically significant ($P=0.017$). 4) The difference in basal FSH levels at the rs6166 locus of the *FSHR* gene among the SS group [(7.48±2.78) U/L], the NN group [(6.08±2.28) U/L] and the NS group [(6.61±1.99) U/L] was statistically significant ($P=0.016$). The proportion of ovarian hyporesponsiveness among the SS group [37.0% (10/26)], the NN group [8.5% (8/99)] and the NS group [10.8% (9/79)] was statistically significant ($P=0.001$). **Conclusion** There were no significant differences between Mongolian and Han ART women in terms of general clinical data, basal sex hormones and ovarian reserve function. The gene polymorphism at rs2236319 of *SIRT*1 gene is associated with ovarian

hyperresponsiveness. *FSHR* rs6165 and rs6166 gene polymorphisms are associated with ovarian hyporesponsiveness. There was no significant correlation between the three polymorphisms and the clinical pregnancy rate of ART.

【Key words】 Polymorphism, single nucleotide; SIRT1; Follicle-stimulating hormone receptor; Ovarian response; Controlled ovarian hyperstimulation

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·实验研究·

模拟海拔 6 500 米低氧环境对雌性小鼠生殖功能的影响

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【摘要】 目的 探讨模拟海拔 6 500 m 低氧环境对 BALB/c 雌性小鼠生殖功能的影响。方法 将 50 只 6 周龄 BALB/c 雌鼠按体质量随机区组法分为对照组和高原组，其中高原组又分为高原 3 d 组、高原 5 d 组、高原 10 d 组及高原 15 d 组，每组 10 只，高原组放置于低压低氧舱模拟海拔 6 500 m 高原环境，每天光照/黑暗比为 12 h∶12 h，然后取卵巢测定卵巢指数，免疫组织化学法（immunohistochemistry，IHC）、蛋白免疫印迹法（Western blotting，WB）测定卵巢组织中低氧诱导因子-1α（hypoxia-inducible factor 1α，HIF-1α）的表达，苏木素-伊红（hematoxylion and eosin，HE）染色评估卵巢卵泡情况，酶联免疫吸附法

（enzyme linked immunosorbent assay，ELISA）测定血清生殖激素水平，了解模拟高原低氧环境对雌性小鼠生殖功能的影响。结果　①生殖激素指标比较：与对照组的抗苗勒管激素（anti-Müllerian hormone，AMH）[（3 417.67±316.02） μg/L]相比，高原各组 AMH 水平均降低，其中高原 10 d 组[（2 643.50±210.01） μg/L]、高原 5 d 组［（2 195.50±160.88） μg/L］、高原 15 d 组［（2 174.40±709.23） μg/L]差异均有统计学意义（均 *P*<0.05）。与对照组卵泡刺激素（follicle-stimulating hormone，FSH）［（68.02±2.80） U/L］相比，高原 5 d 组、高原 10 d 组、高原 15 d 组 FSH 水平均有下降，其中高原 5 d 组［（64.20±4.11） U/L］、高原 10 d 组［（59.05±5.16） U/L］、高原 15 d 组［（57.46±3.58） U/L］差异均有统计学意义（均 *P*<0.05）。与对照组黄体生成素［luteinizing hormone，LH；（6.71±1.01） U/L］相比，高原 5 d 组、高原 10 d 组、高原 15 d 组 LH 水平均有下降，其中高原 10 d 组［（5.18±0.30） U/L］、高原 15 d 组［（4.86±0.53） U/L］差异有统计学意义（*P*=0.005，*P*<0.001）。与对照组雌二醇［（105.56±5.43） pmol/L］相比，高原 5 d 组［（90.92±5.08） pmol/L］、高原 15 d 组［（81.46±3.96） pmol/L］差异有统计学意义（*P*=0.038，*P*<0.001）。与对照组孕酮［（13.63±0.69） μg/L］相比，高原各组孕酮值均下降，高原 3 d 组［（11.45±0.65） μg/L］、高原 5 d 组［（8.86±0.72） μg/L］、高原 10 d 组［（9.56±0.53） μg/L］、高原 15 d 组［（9.29±0.64） μg/L］差异均有统计学意义（均 *P*<0.001）。②卵巢组织学改变：小鼠卵巢 HE 染色显示，与对照组相比，高原组卵巢各级生长卵泡数目减少，闭锁卵泡增多，颗粒细胞凋亡，可见到静脉血管淤血扩张。③HIF-1α 的表达：IHC 检测显示，随低氧时间延长，表达 HIF-1α 的阳性细胞比率增加，WB 检测显示，高原各组较对照组 HIF-1α 蛋白表达升高（均 *P*<0.001）。④卵巢指数比较：与对照组（0.408±0.083）相比，高原各组卵巢指数均降低，高原 3 d 组、高原 5 d 组、高原 10 d 组和高原 15 d 组分别为 0.271±0.087、0.114±0.035、0.076±0.052、0.109±0.026，5 组间比较差异均有统计学意义（均 *P*<0.001）。结论　暴露于模拟海拔 6 500 m 高原低氧环境使得卵巢组织缺氧，对雌性小鼠生育力造成一定的不良影响，为下一步进行女性生育力保护相关研究提供了理论基础。

