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# 育龄人群不孕不育防治临床实践指南 (2024)

中华预防医学会生育力保护分会 中国医师协会生殖医学专业委员会

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**【摘要】** 随着社会的快速发展、人们生活方式以及环境的变迁, 育龄人群的生殖健康正面临日益增多的负面影响。目前, 我国尚缺乏针对育龄人群防范不孕(育)症影响因素的临床实践指南。为推动我国育龄人群健康生育并提高出生人口素质, 中华预防医学会生育力保护分会、中国医师协会生殖医学专业委员会和中国医科大学附属盛京医院联合发起, 基于国内外相关证据, 结合我国临床实践制订了本指南, 旨在为各级医疗卫生保健部门、开展不孕不育临床诊疗工作的医疗机构以及相关医务工作者、教学和科研人员、社区卫生工作者、全科医生和育龄人群提供科学且实用的指导。本指南的应用将有助于改善育龄人群的生育能力、降低不孕不育的患病率, 并为不孕不育的一级预防和管理提供坚实的理论与实践支撑。

**【关键词】** 不孕; 不育; 育龄人群; 临床实践指南

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## **Clinical practice guidelines for the prevention and treatment of infertility in people of childbearing age (2024)**

*Chinese Society for Fertility Preservation of Chinese Preventive Medicine Association, Chinese Association of Reproductive Medicine*

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**【 Abstract 】** As social development accelerates and lifestyles and environmental conditions evolve, the reproductive health of people of childbearing age increasingly suffers adverse impacts. Currently, China lacks comprehensive clinical practice guidelines for preventing infertility in this population. To address the gap in infertility prevention, promote healthy reproduction among people of childbearing age in China, and improve newborn health, Chinese Society for Fertility Preservation of Chinese Preventive Medicine Association, Chinese Association of Reproductive Medicine, and Shengjing Hospital of China Medical University collaborated to develop these guidelines. Grounded in both international and domestic evidence and adapted to Chinese clinical practices, these guidelines provide scientific and practical guidance for different tiers of medical and healthcare providers, infertility centers and clinics, fertility specialists, educators and researchers, community health workers, general practitioners, and individuals of childbearing age. The initiative aims to enhance fertility health, reduce infertility rates, and establish a foundation for the primary prevention and management of infertility.

**【 Key words 】** Infertility; Sterility; People of childbearing age; Clinical practice guidelines

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·临床研究·

# 高尿酸血症对多囊卵巢综合征患者体外受精-胚胎移植助孕临床结局的影响

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章婷和郝好英对本文有同等贡献

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**【摘要】** 目的 探讨高尿酸血症对多囊卵巢综合征 (polycystic ovary syndrome, PCOS) 患者体外受精-胚胎移植 (*in vitro* fertilization and embryo transfer, IVF-ET) 助孕后每移植周期活产率及每取卵周期累积活产率的影响。方法 采用回顾性队列研究, 分析 2016 年 1 月至 2021 年 12 月期间在河南省人民医院生殖医学中心及江西省妇幼保健院生殖医学中心接受 IVF-ET 助孕治疗的 3 959 例 PCOS 患者的资料。根据尿酸水平分为高尿酸 (尿酸值 $>357 \mu\text{mol/L}$ ) 组 (1 126 例) 和正常尿酸 (尿酸值 $\leq 357 \mu\text{mol/L}$ ) 组 (2 833 例), 比较两组患者的基线资料、临床及实验室指标, 并对影响临床结局的各个因素进行单因素及多因素回归分析, 并利用多元 logistic 回归分析比较两组患者的每移植周期活产率及每取卵周期累积活产率, 从而明确高尿酸血症对 PCOS 患者临床结局的影响。结果 两组在年龄、不孕年限、基础睾酮、不孕类型及无可利用胚胎率等方面差异均无统计学意义 (均  $P>0.05$ ), 高尿酸组的体质指数 [  $(25.15 \pm 3.75) \text{ kg/m}^2$  ]、空腹血糖 [  $(4.99 \pm 0.80) \text{ mmol/L}$  ] 和空腹胰岛素 [  $17.19 (11.78, 25.30) \text{ mU/L}$  ] 均高于正常尿酸组 [  $(23.60 \pm 3.64) \text{ kg/m}^2, P<0.001$ ;  $(4.88 \pm 0.81) \text{ mmol/L}, P<0.001$ ;  $12.40 (8.59, 17.86) \text{ mU/L}, P<0.001$  ], 而其基础黄体生成素 [  $7.62 (4.68, 11.18) \text{ U/L}$  ]、抗苗勒管激素 [  $7.62 (5.34, 10.73) \mu\text{g/L}$  ] 均低于正常尿酸组 [  $7.88 (4.98, 11.91) \text{ U/L}, P=0.024$ ;  $7.95 (5.49, 11.73) \mu\text{g/L}, P<0.001$  ], 差异均存在统计学意义; 多元 logistic 回归分析显示女方体质指数、人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 注射日内膜厚度、可移植胚胎数是每移植周期活产率的影响因素 ( $OR=1.02, 95\% \text{ CI: } 1.00 \sim 1.04, P=0.044$ ;  $OR=0.95, 95\% \text{ CI: } 0.92 \sim 0.97, P<0.001$ ;  $OR=0.97, 95\% \text{ CI: } 0.95 \sim 0.99, P=0.006$ ); 空腹血糖、hCG 注射日内膜厚度、可移植胚胎数是每取卵周期累积活产率的影响因素 ( $OR=1.14, 95\% \text{ CI: } 1.01 \sim 1.29, P=0.036$ ;

OR=0.92, 95% CI: 0.87~0.97, P=0.002; OR=0.70, 95% CI: 0.66~0.75, P<0.001); 与正常尿酸组相比, 高尿酸组 PCOS 患者每移植周期活产率和每取卵周期累积活产率没有显著降低 (OR=0.93, 95% CI: 0.72~1.19, P=0.548; OR=1.18, 95% CI: 0.87~1.60, P=0.300)。结论 高尿酸血症对 PCOS 患者 IVF-ET 助孕后每移植周期活产率及每取卵周期累积活产率没有影响。

【关键词】 尿酸; 受精, 体外; 胚胎移植; 多囊卵巢综合征; 活产率; 累积活产率

### Impact of hyperuricemia on the clinical outcomes in patients with polycystic ovary syndrome undergoing *in vitro* fertilization and embryo transfer