【关键词】　高原；　雌性小鼠；　低氧诱导因子-1α；　生殖功能

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Effect of simulated altitude of 6 500 m hypoxia environment on reproductive function of female mice

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【**Abstract**】　**Objective**　To explore the effect of simulated 6 500 m altitude hypoxia on the fertility of BALB/c female mice. **Methods**　In this study, 50 6-week-old BALB/c female mice were randomly divided into control group and plateau groups according to body weight. The plateau group divided into plateau 3-day group,plateau 5-day group,plateau 10-day group and plateau 15-day group, every

group included 10 female mice. A low pressure hypoxic animal test chamber was used to establish a simulated low pressure hypoxia mouse model at an altitude of 6 500 m, the daily light/dark ratio was 12 h ∶ 12 h. In each group, the hypoxia-inducible factor 1α (HIF-1α) level in the mouse ovary was tested by Western blotting (WB) and immunohistochemistry (IHC), mouse ovarian tissue morphology and the changes in the numbers of the egg follicles were observed by hematoxylion and eosin (HE) staining pathological section, enzyme-linked immunosorbent assay (ELISA) was used to get the serum values of reproductive hormone. **Results** 1) Compared with control group [(3 417.67±316.02) μg/L], the levels of anti-Müllerian hormone (AMH) decreased in all groups of the plateau, among them, plateau 10-day group [(2 643.50±210.01) μg/L], the plateau 5-day group [(2 195.50±160.88) μg/L] and plateau 15-day group [(2 174.40±709.23) μg/L] showed significant differences (all P<0.05). Compared with control group [(68.02±2.80) U/L], the levels of follicle-stimulating hormone (FSH) decreased in the plateau 5-day group [(64.20±4.11) U/L, P=0.029], plateau 10-day group [(59.05±5.16) U/L, P<0.001] and plateau 15-day group [(57.46±3.58) U/L, P<0.001]. Compared with control group [(6.71±1.01) U/L], the levels of luteinizing hormone (LH) decreased in the plateau 5-day group, plateau 10-day group and plateau 15-day group, among them, the plateau 10-day group [(5.18±0.30) U/L] and plateau 15-day group [(4.86±0.53) U/L] showed significant differences compared with control group (P=0.005, P<0.001). Compared with control group [(105.56±5.43) pmol/L], the levels of estradiol in the plateau 5-day group [(90.92±5.08) pmol/L] and the plateau 15-day group [(81.46±3.96) pmol/L] showed significant differences compared with control group (P=0.038, P<0.001). Compared with control group[(13.63±0.69) μg/L], the levels of progesterone in plateau groups were decreased, the plateau 3-day group [(11.45±0.65) μg/L], the plateau 5-day group [(8.86±0.72) μg/L], plateau 10-day group [(9.56±0.53) μg/L] and plateau 15-day group [(9.29±0.64) μg/L] showed significant differences compared with control group (all P<0.001). 2) Compared with control group, the numbers of ovarian follicles decreased, atretic follicles increased, granulosa cells apoptosis and venous vascular expansion were observed. 3) IHC showed that the ratio of HIF-1α positive cells increased with the extension of hypoxia. WB showed that the expressions of HIF-1α in the plateau groups increased compared with control group (all P<0.001). 4) Compared with control group (0.408±0.083), the ovarian index were decreased in plateau 3-day group (0.271±0.087), plateau 5-day group (0.114±0.035), plateau 10-day group (0.076±0.052) and plateau 15-day group (0.109±0.026), the difference was significant among the five groups (P<0.001). **Conclusion** Exposure to the simulated low oxygen environment of 6 500 m altitude makes the mouse ovarian tissue hypoxia, which causes certain adverse effects on the fertility of female mice, and provides a theoretical basis for the next research on female fertility protection.

【 Key words 】 Plateau; Female mice; Hypoxia-inducible factor 1α; Reproductive functions

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·实验研究·

肌肽对小鼠卵母细胞体外成熟和胚胎发育的影响

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【摘要】 目的　探讨肌肽对小鼠卵母细胞体外成熟和胚胎发育的影响。方法　获取小鼠卵丘-卵母细胞复合体（cumulus-oocyte complexes，COC），分别用含10 μmol/L、30 μmol/L、50 μmol/L、100 μmol/L、200 μmol/L 肌肽的体外成熟培养液培养 18 h，不含肌肽的培养液设为对照组。根据卵母细胞成熟率、卵裂率和囊胚形成率确定作用的最优浓度。通过检测活性氧（reactive oxygen species，ROS）水平、总谷胱甘肽（total glutathione，T-GSH）含量、皮质颗粒分布、线粒体分布和线粒体拷贝数进一步验证肌肽的作用。结果　肌肽浓度为 100 μmol/L 时，卵母细胞成熟率［69.23%（135/195）］、卵裂率［66.06%（72/109）］和囊胚形成率［48.61%（35/72）］最高，与对照组［44.44%（84/189）、38.67%（29/75）、20.69%（6/29）］相比，差异具有统计学意义（*P*<0.001、*P*<0.001、*P*=0.010），故选定 100 μmol/L 作为肌肽作用的最优浓度。对照组卵母细胞中的 ROS 和 T-GSH 水平为 100 μmol/L 肌肽组的 2.04 倍和 0.64 倍，差异具有统计学意义（均 *P*<0.001）。100 μmol/L 肌肽组的皮质颗粒Ⅲ级的比例显著高于对照组（*P*<0.001）。对照组卵母细胞的线粒体均匀分布在胞质中，100 μmol/L 肌肽组的线粒体聚集在胞质中央区域，且荧光强度高于对照组（*P*=0.040）。100 μmol/L 肌肽组的线粒体拷贝数是对照组的 1.72 倍，差异具有统计学意义（*P*<0.001）。结论　肌肽能够有效改善未成熟卵母细胞的氧化应激，促进小鼠卵母细胞的体外成熟和胚胎发育。

【关键词】 肌肽；　胚胎发育；　线粒体；　未成熟卵母细胞；　体外成熟
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Effects of carnosine on mouse oocyte *in vitro* maturation and embryo development

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【**Abstract**】 **Objective** To explore the effects of carnosine on *in vitro* maturation (IVM) of mouse oocytes and the developmental competency of embryos. **Methods** The mouse cumulus-oocyte complexes (COC) were isolated and cultured in the IVM medium containing 10 μmol/L, 30 μmol/L, 50 μmol/L,100 μmol/L,or 200 μmol/L carnosine for 18 h. IVM medium without carnosine was acted as control group. The optimal concentration was chosen according to the rates of oocyte maturation, embryo cleavage and blastocyst formation. The effect of carnosine was further verified by detecting the levels of reactive oxygen species (ROS), and total glutathione (T-GSH), the distribution of cortical granules and mitochondria, and also the copy numbers of mitochondria. **Results** In the 100 μmol/L carnosine group, the rates of oocyte maturation [69.23% (135/195)], embryo cleavage [66.06% (72/109)] and blastocyst formation [48.61% (35/72)] were the highest and showed statistically significant differences (P<0.001, P<0.001, P=0.010) when compared with control group [44.44% (84/189), 38.67% (29/75), 20.69% (6/29)]. Therefore, 100 μmol/L was selected as the optimal concentration of carnosine. The levels of ROS and T-GSH in control group were 2.04 and 0.64 times as those in the 100 μmol/L carnosine group (both P<0.001). The percentage of grade Ⅲ cortical granules in the 100 μmol/L carnosine group was significantly higher than that in control group (P<0.001). The mitochondria of oocytes in control group were uniformly distributed, while the mitochondria in the 100 μmol/L carnosine group gathered in the central cytoplasmic region, and the fluorescence intensity was higher than that in control group (P=0.040). The mitochondrial copy number in the 100 μmol/L carnosine group was as much 1.72 times as that in control group (P<0.001). **Conclusion** Carnosine effectively improves oxidative stress in the immature oocytes and promotes the mouse oocyte IVM and embryo development.

【**Key words**】 Carnosine; Embryo development; Mitochondria; Immature oocytes; *In vitro* maturation

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·临床报道·

短期不同水平 $PM_{2.5}$ 暴露对早卵泡期降调节方案助孕患者妊娠结局的影响

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【摘要】 目的 探讨短期（30 d）不同水平 $PM_{2.5}$ 暴露对早卵泡期降调节方案助孕患者的卵子质量、胚胎质量和妊娠结局的影响。方法 采用回顾性队列研究的方法，选取 2018 年 12 月至 2019 年 2 月、2019 年 7~9 月期间于湖北医药学院附属人民医院（十堰市人民医院）生殖医学中心进行辅助生殖助孕的早卵泡期降调节方案患者作为研究对象。根据 $PM_{2.5}$ 的空气质量新标准，以 115 μg/m³作为分界值，将患者分为高暴露组（*n*=94）和低暴露组（*n*=254）。患者从开始促排卵到验孕日这一时间段，活动区域均在十堰市市区，计算该时间段大气细颗粒物 $PM_{2.5}$ 总量及日均量。比较两组间细颗粒物 $PM_{2.5}$ 对卵子异常率、胚胎质量（可利用胚胎数、优质胚胎数、优质胚胎率、囊胚形成率）及妊娠结局（妊娠率、流产率、移植周期活产率、低出生体质量儿比例等）的影响。结果 $PM_{2.5}$ 高暴露组的可利用胚胎数［（3.9±1.1）个］、优质胚胎数［（2.9±1.5）个］、优质胚胎率［35.5%（352/992）］与低暴露组［（4.3±1.2）个，*P*=0.005；（3.4±1.7）个，*P*=0.001；40.4%（792/1 959），*P*=0.009］相比，均显著下降，而低出生体质量儿比例［21.4%（12/56）］显著高于低暴露组［5.26%（8/156），*P*<0.001］，差异有统计学意义。结论 短期 $PM_{2.5}$ 高水平暴露对早卵泡期降调节方案的可利用胚胎数、优质胚胎数、优质胚胎率以及低出生体质量儿比例有明显负面影响。

【关键词】 受精，体外； 胚胎移植； $PM_{2.5}$； 胚胎质量； 垂体降调节； 妊娠结局

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Effects of short-term exposure to different levels of $PM_{2.5}$ on pregnancy outcomes in patients with early-follicular phase downregulation scheme