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【Abstract】 **Objective** To investigate the impact of hyperuricemia on the live birth rate per transfer cycle and the cumulative live birth rate per oocyte retrieval cycle in patients with polycystic ovary syndrome (PCOS) undergoing *in vitro* fertilization and embryo transfer (IVF-ET). **Methods** A retrospective cohort study was conducted on data from 3 959 PCOS patients who received IVF-ET treatment at the Reproductive Centers of Henan Provincial People's Hospital and Jiangxi Provincial Maternal and Child Health Hospital between January 2016 and December 2021. The patients were divided into hyperuricemia group (>357  $\mu\text{mol/L}$ ,  $n=1\ 126$ ) and normal uric acid group ( $\leq 357\ \mu\text{mol/L}$ ,  $n=2\ 833$ ) based on their uric acid levels. Baseline data, clinical and laboratory indicators were compared between the two groups. Univariate and multivariate regression analyses were performed on factors influencing clinical outcomes. Multivariate logistic regression analysis was used to compare the live birth rate per transfer cycle and the cumulative live birth rate per oocyte retrieval cycle between the two groups, clarifying the impact of hyperuricemia on clinical outcomes in PCOS patients. **Results** There were no significant differences between the two groups in terms of age, duration of infertility, baseline testosterone level, type of infertility, and the rate of unusable embryos (all  $P>0.05$ ). Body mass index [BMI, (25.15 $\pm$ 3.75)  $\text{kg/m}^2$ ], fasting blood glucose [(4.99 $\pm$ 0.80)  $\text{mmol/L}$ ] and fasting insulin levels [17.19 (11.78, 25.30)  $\text{mU/L}$ ] in hyperuricemia group were higher than those in normal uric acid group [(23.60 $\pm$ 3.64)  $\text{kg/m}^2$ ,  $P<0.001$ ; (4.88 $\pm$ 0.81)  $\text{mmol/L}$ ,  $P<0.001$ ; 12.40 (8.59, 17.86)  $\text{mU/L}$ ,  $P<0.001$ ], while their baseline luteinizing hormone [7.62 (4.68, 11.18)  $\text{U/L}$ ] and anti-Müllerian hormone [7.62 (5.34, 10.73)  $\mu\text{g/L}$ ] levels were lower than those in normal uric acid group [7.88



(4.98, 11.91) U/L,  $P=0.024$ ; 7.95 (5.49, 11.73)  $\mu\text{g/L}$ ,  $P<0.001$ ], with statistically significant differences. Multivariate logistic regression analysis indicated that female BMI, endometrial thickness on human chorionic gonadotropin (hCG) injection day, and the number of transferable embryos were factors influencing the live birth rate per transfer cycle ( $OR=1.02$ , 95%  $CI$ : 1.00–1.04,  $P=0.044$ ;  $OR=0.95$ , 95%  $CI$ : 0.92–0.97,  $P<0.001$ ;  $OR=0.97$ , 95%  $CI$ : 0.95–0.99,  $P=0.006$ ). Fasting blood glucose, endometrial thickness on hCG injection day, and the number of transferable embryos were factors influencing the cumulative live birth rate per oocyte retrieval cycle ( $OR=1.14$ , 95%  $CI$ : 1.01–1.29,  $P=0.036$ ;  $OR=0.92$ , 95%  $CI$ : 0.87–0.97,  $P=0.002$ ;  $OR=0.70$ , 95%  $CI$ : 0.66–0.75,  $P<0.001$ ). Compared with the normal uric acid group, the hyperuricemia group in PCOS patients had not a statistically significant decrease in the live birth rate per transfer cycle and the cumulative live birth rate per oocyte retrieval cycle ( $OR=0.93$ , 95%  $CI$ : 0.72–1.19,  $P=0.548$ ;  $OR=1.18$ , 95%  $CI$ : 0.87–1.60,  $P=0.300$ ). **Conclusion** Hyperuricemia does not affect the live birth rate per transfer cycle or the cumulative live birth rate per oocyte retrieval cycle in PCOS patients undergoing IVF-ET.

**【Key words】** Uric acid; Fertilization *in vitro*; Embryo transfer; Polycystic ovary syndrome; Live birth rate; Cumulative live birth rate

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临床研究

## 不改变宫腔形态的子宫肌瘤对反复种植失败患者助孕结局的影响研究

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**【摘要】** 目的 探讨合并不改变宫腔形态的子宫肌瘤是否对反复种植失败 (recurrent implantation failure, RIF) 患者冻融胚胎移植 (frozen-thawed embryo transfer, FET) 周期的助孕结局产生不利影响。方法 采用双向队列研究,

分析 2018 年 1 月 1 日至 2023 年 12 月 31 日期间就诊于北京大学第三医院妇产科生殖医学中心诊断为 RIF 患者的首次 FET 周期的资料, 根据是否合并不改变宫腔形态的肌壁间肌瘤 [2011 年国际妇产联盟 (International Federation of Gynecology and Obstetrics, FIGO) 分型的 3~6 型], 分为病例组 (肌瘤患者,  $n=457$ ) 和对照组 (非肌瘤患者,  $n=1\ 693$ ), 同时, 通过 SPSS27.0 对两组的年龄、内膜厚度、周期类型、移植胚胎发育天数进行 1:2 倾向性评分匹配, 设定卡钳值为 0.1, 匹配后对照组共 857 例, 比较匹配前后两组的临床妊娠率、人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 阳性率、早期流产率等助孕结局。此后, 在病例组患者中根据肌瘤的个数、大小、位置等特征进行亚组分析, 研究肌瘤特征对 FET 助孕结局的影响。结果 在 RIF 患者 FET 周期中, 病例组患者与匹配后对照组患者的临床妊娠率、早期流产率、hCG 阳性率差异均无统计学意义 (均  $P>0.05$ ); 在肌瘤患者中, 子宫肌瘤的最大直径为  $\geq 2$  cm,  $< 4$  cm 与较低的临床妊娠率 ( $OR=0.441$ , 95%  $CI: 0.218\sim 0.891$ , 调整  $OR=0.408$ ,  $P=0.022$ ) 及 hCG 阳性率 ( $OR=0.374$ , 95%  $CI: 0.185\sim 0.757$ , 调整  $OR=0.337$ ,  $P=0.006$ ) 有关。结论 FIGO 分型的 3~6 型肌壁间肌瘤不影响 RIF 患者的解冻移植结局, 同时, 肌瘤的个数和位置也对助孕结局无影响; 但是, 相对于其他大小的肌壁间肌瘤而言, 直径在 2~4 cm 间的肌瘤可能对胚胎着床存在潜在不利影响。

【关键词】 妊娠结局; 子宫肌瘤; 反复种植失败

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### Impact of uterine fibroids that do not alter uterine cavity morphology on the pregnancy outcome of patients with recurrent implantation failure

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【Abstract】 **Objective** To investigate whether intramural fibroids that do not distort the uterine cavity adversely affect the reproductive outcomes of frozen-thawed embryo transfer (FET) cycles in patients with recurrent implantation failure (RIF). **Methods** A ambispective cohort study analyzed data from patients diagnosed with RIF undergoing their first FET cycle at Reproductive Medicine Center, Obstetrics and Gynecology, Peking University Third Hospital, from January 1, 2018 to December 12, 2023. Patients were categorized into case group (fibroid patients,  $n=457$ ) and control group (non-fibroid patients,  $n=1\ 693$ ) based on whether they had intramural fibroids that did not distort the uterine cavity [type 3-6 according to 2011 International Federation of Obstetrics and Gynecology (FIGO) classification]. Propensity score matching was performed (1:2 ratio) using SPSS27.0 to adjust for age, endometrial thickness, cycle type, and embryo type. After matching, there were 857 cases in control group. Pregnancy outcomes including clinical pregnancy rate, human chorionic gonadotropin (hCG) positive rate, and early miscarriage rate were compared between the two groups. Subgroup analyses were conducted in the case group based on characteristics such as number, size, and location of the fibroids to study their impact on the outcomes of

FET cycles. **Results** In patients with RIF undergoing FET cycles, there were no statistically significant differences between case group and the matched control group in terms of clinical pregnancy rate, early miscarriage rate, and hCG positive rate (all  $P>0.05$ ). Within the fibroid patients, however, fibroids with a maximum diameter  $\geq 2$  cm and  $< 4$  cm were associated with lower clinical pregnancy rate ( $OR=0.441$ , 95%  $CI$ : 0.218–0.891,  $aOR=0.408$ ,  $P=0.022$ ) and lower hCG positive rate ( $OR=0.374$ , 95%  $CI$ : 0.185–0.757,  $aOR=0.337$ ,  $P=0.006$ ) compared with the other sizes of intramural fibroids. **Conclusion** Type 3–6 intramural fibroids according to the FIGO classification do not affect the outcomes of FET cycles in patients with RIF. Additionally, the number and location of fibroids also do not affect reproductive outcomes. However, intramural fibroids with a diameter between 2–4 cm may potentially have adverse effects on embryo implantation compared with other sizes of intramural fibroids.