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【Abstract】 **Objective** To study the effects of short-term (30 d) exposure to different levels of $PM_{2.5}$ on oocyte quality, embryo quality and pregnancy outcomes in patients with early-follicular phase downregulation scheme. **Methods** From December 2018 to February 2019, and from July to September 2019, 348 patients with early-follicular phase downregulation scheme who underwent assisted reproduction and assisted pregnancy in the Reproductive Medicine Center, Renmin Hospital, Hubei University of Medicine were selected as the research objects in this retrospective cohort study. According to $PM_{2.5}$ new air quality standard, with 115 μg/m^3 as the cut-off value, the patients were divided into high exposure group (*n*=94) and low exposure group (*n*=254). During the period from the start of ovulation induction to the pregnancy test day, the activity areas of the patients are in the urban area of Shiyan City. The $PM_{2.5}$ of atmospheric fine particles during this period was calculated, including total amount and daily average amount. The effects of fine particulate matter $PM_{2.5}$ on ovum abnormality rate, embryo quality (number of available embryos, number of high-quality embryos, high-quality embryo rate, and blastocyst formation rate) and pregnancy outcome (pregnancy rate, abortion rate, live birth rate and proportion of low birth weight infants) were compared between the two groups. **Results** Compared with the low exposure group, the number of available embryos (3.9±1.1 *vs.* 4.3±1.2, *P*=0.005), the number of high-quality embryos (2.9±1.5 *vs.* 3.4±1.7, *P*=0.001), high-quality embryo rate [35.5% (352/992) *vs.* 40.4% (792/1 959), *P*=0.009] and proportion of low birth weight infants [21.4% (12/56) *vs.* 5.13% (8/156), *P*<0.001] in the high exposure group were significantly decreased, and there was no significant difference in other data. **Conclusion** Short-term exposure to high levels of $PM_{2.5}$ had significant negative effects on the number of available embryos, the number of high-quality embryos, the rate of high-quality embryos and proportion of low birth weight infants in the early-follicular phase down-regulation scheme.

【Key words】 Fertilization *in vitro*; Embryo transfer; $PM_{2.5}$; Embryo quality; Pituitary down-regulation; Pregnancy outcome

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·临床报道·

PPOS 方案促排卵全胚冷冻患者首次冻融胚胎移植时机对临床及围产期结局的影响：一项倾向性评分匹配研究

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【摘要】　目的　探讨应用醋酸甲羟孕酮（medroxyprogesterone acetate，MPA）行高孕激素状态下促排卵（progestin primed ovarian stimulation，PPOS）方案，全胚冷冻患者首次冻融胚胎移植（frozen-thawed embryo transfer，FET）时机对临床结局的影响。方法　回顾性队列研究分析 2015 年 1 月至 2021 年 11 月期间在郑州大学第三附属医院生殖医学中心行 PPOS 方案促排卵全胚冷冻后首次 FET 患者的临床资料，根据其促排卵周期取卵日与首次 FET 日的时间间隔分为两组，A 组为取卵后首次月经周期进行移植（时间间隔≥24 d 且<45 d，*n*=80），B 组为取卵后至少间隔 1 个月进行移植（时间间隔≥45 d，*n*=1 040）。经倾向性评分匹配（propensity score matching，PSM）后，比较两组患者一般资料、临床促排卵情况、胚胎实验室指标、首次 FET 周期相关指标、临床及围产期结局。结果　匹配前 A 组年龄［38（35，41）岁］明显高于 B 组［37（32，40）岁，*P*=0.020］。PSM 后 A 组为 80 个周期，B 组为 240 个周期。匹配后两组患者一般资料比较差异均无统计学意义（均 *P*>0.05）；两组促排卵周期资料、胚胎实验室指标、临床妊娠率、活产率及围产期结局差异均无统计学意义（均 *P*>0.05）。结论　相比于取卵后至少间隔 1 个月行 FET，PPOS 方案取卵后首次月经来潮周期行 FET 并不会影响临床及围产期结局。可根据患者情况考虑在取卵后尽早行 FET，以缩短患者到达首次活产的时间。

【关键词】　高孕激素状态下促排卵；　冻融胚胎移植；　移植时机；　临床妊娠率；　围产期结局

Effect of timing of first frozen-thawed embryo transfer on clinical and perinatal outcomes in whole embryo cryopreservation patients with PPOS protocol: a propensity score matching study

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【Abstract】 **Objective** To investigate the timing of the first frozen-thawed embryo transfer (FET) on clinical and perinatal outcomes in whole embryo freezing patients, who used the medroxyprogesterone acetate (MPA) in progestin primed ovarian stimulation (PPOS). **Methods** A retrospective cohort study was conducted to analyze the clinical data of patients with the first FET after ovulation induction by PPOS protocol in Reproductive Medicine Center of the Third Affiliated Hospital of Zhengzhou University from January 2015 to November 2021. According to the time interval between the day of oocytes retrieved and the day of the first FET in the ovulation induction cycle, they were divided into two groups. Group A: transplantation was performed during the first menstrual cycle after oocyte retrieval (time interval ≥24 d and <45 d, *n*=80), group B: transplantation was performed at least one month apart after oocytes retrieved (time interval ≥45 d, *n*=1 040). After propensity score matching (PSM), the general data, clinical excretion promotion, embryo laboratory indicators, indicators related to the first FET cycle, clinical and perinatal outcomes were compared between the two groups. **Results** Before PSM, the age of group A was significantly higher than that of group B [38 (35, 41) years *vs*. 37 (32, 40) years, *P*=0.020]. After PSM, there were no significant differences in general data, ovulation induction cycle data, embryo laboratory indicators, clinical pregnancy rate, live birth rate and perinatal outcomes between the two groups (all *P*>0.05). **Conclusion** Compared with FET at least one month after oocytes retrieval, FET during the first menstrual cycle after PPOS does not affect clinical or perinatal outcomes. FET can be performed as early as possible after oocytes retrieval according to the condition of patients to shorten the time to reach their first live birth.

【Key words】 Progestin primed ovarian stimulation; Frozen-thawed embryo transfer; Time to transfer; Clinical pregnancy rate; Perinatal outcome

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·临床报道·

胚胎移植后早期自然流产伴绒毛染色体异常患者再次移植临床结局分析

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【摘要】 目的 分析体外受精-胚胎移植（*in vitro* fertilization and embryo transfer，IVF-ET）和冻融胚胎移植（frozen-thawed embryo transfer，FET）妊娠后染色体异常患者再次胚胎移植的临床结局。方法 回顾性病例对照研究分析 2015 年 7 月至 2019 年 12 月期间于烟台毓璜顶医院生殖医学科行 IVF-ET/FET 助孕妊娠后 172 例早期自然流产伴绒毛染色体异常患者（绒毛染色体异常组），及 127 例同期早期自然流产伴绒毛染色体正常患者（绒毛染色体正常组）的临床资料。对上述患者进行针对年龄、抗苗勒管激素、基础卵泡刺激素的倾向性评分匹配（propensity score matching， PSM），再比较两组患者胚胎移植后临床结局。结果 PSM 前，绒毛染色体异常组患者年龄［34.0（30.0，38.0）岁］大于绒毛染色体正常组患者［32.0（30.0，36.0）岁，*P*=0.015］。两组患者再次移植后，临床妊娠率、早期流产率、近似活产率、累积活产率比较，差异均无统计学意义（均 *P*>0.05）。PSM 后两组患者临床妊娠率、早期流产率、近似活产率、累积活产率比较，差异均无统计学意义（均 *P*>0.05）。结论 绒毛染色体异常患者再次胚胎移植后可达到与绒毛染色体正常患者相似的临床结局，建议患者尽早继续助孕治疗。

【关键词】 自然流产； 受精，体外； 胚胎移植； 冻融胚胎移植； 绒毛染色体

Analysis of clinical outcomes after embryo transfer again in IVF-ET/FET patients with previous spontaneous abortion in early pregnancy and fetal chromosomal abnormalities

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【Abstract】 **Objective** To investigate clinical outcomes after embryo transfer again in *in vitro* fertilization and embryo transfer/frozen-thawed embryo transfer (IVF-ET/FET) patients with previous fetal chromosomal abnormalities. **Methods** In this retrospective case-control study, data of patients who received IVF-ET/FET treatment at the Department of Reproductive Medicine, Yantai Yuhuangding Hospital between July 2015 and December 2019 and had embryo

chromosomes tested after spontaneous abortion were analyzed. Among 299 patients, 172 cases were found to have fetal chromosomal abnormalities (abnormal group) and 127 cases were found to have normal results (normal group). We matched the above patients cycles with age, anti-Müllerian hormone and basal follicle-stimulating hormone using propensity score matching (PSM). Clinical data were analyzed again after PSM. **Results** Before PSM, patients in abnormal group [34.0 (30.0,38.0) years] were significantly older than those in normal group [32.0 (30.0,36.0) years, *P*=0.015]. There were no statistically significant differences in clinical pregnancy rate, early miscarriage rate, approximate live birth rate and cumulative live birth rate (all *P*>0.05). After PSM matching, there were also no statistically significant differences in clinical pregnancy rate, early miscarriage rate, approximate live birth rate and cumulative live birth rate (all *P*>0.05). **Conclusion** Patients with fetal chromosomal abnormalities can achieve similar clinical outcomes after embryo transfer again. Therefore IVF-ET or FET is recommended as early as possible.

【Key words】 Abortion, spontaneous; Fertilization *in vitro*; Embryo transfer; Frozen-thawed embryo transfer; Villus chromosome

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·现场调查·

我国辅助生殖机构女性不孕症患者基本特征、就医情况和地区差异研究

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【摘要】 目的　描述我国辅助生殖机构女性不孕症患者的基本特征和就医情况，并比较东、中、西部之间的差异。方法　本研究使用中国疾病预防控制中心妇幼保健中心辅助生殖技术管理部自 2018 年起参与的国家重点研发计划“生殖健康及重大出生缺陷防控研究”中单元六——育龄人群生殖健康及医疗保健服务匹配情