**【Key words】** Pregnancy outcome; Uterine fibroids; Recurrent implantation failure

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临床研究

## 体脂率对不孕症女性 IVF/ICSI 妊娠结局的影响

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**【摘要】** 目的 探讨体脂率对进行体外受精/卵胞质内单精子注射 (*in vitro* fertilization/intracytoplasmic sperm injection, IVF/ICSI) 新鲜周期移植患者妊娠结局的影响。方法 采用回顾性队列研究方法, 对 2022 年 3 月至 2023 年 10 月期间于郑州大学第三附属医院生殖健康医院就诊的 20~45 岁行 IVF/ICSI 治疗

的患者临床资料进行分析。根据体脂率将研究对象分为非肥胖组(体脂率<35%) 800例和肥胖组(体脂率≥35%) 742例。比较两组患者基线数据、促排卵结局及新鲜移植周期临床妊娠结局的差异。结果 ①肥胖组患者体质量指数[body mass index, BMI, 25.85 (24.22, 28.04) kg/m<sup>2</sup>]、基础睾酮 [0.80 (0.45, 1.12) nmol/L]、甘油三酯 [1.29 (1.03, 1.59) mmol/L]、血清总胆固醇 [4.55 (4.29, 4.81) mmol/L]、低密度脂蛋白胆固醇 [3.17 (2.90, 3.40) mmol/L]、空腹葡萄糖 [5.40 (5.10, 5.75) mmol/L]、空腹胰岛素 [12.99 (9.01, 18.31) mU/L]、胰岛素抵抗指数 [3.09 (2.14, 4.50)]、窦卵泡计数 [16.00 (11.00, 22.00)]、合并多囊卵巢综合征占比 [9.4% (70/742)] 均高于非肥胖组 [21.94 (20.32, 23.51) kg/m<sup>2</sup>,  $P<0.001$ ; 0.69 (0.43, 0.98) nmol/L,  $P<0.001$ ; 1.00 (0.79, 1.21) mmol/L,  $P<0.001$ ; 4.42 (4.19, 4.66) mmol/L,  $P<0.001$ ; 2.91 (2.67, 3.15) mmol/L,  $P<0.001$ ; 5.22 (5.00, 5.45) mmol/L,  $P<0.001$ ; 11.30 (8.33, 14.82) mU/L,  $P<0.001$ ; 2.61 (1.86, 3.48),  $P<0.001$ ; 14.00 (10.00, 20.00),  $P<0.001$ ; 4.8% (38/800),  $P<0.001$ ]; 肥胖组基础卵泡刺激素 [6.58 (5.64, 7.73) U/L]、基础雌二醇 [133.01 (102.35, 171.56) pmol/L]、基础黄体生成素 [4.80 (3.62, 6.53) U/L]、高密度脂蛋白胆固醇 [1.29 (1.17, 1.39) mmol/L] 均低于非肥胖组 [6.91 (5.86, 8.33) U/L,  $P<0.001$ ; 145.52 (105.23, 187.95) pmol/L,  $P=0.001$ ; 5.16 (3.82, 6.94) U/L,  $P=0.022$ ; 1.45 (1.36, 1.55) mmol/L,  $P<0.001$ ]。②肥胖组患者促性腺激素 (gonadotropin, Gn) 起始剂量 [187.50 (150.00, 225.00) U]、Gn 使用总量 [2 481.25 (1 856.25, 3 225.00) U] 均高于非肥胖组 [225.00 (175.00, 250.00) U,  $P<0.001$ ; 2 925.00 (2 250.00, 3 675.00) U,  $P<0.001$ ]，人绒毛膜促性腺激素 (human chorionic gonadotropin, hCG) 注射日血雌二醇水平 [8 984.00 (6 087.75, 11 978.25) pmol/L]、hCG 注射日黄体生成素水平 [1.23 (0.87, 1.79) U/L]、囊胚形成率 [55.56% (33.33%, 75.00%)] 均低于非肥胖组 [9 378.50 (6 528.50, 12 624.50) pmol/L,  $P=0.016$ ; 1.37 (0.94, 2.01) U/L,  $P=0.001$ ; 60.00% (37.86%, 80.00%),  $P=0.014$ ]。③两组间着床率、临床妊娠率、流产率及活产率差异均无统计学意义 (均  $P>0.05$ )。肥胖组持续妊娠率 [41.5% (308/742)] 低于非肥胖组 [47.6% (381/800),  $P=0.016$ ]。④多因素 logistic 回归分析显示: 体脂率不是临床妊娠率和活产率的独立影响因素 (均  $P>0.05$ )。⑤BMI 和体脂率预测获得临床妊娠的受试者工作特征曲线下面积 (area under the curve, AUC) 分别为 0.509 与 0.518, 差异无统计学意义 (AUC<sub>差值</sub>=0.009, 95% CI: -0.010~0.028,  $P=0.376$ )。BMI 和体脂率预测获得活产的 AUC 分别为 0.501 与 0.513, 差异无统计学意义 (AUC<sub>差值</sub>=0.012, 95% CI: -0.007~0.030,  $P=0.221$ )。结论 高体脂率可增加 Gn 使用总量, 降低囊胚形成率及持续妊娠率。

【关键词】 胚胎移植; 不孕症; 体脂率; 助孕结局

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## Effects of body fat percent on outcome of IVF/ICSI in infertile women