况现状分析和诊疗示范推广研究子课题的数据。选取我国东、中、西部不同地区的8个省会城市中2018年体外受精技术取卵周期数在1 000以上和1 000以下的辅助生殖机构各1家，对16家机构门诊首次就诊的20~49岁不孕症女性患者的问卷数据进行分析。采用频率描述、χ^2检验、Kruskal-Wallis *H*检验等方法对患者年龄、文化程度、个人年收入、试孕时长、单程交通时间等指标进行分析。结果　最终纳入3 673例女性患者作为研究对象。患者的年龄为（31.0±4.6）岁，59.0%（2 156/3 660）为本科/大专以上学历，中位试孕时长2.0（1.3，3.5）年。人口学特征方面，东部和西部地区35岁以上患者在小机构中占比更大，分别为22.8%（216/948）和26.4%（148/561），中部地区高中及以下学历患者的比例更高，在大机构中为49.1%（216/440），小机构中为47.0%（275/585）。经济方面，30.5%（521/1 708）的东部患者达到10万元以上的个人年收入，而只有2.8%（26/939）愿意接受10万元以上的治疗费用，中、西部地区患者无论从个人年收入方面，还是可接受的治疗费用方面，均低于东部地区（*P*<0.001）。交通方面，西部地区患者所耗费的单程交通时间最长，30.9%（117/379）的大机构患者和29.8%（167/561）的小机构患者需要花费3 h以上；东部地区的大机构内异地就医的患者比例最高，为21.6%（164/758）。结论　我国辅助生殖机构的不孕症患者年龄普遍超过女性最佳生育年龄，受教育程度较高，因此在年轻人和受教育程度较低的人群中，应加强生育知识的宣传，鼓励有生育意愿的夫妻尽早开始准备；另外，西部地区大龄患者更多，经济和交通条件更加不利，需要政策层面的更多关注。

【关键词】　生殖技术，辅助；　不孕症；　患者特征；　地区差异

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Basic characteristics, treatment seeking behavior and regional differences of female infertility patients in assisted reproductive institutions in China

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【**Abstract**】　**Objective**　To describe the characteristics and medical seeking behaviors of female infertility patients in assisted reproductive institutions in China overall and geographical regions, and compare the differences among the eastern, the middle and the western regions. **Methods**　This study used the data from Unit 6-Analysis on the matching status of reproductive health and health care services among reproductive age population and demonstration and promotion study of diagnosis and treatment in National Key R&D Program "Reproductive Health and Major Birth Defects Prevention and Control Study" participated by the Assisted Reproductive Technology Management Department of Maternal and Child Health Care Center, Chinese Center for Disease Control and Prevention. One assisted reproductive institution with more than 1 000 and less than 1 000 oocyte retrieval cycles by *in vitro* fertilization techniques in 2018 was selected from 8 provincial capital cities in different regions of eastern and western China, and the questionnaire data of infertile female patients aged 20–49 years who first visited the outpatient

clinics of 16 institutions were analyzed. The patient's age, degree of culture, annual personal income, try-to-conceived time, and one-way transportation time were analyzed using the frequency description, χ^2 test, Kruskal-Wallis *H* test and other methods. **Results** A total of 3 673 female patients were finally included as study subjects. The patient's age was (31.0±4.6) years old, and 59.0% (2 156/3 660) was an undergraduate/college degree or above, with a median pregnancy test duration of 2.0 (1.3, 3.5) years. In terms of demographic characteristics, the proportion of patients over 35 years old in the eastern and western regions was greater in small institutions, 22.8% (216/948) and 26.4% (148/561), respectively. The proportion of patients with academic degrees in high school and below in the central region was higher, 49.1% (216/440) in large institutions and 47.0% (275/585) in small institutions. In terms of economics, 30.5% (521/1 708) of eastern patients reached an annual income of more than RMB 100 000, while only 2.8% (26/939) were willing to accept more than RMB 100 000 in treatment costs, and patients in the central and western regions were lower than those in the eastern region in terms of their annual income and acceptable treatment costs (P<0.001). In terms of transportation, patients in the western region spent the longest amount of one-way transportation time, with large institutions of 30.9% (117/379) and small institutions of 29.8% (167/561) needing to spend more than 3 h; the proportion of patients in the eastern region who seek medical treatment from overseas was the highest, with 21.6% (164/758). **Conclusion** The age of infertility patients in assisted reproductive institutions in China generally exceeds the optimal reproductive age of women and has a higher degree of education. Therefore, in young and people with a lower degree of education, the publicity of reproductive knowledge should be strengthened to encourage couples with fertility willingness to start preparation as early as possible. ln addition, there are more older patients in the western region, as well as the economic and transportation conditions are more unfavorable, and more attention needs to be paid at the policy level.

【 Key words 】 Reproductive technology, assisted; Infertility; Patient characteristics; Regional differences

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·个案报道·

宫内合并特殊部位复合妊娠 5 例临床分析并文献复习

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【摘要】 目的　探讨宫内合并特殊部位复合妊娠的诊治方法，以提高特殊复合妊娠的诊治水平。方法　回顾性分析 2017 年 1 月至 2020 年 12 月期间在重庆市妇幼保健院妇产科诊断为宫内合并特殊部位复合妊娠 5 例的临床资料，总结特殊复合妊娠的临床特点、治疗方案及结局。结果　5 例患者有 2 例采取减胎术，有 3 例采取腹腔镜下妊娠物清除术。5 例患者均保留了子宫的完整性，1 例早产，4 例足月产，母婴结局良好。结论　早诊断、早治疗是改善宫内合并特殊部位复合妊娠预后的重要因素之一；治疗方案要根据患者对宫内妊娠的期望值、异位妊娠部位及医疗资源进行个体化的治疗。

【关键词】 生殖技术，辅助；　妊娠结局；　特殊部位复合妊娠
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Clinical analysis of 5 cases of rare heterotopic pregnancy and literature review

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【**Abstract**】 **Objective** To analyze and improve the diagnosis and treatment of rare heterotopic pregnancy. **Methods** We retrospectively analyzed the clinical data of 5 patients diagnosed with rare heterotopic pregnancy at the Department of Obstetrics and Gynecology, Chongqing Health Center for Women and Children from January 2017 to December 2020 and reviewed the clinical characteristics, treatment options, and outcomes of them. **Results** Two of the 5 patients underwent ectopic pregnancy reduction, 3 patients underwent laparoscopic ectopic gestational sac removal. Five patients had preservation of uterine integrity, a patient had preterm birth, 4 patients had term birth, and the mother and baby had good outcomes. **Conclusion** Early diagnosis and treatment are important factors in improving the prognosis of the disease. Treatment regimens should be individualized based on patient expectations of intrauterine pregnancy, location of ectopic pregnancy, and medical resources.

【**Key words**】 Reproductive techniques, assisted; Pregnancy outcome; Rare heterotopic pregnancy

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·综述·

白藜芦醇在多囊卵巢综合征治疗中的研究进展

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【摘要】 多囊卵巢综合征（polycystic ovary syndrome，PCOS）是育龄期妇女最常见的生殖内分泌代谢性疾病，主要表现为排卵功能障碍、高雄激素血症、不孕和卵巢多囊样改变，常伴有肥胖、胰岛素抵抗（insulin resistance，IR）和糖耐量异常。近年来，其发病率逐年上升，且尚无完全有效的治疗手段。越来越多的研究显示，白藜芦醇对 PCOS 具有潜在的治疗价值。本文主要对白藜芦醇改善 PCOS 的 IR 及糖脂代谢紊乱、高雄激素血症、炎症与氧化应激的相关研究和机制进展，以及白藜芦醇在 PCOS 合并不孕症中的应用进行综述。

【关键词】 多囊卵巢综合征；　白藜芦醇；　胰岛素抵抗；　高雄激素血症

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Research progress of resveratrol in the treatment of polycystic ovary syndrome

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【Abstract】 Polycystic ovary syndrome (PCOS) is the most common reproductive endocrine and metabolic disease in women of childbearing age, which is characterized by ovulatory dysfunction, hyperandrogenemia, infertility and polycystic changes of the ovary, often accompanied by obesity, insulin resistance (IR) and impaired glucose tolerance. In recent years, its incidence has increased year by year, and there is no completely effective treatment. More and more studies have shown that resveratrol has potential therapeutic value for PCOS. This article mainly reviews the related research and mechanism progress of resveratrol in improving

IR, glucose and lipid metabolism disorders, hyperandrogenism, inflammation and oxidative stress in PCOS, as well as the application of resveratrol in PCOS with infertility.

【**Key words**】 Polycystic ovary syndrome; Resveratrol; Insulin resistance; Hyperandrogenism

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·综述·

m6A 修饰在女性生殖发育及相关疾病中的研究进展

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【摘要】 N6-甲基腺嘌呤（N6-methyladenosine，m6A）修饰是由 m6A 甲基转移酶、去甲基化转移酶、阅读蛋白进行调控的一种 RNA 转录后水平修饰，在最为广泛，且在哺乳动物的生殖发育中发挥重要作用。一方面，m6A 修饰调控着卵母细胞成熟和早期胚胎发育过程中 RNA 的代谢过程；另一方面，m6A 修饰与卵巢和子宫疾病密切相关，尤其是妇科肿瘤，m6A 修饰影响着肿瘤细胞的增殖和迁移。本文对 m6A 修饰在女性生殖生理及其相关疾病中的研究进展做一综述，旨在为临床治疗提供新的思路。

【关键词】 胚胎发育； 生殖器肿瘤，女性； N6-甲基腺嘌呤

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Research progress of m6A modification in female reproductive development and related diseases

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【 Abstract 】 N6-methyladenine (m6A) modification is an RNA post-transcriptional level modification regulated by m6A methyltransferase, demethylated transferase and reading protein, which is the most widespread in messenger RNA. And it plays an important role in the reproductive development of mammals. On the one hand,m6A regulates RNA metabolism during oocyte maturation and early embryonic development, and on the other hand, m6A is closely associated with ovarian and uterine diseases, especially in gynecological tumors, m6A affects the proliferation and migration of tumor cells. This article reviews the research progress of m6A modification in female reproductive physiology and related diseases in order to provide new ideas for clinical treatment.