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**【Abstract】 Objective** To explore the effect of body fat percent (BFP) on assisted reproductive outcomes in infertile women undergoing *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) and fresh embryo transfer. **Methods** We analyzed clinical data on infertile women in a retrospective cohort study, who underwent IVF/ICSI and embryo transfer at the Reproductive Health Hospital of the Third Affiliated Hospital of Zhengzhou University from March 2022 to October 2023. The study subjects were divided into non-obese group (BFP<35%, 800 cases) and obese group (BFP≥35%, 742 cases) according to BFP. The baseline data, ovulation induction outcomes and clinical pregnancy outcomes were compared between the two groups. **Results** 1) The body mass index [BMI, 25.85 (24.22, 28.04) kg/m<sup>2</sup>], basal testosterone [0.80 (0.45, 1.12) nmol/L], triglyceride [1.29 (1.03, 1.59) mmol/L], serum total cholesterol [4.55 (4.29, 4.81) mmol/L], low-density lipoprotein cholesterol [3.17 (2.90, 3.40) mmol/L], fasting glucose [5.40 (5.10, 5.75) mmol/L], fasting insulin [12.99 (9.01, 18.31) mU/L], homeostasis model assessment-insulin resistance [3.09 (2.14, 4.50)], antral follicle count [16.00 (11.00, 22.00)], the patients combined with polycystic ovary syndrome [9.4% (70/742)] in obese group were significantly higher than those in non-obese group [21.94 (20.32, 23.51) kg/m<sup>2</sup>,  $P<0.001$ ; 0.69 (0.43, 0.98) nmol/L,  $P<0.001$ ; 1.00 (0.79, 1.21) mmol/L,  $P<0.001$ ; 4.42 (4.19, 4.66) mmol/L,  $P<0.001$ ; 2.91 (2.67, 3.15) mmol/L,  $P<0.001$ ; 5.22 (5.00, 5.45) mmol/L,  $P<0.001$ ; 11.30 (8.33, 14.82) mU/L,  $P<0.001$ ; 2.61 (1.86, 3.48),  $P<0.001$ ; 14.00 (10.00, 20.00) mmol/L,  $P<0.001$ ; 4.8% (38/800),  $P<0.001$ ]. Basal follicle-stimulating hormone [6.58 (5.64, 7.73) U/L], basal estradiol [133.01 (102.35, 171.56) pmol/L], basal luteinizing hormone [4.80 (3.62, 6.53) U/L] and high-density lipoprotein cholesterol [1.29 (1.17, 1.39) mmol/L] in obese group were significantly lower than those in non-obese group [6.91 (5.86, 8.33) U/L,  $P<0.001$ ; 145.52 (105.23, 187.95) pmol/L,  $P=0.001$ ; 5.16 (3.82, 6.94) U/L,  $P=0.022$ ; 1.45 (1.36, 1.55) mmol/L,  $P<0.001$ ]. 2) The initiated dosage of gonadotropin (Gn) used [187.50 (150.00, 225.00) U] and the total dosage of Gn used [2 481.25 (1 856.25, 3 225.00) U] in obese group were significantly higher than those in non-obese group [225.00 (175.00, 250.00) U,  $P<0.001$ ; 2 925.00 (2 250.00, 3 675.00) U,  $P<0.001$ ]. Serum estradiol level on the day of human chorionic gonadotropin (hCG) injection [8 984.00 (6 087.75, 11 978.25) pmol/L], luteinizing hormone level on the day of hCG injection [1.23 (0.87, 1.79) U/L], the rate of blastocyst formation [55.56% (33.33%, 75.00%)] in obese group were significantly lower than those in non-obese group [9 378.50 (6 528.50, 12 624.50) pmol/L,  $P=0.016$ ; 1.37 (0.94, 2.01) U/L,  $P=0.001$ ; 60.00% (37.86%, 80.00%),  $P=0.014$ ]. 3) Sustained pregnancy rate in obese group [41.5% (308/742)] was lower than that in non-obese group [47.6% (381/800),  $P=0.016$ ]. The number of embryo transfer, embryo transfer type, implantation rate, clinical pregnancy rate, abortion rate and live birth rate were not statistically significant between the two groups (all  $P>0.05$ ). 4) BFP was not an independent factor of clinical pregnancy rate and live birth rate (all  $P>0.05$ ). 5) The area under the curve (AUC) of BMI and BFP to predict clinical pregnancy was 0.509 and 0.518, and there was no significant difference between them ( $AUC_{\text{difference}}=0.009$ , 95% *CI*:

-0.010-0.028,  $P=0.376$ ). The AUC of BMI and BFP for predicting live birth was 0.501 and 0.513, with no statistically significant difference ( $AUC_{\text{difference}}=0.012$ , 95% CI: -0.007-0.030,  $P=0.221$ ). **Conclusion** High BFP can increase total dosage of Gn used, decrease blastocyst formation rate and continuous pregnancy rate.

**【Key words】** Embryo transfer; Infertility; Body fat percent; Outcomes of assisted pregnancy

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临床研究

## 重组人促卵泡激素(芳乐舒<sup>®</sup>) 6.5年的三期随访研究

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**【摘要】** 目的 对重组人促卵泡激素(芳乐舒<sup>®</sup>)三期临床研究进行随访, 评估患者的累积妊娠率、累积活产率和新生儿结局指标。方法 对芳乐舒<sup>®</sup>中国三期临床研究(NCT03506243/CTR20150341, 2015年5月15日至2016年6月27日)进行随访至2022年12月31日。本研究分为芳乐舒<sup>®</sup>组和果纳芬<sup>®</sup>组, 按照年龄分为

20~30岁、31~35岁和36~39岁三个亚组。对患者的累积妊娠率、累积活产率、移植胚胎数、每获胚活产数、每获卵活产数、鲜胚移植和冻胚移植的临床妊娠率、鲜胚移植和冻胚移植的活产率、新生儿表征（双胎妊娠率、体质量、性别、出生缺陷率）等指标进行评估和分析。结果 共446例患者纳入分析，其中芳乐舒<sup>®</sup>组336例，果纳芬<sup>®</sup>组110例，随访时间为6.5年。芳乐舒<sup>®</sup>组和果纳芬<sup>®</sup>组的累积妊娠率、累积活产率差异均无统计学意义（均 $P>0.05$ ）。各年龄亚组两组间累积妊娠率和累积活产率差异均无统计学意义（均 $P>0.05$ ），36~39岁亚组中芳乐舒<sup>®</sup>组累积妊娠率[60.0% (12/20)]、累积活产率[55.0% (11/20)] 相比于果纳芬<sup>®</sup>组[28.6% (2/7)，14.3% (1/7)] 有增高趋势，但差异均无统计学意义（均 $P>0.05$ ）。芳乐舒<sup>®</sup>组和果纳芬<sup>®</sup>组的双胎妊娠率、每获胚活产数、每获卵活产数、新生儿性别、新生儿体质量、出生缺陷率差异均无统计学意义（均 $P>0.05$ ）。结论 芳乐舒<sup>®</sup>在控制性超促排卵中的安全性、有效性与果纳芬<sup>®</sup>相似。相比于果纳芬<sup>®</sup>，芳乐舒<sup>®</sup>在高龄人群中的累积妊娠率和累积活产率有增高趋势，但差异无统计学意义。

【关键词】 控制性超促排卵； 累积活产率； 重组人促卵泡激素； 高龄  
基金项目：国家自然科学基金青年科学基金（81801448）

### A phase III follow-up study of recombinant human follicle-stimulating hormone (Follitrope<sup>®</sup>) over 6.5 years

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【Abstract】 **Objective** To follow-up the previous phase III clinical trial of recombinant human follicle-stimulating hormone (Follitrope<sup>®</sup>), and to evaluate the cumulative pregnancy rate, the cumulative live birth rate, and the neonatal outcomes of subjects. **Methods** The phase III clinical study of Follitrope<sup>®</sup> in China (CTR20150341/CTR20150341, May 15, 2015—June 27, 2016) was followed up until December 31, 2022. Patients were divided into Follitrope<sup>®</sup> group and Gonal-F<sup>®</sup> group. According to the age, patients were divided into three subgroups: 20–30 years old subgroup, 31–35 years old subgroup and 36–39 years old subgroup. Cumulative pregnancy rate, cumulative live birth rate, number of embryos transferred per cycle, live births per embryo transfer cycle, live births per oocyte retrieved, and neonatal characteristics were analyzed. **Results** A total of 446 patients were included in the analysis, of which 336 (75.3%) were in the Follitrope<sup>®</sup> group and 110 (24.7%) in the Gonal-F<sup>®</sup> group, with a follow-up period

of 6.5 years. There were no statistically significant differences between the Follitrope® group and the Gonal-F® group in terms of cumulative pregnancy rate and cumulative live birth rate (all  $P>0.05$ ). Similar cumulative pregnancy rates and cumulative live birth rates were observed between the two groups within each age subgroup (all  $P>0.05$ ). In the 36–39 years old subgroup, the Follitrope® group showed a trend towards higher cumulative pregnancy rate [60.0% (12/20)] and cumulative live birth rate [55.0% (11/20)] compared with the Gonal-F® group [28.6% (2/7), 14.3% (1/7)], however, none of the differences were statistically significant (all  $P>0.05$ ). Twin pregnancy rates, live births per embryo, live birth per oocyte, newborn gender, birth weight, and birth defect rates were similar between the Follitrope® group and the Gonal-F® group without statistically significant differences (all  $P>0.05$ ). **Conclusion** The safety and effectiveness of Follitrope® in controlled ovarian hyperstimulation are similar to those of Gonal-F®. Compared with Gonal-F®, there is a trend toward higher cumulative pregnancy rates and cumulative live birth rates in elderly patients with Follitrope®, although there is no statistical difference.

**【Key words】** Controlled ovarian hyperstimulation; Cumulative live birth rate; Recombinant human follicle-stimulating hormone; Advanced maternal age

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·实验研究·

## 氯化锂对雄性小鼠睾酮生成障碍的影响及槲皮素保护作用的体内外研究

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**【摘要】** 目的 研究氯化锂 (lithium chloride, LiCl) 对雄性小鼠生殖毒性的作用, 探讨槲皮素对睾酮生成障碍保护效应的分子机制。方法 25 只 4~5 周龄的雄性 C57BL/6 小鼠按照随机数字表法分为 5 组, 分别为对照组、LiCl 染毒组 [38.4 mg/ (kg·d) LiCl+玉米油, 记为 LiCl 组]、槲皮素对照组 [50 mg/ (kg·d) 槲皮素, 记为 High-Quer 组]、低剂量槲皮素联合 LiCl 染毒组 [38.4 mg/ (kg·d) LiCl+10 mg/ (kg·d) 槲皮素, 记为 Low-Quer+LiCl 组] 和高剂量槲皮素联合 LiCl 染毒组 [38.4 mg/ (kg·d) LiCl+50 mg/ (kg·d) 槲皮素, 记为 High-Quer+LiCl 组]。HE 染色观察睾丸组织结构, 计算机辅助精子分析 (computer-aided sperm analysis, CASA) 系统检测精液参数, 透射电子显微镜观察小鼠睾丸间质细胞超微结构。采用 0 mmol/L、5 mmol/L、10 mmol/L、20 mmol/L 的 LiCl 染毒小鼠睾丸间质细胞株 TM3 细胞 24 h 后, 测定细胞总超氧化物歧化酶 (superoxide dismutase, SOD) 和谷胱甘肽过氧化物酶 (glutathione peroxidase, GSH-Px) 活性, TMRE 探针检测细胞线粒体膜电位 (mitochondrial membrane potential, MMP), Image-iT™ 脂质过氧化探针检测细胞脂质过氧化水平, 分别使用 Fe<sup>2+</sup> 含量检测试剂盒和 FerroOrange 探针检测细胞内 Fe<sup>2+</sup> 含量, 酶联免疫吸附法测定睾酮、孕酮和雌二醇水平, Western blotting 测定睾酮等相关蛋白表达水平。结果 LiCl 组小鼠精子总数 [ (36.78±1.81) ×10<sup>6</sup> ]、精子浓度 [ (18.39±0.90) ×10<sup>6</sup>/mL ]、精子活力 [ (25.70±3.32) % ] 和血清睾酮水平 [ (7.26±0.29) μg/L ] 均比对照组 [ (51.60±4.96) ×10<sup>6</sup>、(25.80±2.48) ×10<sup>6</sup>/mL、(41.47±2.83) %、(7.87±0.29) μg/L ] 低 (P=0.002、P=0.002、P=0.001、P=0.013); LiCl 组小鼠睾丸间质细胞出现线粒体空泡化、肿胀, 睾丸组织睾酮合成关键酶胆固醇侧链裂解酶 (cholesterol side-chain cleavage enzyme, Cyp11a1)、类固醇生成急性调节蛋白 (steroidogenic acute regulatory, StAR) 和细胞色素 P450 17α-羟化酶 (cytochrome P450 17α-hydroxylase, Cyp17a1)、睾丸间质细胞生物标志物 (3β-HSD1 和 17β-HSD3) 和铁死亡调控蛋白 (GPX4、SLC7A11 和 Nrf2) 的表达水平均较对照组显著下调 (均 P<0.001), 而低剂量槲皮素干预可显著改善 LiCl 诱导的上述损伤 (精子总数: P<0.001, 精子浓度: P<0.001, 精子活力: P=0.015, 血清睾酮: P=0.026, Cyp11a1、StAR、Cyp17a1、3β-HSD1、17β-HSD3、GPX4、SLC7A11 和 Nrf2: 均 P<0.001)。20 mmol/L LiCl 组 TM3 细胞睾酮水平 [ (7.28±0.24) μg/L ] 比 0 mmol/L LiCl 组 [ (12.50±0.38) μg/L ] 低 (P<0.001), 睾酮合成关键酶 Cyp11a1、StAR 和 Cyp17a1 蛋白水平均较 0 mmol/L LiCl 组显著下调 (均 P<0.001), SOD [ (2.42±0.11) U/mg ]、GSH-Px 活性 [ (1.29±0.03) mU/mg ] 和 MMP [ (57.24±1.69) % ] 均比 0 mmol/L LiCl 组 [ (3.11±0.09) U/mg、(1.54±0.01) mU/mg、(100.00±0) % ] 低 (均 P<0.001), 脂质过氧化水平 [ (211.18±3.60) % ] 和 Fe<sup>2+</sup> 含量 [ (26.44±0.94) μmol/L ] 均比 0 mmol/L LiCl 组 [ (100.00±0) %、(7.12±0.29) μmol/L ] 高 (均 P<0.001), GPX4、SLC7A11 和 Nrf2 蛋白表达水平均较 0 mmol/L LiCl 组显著下调 (均 P<0.001)。与 20 mmol/L LiCl 染毒组 [ 脂质过氧化: (194.46±3.16) %、(194.70±3.93) %; MMP: (78.74±0.52) %、(75.32±1.29) % ] 比较, 铁死亡抑制剂 Fer-1 和槲皮素均显著降低细胞脂质过氧化水平 [ (181.71±3.80) %, P=0.004; (166.88±3.22) %, P<0.001 ], 提高细胞 MMP [ (86.26±0.79) %, P=0.040; (81.09±1.32) %, P=0.001 ], 并显著上调睾酮合成关键酶以及铁死亡调控蛋白的表达水平 (均 P<0.05)。结论 槲皮素可能通过抑制细胞铁死亡保护 LiCl 诱导的睾丸间质细胞损伤和睾酮生成障碍。

**【关键词】** 氯化锂; 槲皮素; 睾丸间质细胞; 睾酮; 铁死亡

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### **Effect of lithium chloride on testosterone production dysfunction in male mice and protective effect of quercetin *in vivo* and *in vitro***