【 Key words 】 Embryonic development; Genital neoplasms, female; N6-methyladenosine

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·综述·

类器官及器官芯片技术在体外胎盘模型构建中的研究进展

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【摘要】 胎盘具有物质交换及屏障功能，对维持胎儿生长发育至关重要。胎盘功能异常与多种不良妊娠结局有关。现有的体外胎盘模型均存在一定局限性，无法满足研究需要。目前类器官及器官芯片技术发展迅速，在药物研发、基础医学研究等方面展示出了极大的应用前景。构建自真实胎盘的类器官在细胞表型、基因表达等方面均与源组织具有高度一致性。胎盘芯片可体外模拟胎盘屏障，并在药物的胎盘通透性研究中被广泛应用。构建胎盘类器官芯片，或构建包含胎盘、子宫内膜等成分的多器官芯片，对于生殖及围产医学领域的发展具有重要意义。

【关键词】 类器官； 器官芯片； 胎盘屏障； 体外模型

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Recent development of organoids and organ-on-a-chip in creation of an *in vitro* model of the placenta

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【Abstract】 The placenta is the site of material exchange and barrier between mother and the offspring, plays a crucial role in the growth of fetus. Dysfunction of placenta is responsible for varies of adverse pregnancy outcome. Current *in vitro* experimental models of the placenta all have their limitations and are insufficient for research. Recently, organoid and organ-on-a-chip technology develop rapidly, and provide a potentially powerful approach to drug discovery and basic medical research. Organoids derived from human placenta closely resemble origin trophoblast in cell phenotype, genetic expression and so on. Placenta organ-on-a-chip mimics the placenta barrier and has been used in research of drug transport across the placenta. Establishment of placenta organoid-on-a-chip, or multi-organ chip contains placenta and endometrium cells can be a potential direction of research in the future.

【Key words】 Organoid; Organ-on-a-chip; Placental barrier; *In vitro* model

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·综述·

Keap1-Nrf2/ARE 系统抵抗蜕膜化缺陷的研究进展

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【摘要】 蜕膜化缺陷可导致不孕症以及其他不良妊娠结局的发生，氧化应激、炎症、毒物暴露等多种不良应激源均是蜕膜化缺陷的诱因。近年来，Keap1-Nrf2/ARE 系统作为细胞防御机制的关键调节因子，成为多种慢性疾病的研究热点。越来越多的证据支持 Keap1-Nrf2/ARE 系统在抵抗蜕膜化缺陷过程中发挥重要作用，除了经典的细胞防御作用外，Nrf2 被证实可以被雌孕激素激活，并可能通过 FoxO1 通路调控蜕膜化过程，因此该系统有望成为临床改善不良妊娠结局的重要靶点。本文综述了 Keap1-Nrf2/ARE 系统通过抵抗应激损伤、与雌孕激素相互作用、调控 FoxO1 因子等方面参与调控蜕膜化过程的依据。

【关键词】 妊娠结局；　Nrf2；　蜕膜化；　细胞防御
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Research on Keap1-Nrf2/ARE system resisting defective decidualization

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【Abstract】 Defective decidualization can lead to infertility and other poor pregnancy outcomes. A variety of adverse stressors such as oxidative stress, inflammation, and toxic exposure are all triggers of defective decidualization. In recent years, the Keap1-Nrf2/ARE system, as a key regulator of cellular defense

mechanisms, has become a hot topic of research in various chronic diseases. In addition to its classical cellular defense role, Nrf2 has been confirmed to be activated by estrogen and progesterone, and may regulate decidualization through the FoxO1 pathway, thus making it an important target for clinical improvement of adverse pregnancy outcomes. This article provides an overview of the evidence supporting the involvement of the Keap1-Nrf2/ARE system in regulating the decidualization process through mechanisms such as combating stress-induced damage, interacting with female pregnancy hormones, and regulating the FoxO1 factor.

【Key words】 Pregnancy outcome; Nrf2; Decidualization; Cellular defense

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·综述·

2 型糖尿病引起的男性生殖功能障碍病因机制的研究进展

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【摘要】 2 型糖尿病（type 2 diabetes，T2D）是一种因胰岛素相对分泌不足或作用障碍导致的代谢性疾病，已成为严重危害人民健康最常见的慢性病之一。我国是糖尿病高发的国家，尤其受高脂高糖饮食的影响，越来越多处于育龄期的男性遭受了此病的困扰。T2D 男性患者并发生殖功能障碍会产生性欲减退、阴茎勃起功能障碍、生精障碍、异常射精等。本文就它们的相关机制进行综述，以期为临床上解决此类生殖问题提供借鉴与参考。

【关键词】 2 型糖尿病； 男性； 氧化应激； 胰岛素抵抗； 生殖功能障碍

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Research progress on etiological mechanism of male reproductive dysfunction caused by type 2 diabetes

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【Abstract】 Type 2 diabetes (T2D), a metabolic disease caused by inadequate insulin secretion or dysfunction, is one of the most common chronic illnesses causing serious health complications in human. The incidence of diabetes in China is high. Increasingly, men in their reproductive years are afflicted with the disease, particularly due to high-fat and high-sugar diets. Male patients with T2D often suffer from reproductive dysfunction, which is characterized by hyposexual desire, penile erectile dysfunction, spermatogenic dysfunction and abnormal ejaculation, etc. In this paper, we review their related mechanisms, in order to provide reference for the clinical solution of these reproductive problems.

【Key words】 Type 2 diabetes; Men; Oxidative stress; Insulin resistance; Reproductive dysfunction

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