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**【 Abstract 】 Objective** To study the reproductive toxicity of lithium chloride (LiCl) in male mice and to explore the molecular mechanism of the protective effect of quercetin on testosterone production dysfunction. **Methods** Twenty-five male C57BL/6 mice aged 4–5 weeks were randomly divided into five groups according to the random number table method: control group, LiCl infected group [38.4 mg/(kg·d) LiCl+corn oil, noted as LiCl group], quercetin control group [50 mg/(kg·d) quercetin, noted as High-Quer group], low-dose quercetin combined with LiCl infection group [38.4 mg/(kg·d) LiCl+10 mg/(kg·d) quercetin, noted as Low-Quer+LiCl group] and high dose quercetin combined with LiCl infected group [38.4 mg/(kg·d) LiCl+50 mg/(kg·d) quercetin, noted as High-Quer+LiCl group]. The structure of testicular tissue, semen parameters, and the ultrastructure of Leydig cells in mice were detected by HE staining, computer-aided sperm analysis system (CASA), and transmission electron microscopy, respectively. TM3 mouse Leydig cells were treated with 0 mmol/L, 5 mmol/L, 10 mmol/L, 20 mmol/L LiCl for 24 h. The activities of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), mitochondrial membrane potential (MMP), lipid peroxidation levels, and expression levels of testosterone-related protein were measured by SOD and GSH-Px kits, TMRE probe, Image-iT™ lipid peroxidation probe, and Western blotting, respectively. Intracellular Fe<sup>2+</sup> concentration was detected by Fe<sup>2+</sup> detection kit and FerroOrange probe. The levels of testosterone, progesterone, and estradiol were measured using enzyme-linked immunosorbent assay kits. **Results** In the LiCl group, the total sperm count [(36.78±1.81)×10<sup>6</sup>], sperm concentration [(18.39±0.90)×10<sup>6</sup>/mL], sperm motility [(25.70±3.32)%] and serum testosterone level [(7.26±0.29) μg/L] were lower than those of control group [(51.60±4.96)×10<sup>6</sup>, *P*=0.002; (25.80±2.48)×10<sup>6</sup>/mL, *P*=0.002; (41.47±2.83)%, *P*=0.001; (7.87±0.29) μg/L, *P*=0.013], the expression levels of Cyp11a1, StAR and Cyp17a1, Leydig cell biomarkers (3β-HSD1, 17β-HSD3) and ferroptosis regulatory proteins (GPX4, SLC7A11 and Nrf2) in testis were significantly down-regulated compared with control group (all *P*<0.001). LiCl also induced mitochondrial vacuoles and swelling of Leydig cells. However, low-dose quercetin intervention could significantly ameliorate the above LiCl-induced damage (total sperm count: *P*<0.001, sperm concentration: *P*<0.001, sperm motility: *P*=0.015, serum testosterone level: *P*=0.026, Cyp11a1, StAR, Cyp17a1, 3β-HSD1, 17β-HSD3, GPX4, SLC7A11, and Nrf2: all *P*<0.001). In 20 mmol/L LiCl group, the testosterone level [(7.28±0.24) μg/L] in TM3 cells was lower than that of 0 mmol/L LiCl group [(12.50±0.38) μg/L,

$P<0.001$ ], the protein levels of Cyp11a1, StAR and Cyp17a1 were significantly down-regulated compared with 0 mmol/L LiCl group (all  $P<0.001$ ), the activities of SOD [(2.42±0.11) U/mg], GSH-Px [(1.29±0.03) mU/mg] and MMP [(57.24±1.69)%] were lower than those of 0 mmol/L LiCl group [(3.11±0.09) U/mg, (1.54±0.01) mU/mg, (100.00±0)%], all  $P<0.001$ ], the level of lipid peroxidation [(211.18±3.60)%] and the concentration of  $Fe^{2+}$  [(26.44±0.94)  $\mu\text{mol/L}$ ] were higher than those of 0 mmol/L LiCl group [(100.00±0)%, (7.12±0.29)  $\mu\text{mol/L}$ , all  $P<0.001$ ], and the expression of ferroptosis regulatory proteins was significantly down-regulated compared with 0 mmol/L LiCl group (all  $P<0.001$ ). Compared with 20 mmol/L LiCl group cells [lipid peroxidation: (194.46±3.16)%, (194.70±3.93)%; MMP: (78.74±0.52)%, (75.32±1.29)%], ferroptosis inhibitors Fer-1 and quercetin significantly decreased the level of lipid peroxidation [(181.71±3.80)%,  $P=0.004$ ; (166.88±3.22)%,  $P<0.001$ ], increased the level of MMP [(86.26±0.79)%,  $P=0.040$ ; (81.09±1.32)%,  $P=0.001$ ], and significantly up-regulated the expression of key enzymes in testosterone synthesis and ferroptosis regulatory proteins (all  $P<0.05$ ).

**Conclusion** Quercetin may protect LiCl-induced Leydig cells injury and testosterone production dysfunction by inhibiting cell ferroptosis.

**【 Key words 】** Lithium chloride; Quercetin; Leydig cells; Testosterone; Ferroptosis

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·临床报道·

## 不孕女性亚临床结核病的临床特征分析

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**【摘要】** 目的 探讨不孕女性亚临床结核病的临床特征。方法 收集 2019 年 1 月至 2024 年 1 月期间，因结核免疫学阳性在西安市胸科医院妇儿结核科进行结核活动性排查的不孕女性 2 129 例，对其中亚临床结核病例的临床资料进行回顾性分析。结果 亚临床结核病的不孕女性 69 例，占总体排查女性的 3.2%。发病年龄为 (31.16±4.68) 岁，不孕年限为 (3.81±2.58) 年，94.2% (65/69) 为原发性不孕。部分患者有不良孕产史，如异位妊娠、反复助孕失败、稽留流产、先兆流产。胸部 CT 多表现为纤维条索硬结灶、结节及结节钙化灶、胸膜粘连或少量胸腔积液、肺门或纵隔淋巴结钙化、斑片状合并条索状增殖灶。宫腔镜表现有慢性子宫内膜炎、子宫内膜息肉、宫腔粘连。子宫输卵管造影多为双侧输卵管不通、梗阻、积水；结核病原学结果提示分子生物学阳性占多数，提示较低的结核菌载量。结论 不孕女性亚临床结核病的临床特征不典型，胸部 CT 肺部病灶隐匿，常被忽视。

**【关键词】** 不孕；结核分枝杆菌潜伏感染；亚临床结核病；评估  
基金项目：陕西省科学基础研究计划项目 (2022JQ-924)

## **Analysis of clinical characteristics of subclinical tuberculosis in infertile women**

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**【 Abstract 】 Objective** To investigate the clinical characteristics of subclinical tuberculosis in infertile women. **Methods** A total of 2 129 infertile women screened for active tuberculosis were collected from January 2019 to January 2024 at Department of Gynecology and Pediatrics Tuberculosis in Xi'an Chest Hospital due to latent tuberculosis infection, and the clinical data of subclinical tuberculosis cases were retrospectively analyzed. **Results** The study identified 69 cases [3.2% (69/2 129)] of subclinical tuberculosis among these women. The age at diagnosis was (31.16±4.68) years, with an infertility duration of (3.81±2.58) years. About 94.2% (65/69) of these women had primary infertility. Some patients had adverse reproductive histories, including ectopic pregnancies, repeated assisted reproduction failures, missed miscarriages, and threatened miscarriages. Chest CT scans typically revealed fibrous cord-like consolidations, nodules and calcified nodules, pleural adhesions or minimal pleural effusions, calcification of hilar or mediastinal lymph nodes, and speckled combined with linear proliferative lesions. Hysteroscopic findings included chronic endometritis, endometrial polyps, and intrauterine adhesions. Hysterosalpingography frequently showed bilateral tubal occlusions, stenosis, and hydrosalpinx. Molecular biological assays indicated a lower bacillary load in most cases. **Conclusion** The clinical presentation of subclinical tuberculosis in infertile women is often atypical, with pulmonary lesions on chest CT being subtle and indicative of chronic conditions, which are frequently overlooked.

**【 Key words 】** Infertility; Latent tuberculosis infection; Subclinical tuberculosis; Assessment

**Fund program:** Scientific Basic Research Project of Shaanxi Province  
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·个案报道·

## 胚胎移植术前发现重复右肾、输尿管伴输尿管 异位开口于阴道1例

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**【摘要】** 回顾分析1例胚胎移植术前发现重复右肾、输尿管伴输尿管异位开口于阴道的病例并进行文献复习。该患者拟行第3次胚胎移植,移植术前因“右输卵管积水”行腹腔镜下双侧输卵管切除术,术后1周余开始出现阴道持续分泌物增多伴异味50 d余,门诊反复抗炎治疗无效。阴道超声检测见右附件区囊肿,后经多次妇科检查、阴道超声、泌尿系超声、全腹CT、磁共振泌尿系水成像等检查诊断为右肾、输尿管畸形伴输尿管异位开口于阴道。复读患者输卵管切除术前影像,发现扩张的右重复输尿管被误诊为右输卵管积水。女性附件区囊肿伴持续阴道流液需考虑有无重复输尿管合并输尿管异位开口的可能,应注意与输卵管积水鉴别。

**【关键词】** 泌尿生殖系统畸形; 输尿管疾病; 输卵管疾病; 鉴别诊断  
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**Diagnosis of duplicated kidney and ureter with ectopic opening of ureter in  
vagina before embryo transfer**

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**【Abstract】** A retrospective analysis was conducted on a case of duplicate right kidney and ureter with ectopic opening in the vagina discovered before embryo transfer, and literature review was conducted. The patient planned to undergo a third embryo transfer. Prior to the transfer, laparoscopic bilateral salpingectomy was performed due to "right fallopian tube hydrosalpinx". About a week after the surgery, there was a continuous increase in vaginal discharge with an odor for more than 50 d. Repeated antibiotic treatments in the outpatient department were ineffective. Vaginal ultrasound examination revealed a cyst in the right adnexal area. After multiple gynecological examinations, vaginal ultrasound, urological ultrasound, whole abdominal CT, magnetic resonance urography, etc., the diagnosis was right kidney and ureteral malformation with ectopic opening of the ureter in the vagina. Upon reviewing the preoperative images of the patient undergoing salpingectomy, it was found that the dilated right repeated ureter was misdiagnosed as hydrosalpinx. Women with adnexal cysts accompanied by continuous vaginal discharge should consider the possibility of repeated ureters and ectopic ureteral opening, and should pay attention to distinguishing it from hydrosalpinx.

**【Key words】** Urogenital abnormalities; Ureteral diseases; Fallopian tube diseases; Diagnosis, differential

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个案报道

## 单侧输卵管双胎妊娠 2 例病例报道并文献复习

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**【摘要】** 单侧输卵管双胞胎妊娠是一种比较罕见的异位妊娠。本文报道了 2015 年、2023 年青岛市胶州中心医院收治的 2 例单侧输卵管双胞胎妊娠的诊疗经过，并复习相关文献，总结了单侧输卵管双胞胎妊娠的发病危险因素、临床病例特点、临床诊疗方法，以期对单侧输卵管双胞胎妊娠的早期识别、准确诊断和及时治疗提供有益的参考，降低其发病率和病死率。

**【关键词】** 超声检查； 发病率； 危险因素； 腹腔镜手术； 单侧输卵管双胞胎妊娠

### Unilateral tubal twin pregnancy: report of two cases and literature review

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**【Abstract】** Unilateral tubal twin pregnancy is a relatively rare ectopic pregnancy. This paper reported the diagnosis and treatment of two cases of unilateral tubal twin pregnancy admitted to Jiaozhou Central Hospital of Qingdao in 2015 and 2023, respectively, and the relevant literatures were reviewed. This paper summarized the risk factors, clinical case characteristics, clinical diagnosis and treatment methods of unilateral tubal twin pregnancy, in order to provide useful reference for early recognition, accurate diagnosis and timely treatment of unilateral tubal twin pregnancy, and reduce its incidence rate and mortality.

**【Key words】** Ultrasonography; Incidence rate; Risk factors; Laparoscopic surgery; Unilateral tubal twin pregnancy

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·综述·

## 减重干预对超重或肥胖不孕女性生育力和辅助生殖结局的影响

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**【摘要】** 超重和肥胖全球发病率逐年上升, 已成为重要的世界性医学社会问题。育龄期超重或肥胖女性生育力广受影响, 围产期各种并发症风险显著增加, 减重干预被认为是改善这部分不孕女性生育结局的有效手段。但目前关于减重干预是否能够有效改善超重或肥胖不孕女性生育结局等仍在探讨中。本文拟从减重干预对超重或肥胖不孕女性生育力、辅助生殖结局和围产期结局影响等多个角度探讨减重干预对超重或肥胖女性的作用, 旨在为减重干预临床实践提供更多思路和参考。

**【关键词】** 减重; 超重; 肥胖; 生育力; 辅助生殖

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## **Effect of weight loss interventions on fertility and assisted reproductive outcomes in overweight or obese infertile women**

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**【 Abstract 】** Overweight and obesity are getting more commonplace worldwide and increasingly developing serious health and social issues. Weight loss intervention is regarded as an effective way to improve the fertility outcomes of overweight or obese women of childbearing age who have a substantial impact on their ability to conceive as well as an elevated risk of various perinatal complications. The effectiveness of weight loss therapies in improving fertility outcomes in overweight or obese infertile women is still being investigated. This article aims to investigate the impact of weight loss therapies on overweight or obese women from multiple perspectives, including the effects of weight loss intervention on fertility, assisted reproductive outcomes, and perinatal outcomes to provide more ideas and references for the clinical practice of weight loss interventions.

**【 Key words 】** Weight loss; Overweight; Obese; Fertility; Assisted reproduction

**Fund program:** International Scientific and Technological Cooperation Project of Hubei Province (2021EHB025); National Key Research and Development Program of China (2022YFC2702503)



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综述

## 抑郁症影响生育力的研究进展

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**【摘要】** 抑郁症在我国发病率较高, 但因精神卫生资源缺乏及民众认识较为落后, 抑郁症患者得不到及时的识别和充分的治疗, 为家庭和社会带来了沉重的负担。抑郁症可影响机体多系统功能, 与多种疾病的发生密切相关。目前的证据提示, 抑郁会对生育力造成损害, 其表现涵盖性功能障碍、卵母细胞与精子的发育异常以及胚胎发育和植入受损等情况。本文主要总结了抑郁症影响生育力的临床研究及基础研究, 以期揭示抑郁对于生育力的影响和机制。

**【关键词】** 抑郁症; 生育力; 皮质醇; 下丘脑-垂体-性腺轴

### Research progress on the impact of depression on fertility

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**【Abstract】** The incidence of depression is high in China. However, due to the lack of mental health resources and the insufficient understanding of depression among the public, patients with depression cannot be identified in time and treated adequately, which brings heavy burdens to families and society. Depression can affect the functions of multiple systems in the body. It is closely related to the occurrence of various diseases. Current evidence indicates that depression can cause damage to fertility. Its manifestations include sexual dysfunction, abnormal development of oocytes and sperm, and impaired development and implantation of embryos. This article mainly summarizes the clinical and basic research on the impact of depression on fertility. We hope this article reveal the influence and mechanism of depression on fertility.

**【 Key words 】** Depression; Fertility; Cortisol; Hypothalamic-pituitary-gonadal axis

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综述

## 糖尿病影响男性生育能力的研究进展

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**【摘要】** 糖尿病是一种全球流行病, 具有高发病率和高死亡率的特点。糖尿病可导致急性和慢性全身并发症。糖尿病所致的男性生殖障碍成为了人类关注的热点。多项研究表明, 糖尿病通过多种途径诱发男性生育力损伤, 包括勃起及射精功能障碍、下丘脑-垂体-性腺轴的紊乱、附睾和睾丸内损害、精液质量损害、睾丸和精子糖代谢异常以及影响子代健康等。其涉及到的机制包括氧化应激、炎症、自噬、凋亡、表观遗传调控及线粒体损伤等。针对男性生育力损伤的干预措施有糖尿病治疗药物、抗氧化剂、中药及针灸、间充质干细胞疗法、运动及体育锻炼和肠道菌群干预等。本文通过总结目前关于糖尿病与男性生育力之间关系的研究进展, 探讨其导致男性不育的内在机制, 探寻其潜在的干预措施, 为提高男性生殖健康提供参考。

**【关键词】** 糖尿病; 高血糖症; 不育, 男性

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### Research progress on the impact of diabetes mellitus in male fertility

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**【Abstract】** Diabetes mellitus is a global epidemic characterized by high incidence and mortality rates. It can lead to both acute and chronic systemic complications. Diabetes-induced male reproductive disorders have become a focal point of concern. Numerous studies have shown that hyperglycemia can impair male fertility through various pathways, including erectile and ejaculatory dysfunction, disruption of the hypothalamic-pituitary-gonadal axis, damage to the epididymis and testis, impaired semen quality, abnormalities in testicular and sperm glucose metabolism, and adverse effects on offspring health. The mechanisms involved include oxidative stress, inflammation, autophagy, apoptosis, epigenetic regulation, and mitochondrial damage. Interventions for male fertility impairment include diabetes treatment drugs, antioxidants, Traditional Chinese Medicine and acupuncture, mesenchymal stem cell therapy, exercise and physical training, as well as gut microbiota interventions. This article aims to review the current research on the relationship between diabetes and male fertility, explore the underlying mechanisms leading to male infertility, and identify potential interventions to improve male reproductive health, which holds significant clinical value.

**【Key words】** Diabetes mellitus; Hyperglycemia; Infertility, male

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综述

## 微塑料对生殖系统的损害及相关机制研究进展

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**【摘要】** 微塑料是指直径小于5 mm的疏水性固体或聚合物基质,其主要来源于日常塑料制品的降解,根据形成过程可分为初级微塑料和次级微塑料。微塑料广泛存在于环境中,能够在生物体各组织内原位沉积并且进入血液循环转移至机体其他器官。目前发现微塑料与生殖器官功能损害存在一定关联,其造成卵泡结构破

坏、颗粒细胞凋亡、卵泡数量减少、生精细胞层数减少、排列紊乱、精子发育畸形等问题。本文对微塑料引起生殖系统结构和功能损害及产生损害的可能机制进行了相关总结和综述。

【关键词】 微塑料； 生殖系统； 毒性作用； 氧化应激

## Research progress on the damage and related mechanisms to the reproductive system caused by microplastics

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【Abstract】 Microplastics are hydrophobic solids or polymer matrices with a diameter less than 5 mm, which mainly originate from the degradation of daily plastic products. Based on their formation process, microplastics can be classified into primary microplastics and secondary microplastics. Microplastics are widely present in the environment, able to deposit *in situ* within various tissues of organisms and enter the blood circulation system to be transported to other organs of the body. Current research has found a certain correlation between microplastics and reproductive organ dysfunction, leading to the destruction of follicular structure, apoptosis of granulosa cells, and a reduction in the number of follicles, a decrease in the number of spermatogenic cell layers, disordered arrangement, and developmental malformations of sperm. This review summarized the structural and functional damage to the reproductive systems caused by microplastics and the possible mechanisms underlying such damage.

【Key words】 Microplastics; Reproductive system; Toxic effects; Oxidative stress

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综述

## 从受精卵到囊胚期胚胎在体外培养发育过程中的果糖代谢

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**【摘要】** 哺乳动物胚胎在早期发育阶段是以丙酮酸和乳酸为主要代谢途径产生 ATP, 但是随着胚胎基因组的激活和生物合成的增加, 其能量代谢也会发生动态变化, 随着胚胎发育到囊胚阶段, 能量来源逐步转变为葡萄糖代谢。早期研究表明, 培养液中的葡萄糖会抑制早期胚胎发育。动物研究显示, 果糖可以代替葡萄糖作为能量基质被胚胎摄取利用。培养液中添加果糖可以提高动物胚胎体外培养的囊胚形成率。培养液中混合添加果糖与葡萄糖还可以改善动物囊胚质量、降低细胞凋亡比例。由此推测, 果糖和葡萄糖在培养液中具有一定的代谢协同作用可改善胚胎的发育。本文通过分析讨论受精卵到囊胚期胚胎在体外培养发育过程中的能量底物需求, 从而对胚胎培养液中添加果糖可能的代谢途径进行概述。

**【关键词】** 受精卵; 囊胚; 胚胎发育; 果糖; 能量代谢

### **Fructose metabolism from zygote to blastocyst stage development during culture *in vitro***

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**【Abstract】** Dynamic changes of energetic metabolism occur in mammalian embryonic development from zygote to blastocyst stage. Pyruvate and lactate play an important role in early cleavage stage for ATP production, and glucose may play a key role for blastocyst development after zygote genome activation. Although the early cleavage development is inhibited by glucose, the late blastocyst formation is required for existing glucose in the culture medium *in vitro*. It has been reported that the role of glucose in the culture medium can be replaced by fructose. In animal studies, it also has been reported that the blastocyst formation rate is increased by fructose supplementation in the culture medium, and further indicated that combined use of glucose and fructose in the culture medium as energetic sources not only increases the blastocyst formation rate but also improves the quality of blastocyst and reduces the cell apoptosis. Those results indicated that there is synergic function of glucose and fructose in the culture medium during embryonic development. In this review, we will discuss the possibility of fructose metabolic routes from the development of zygote to blastocyst stage and explain the functional role of fructose in the culture medium.

**【Key words】** Zygote; Blastocyst; Embryo development; Fructose; Energetic metabolism