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# 基础抗苗勒管激素在卵泡期长效促性腺激素释放激素激动剂长方案中对卵巢反应性及妊娠结局的预测价值

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**【摘要】目的** 探讨在卵泡期长效促性腺激素释放激素 (GnRH) 激动剂长方案中, 血清抗苗勒管激素 (AMH) 浓度对卵巢反应性、临床妊娠的预测价值。**方法** 本研究为基于电子医疗记录的聚合式队列研究, 回顾性分析接受试管婴儿助孕治疗的 4 075 名患者, 根据卵巢反应性分为低反应、正常反应及高反应组, 根据妊娠结局分为妊娠组和未妊娠组, 采用 logistic 回归及受试者工作特征曲线 (ROC) 分析 AMH 对卵巢反应性及妊娠结局的预测价值。**结果** AMH 是卵巢反应性的有效预测因子, 预测卵巢低反应、高反应的曲线下面积分别为 0.853、0.764, 临界值分别为 1  $\mu\text{g/L}$ 、2.75  $\mu\text{g/L}$ , 但对临床妊娠的预测价值较低。**结论** AMH 是卵巢反应性的有效独立预测因子, 且对低反应的预测价值高于高反应, 但不能有效预测临床妊娠结局。

**【关键词】** 抗苗勒管激素 (AMH); 卵泡期长效促性腺激素释放激素 (GnRH) 激动剂长方案; 卵巢反应性; 妊娠结局

· 临床研究 ·

**The value of basal anti-Müllerian hormone in predicting ovarian response and pregnancy outcomes in follicular-phase long-acting gonadotropin releasing hormone agonist long protocol** Huang Huixia,

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Huang Huixia and Yu Yiping are the first authors who contributed equally to the article

**【Abstract】 Objective** To explore the potential value of basal serum anti-Müllerian hormone (AMH) concentration in predicting ovarian response and pregnancy outcomes in follicular-phase long-acting gonadotropin releasing hormone (GnRH) agonist long protocol. **Methods** This study is an aggregated cohort study based on electronic medical records and a total number of 4 075 patients were recruited in this retrospective study. These patients were divided into three groups (low, normal and high response) according to the ovarian response and were divided into two groups (pregnancy and non-pregnancy) according to pregnancy outcomes. The logistic regression analysis and receiver operating characteristic curve (ROC) were used to compare the predictive value of AMH on ovarian response and pregnancy outcomes. **Results** Basal AMH was the most effective factor for predicting ovarian response. The area under the receiver operating characteristic curve (AUC) analysis of AMH for low and high ovarian response prediction was 0.853 and 0.764, respectively. The cut-off point of AMH for predicting low and high ovarian response is 1  $\mu\text{g/L}$  and 2.75  $\mu\text{g/L}$ , respectively. AMH has a low predictive value for clinical pregnancy outcomes. **Conclusion** Basal AMH is the most powerful predicting factor for ovarian response, especially for low ovarian response, but not a significant predicting factor for pregnancy outcomes.

**【Key words】** anti-Müllerian hormone (AMH); Follicular long-acting gonadotropin releasing hormone (GnRH) agonist long protocol; Ovarian response; Pregnancy outcomes

# 移植冻融第 4 日 8- 细胞胚胎至第 3 日内膜后的临床结局分析

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**【摘要】** 目的 探讨为第 3 日胚胎准备的内膜移植第 4 日 8- 细胞胚胎后的临床结局。方法 观察性分析 1 190 个第 3 日滞后胚胎。将延长培养后优选的 176 个第 4 日 8- 细胞胚胎作为研究组, 以同期 660 个第 3 日 8- 细胞胚胎作对照组。比较两组胚胎移植的临床结局。结果 研究组的种植率 (20.45%)、临床妊娠率 (15.91%) 和活胎分娩率 (14.20%) 低于对照组 (30.45%、27.42%、20.91%;  $P=0.009$ 、 $0.002$ 、 $0.046$ ), 但流产率 (4.55%) 与对照组相似 (3.33%) ( $P>0.05$ )。研究组的新生儿出生体质量  $[(3\ 556\pm\ 381)\ \text{g}]$  高于对照组  $[(3\ 311\pm\ 570)\ \text{g}]$  ( $P=0.012$ )。结论 移植第 4 日 8- 细胞胚胎到为第 3 日胚胎准备的内膜可以作为滞后胚胎安全有效的备选方法。

**【关键词】** 滞后胚胎; 延长培养; 冷冻胚胎移植; 同步性; 种植率

· 临床研究 ·

**Clinical outcomes of transfer vitrified-thawed day 4 8-cell embryos into endometrium prepared for day 3 embryos** Si Jiqiang, Zhang Yaning, Kuang Yanping, Lyu Qifeng

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**【Abstract】 Objective** To determine the clinical outcomes when day 4 8-cell embryo is transferred into endometrium prepared for day 3 embryos. **Methods** This study performed a retrospective analysis of 1 190 retarded embryos by extended culture *in vitro*. Among them, 176 day 4 8-cell embryos were chosen and transferred as study group, and 660 day 3 8-cell embryo were matched as control group. Pregnancy outcomes were compared between the two groups. **Results** Achieved successful implantation rates, clinical pregnancy rate and live birth rate in study group (20.45%, 15.91% and 14.20%) were lower than those in control group (30.45%, 27.42% and 20.91%;  $P=0.009, 0.002, 0.046$ ). Miscarriage rate was similar to the control (3.33%) ( $P>0.05$ ), and mean birth weight of study group [(3 556±381) g] was higher than that in control group [(3 311±570) g,  $P=0.012$ ]. **Conclusion** Transferring day 4 8-cell frozen embryo into endometrium prepared for day 3 embryos can be a new and safe alternative for patients with slow embryos.

**【Key words】** Retarded embryo; Extended culture; Frozen embryo transfer; Synchronization; Implantation rate

# 曼月乐治疗对子宫腺肌症患者冻融胚胎移植结局的影响

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**【摘要】目的** 探讨用左炔诺孕酮宫内缓释系统 (LNG-IUS, 曼月乐) 治疗子宫腺肌症后对体外受精-胚胎移植 (IVF-ET) 患者冻融胚胎移植 (FET) 结局的影响。**方法** 回顾性病例对照分析在本中心就诊的子宫腺肌症的不孕症患者资料, 分为治疗组, 即接受曼月乐治疗患者, 共 122 个 FET 周期; 对照组, 即未经曼月乐治疗患者, 共 196 个 FET 周期。比较两组患者促排卵和临床结局。**结果** 治疗组和对照组相比, 基础情况、治疗结束时直径 >14 mm 的卵泡数、获卵数、成熟卵数、正常受精卵数、优质胚胎数、有效胚胎总数等组间比较差异均无统计学意义 ( $P>0.05$ )。治疗组的生化妊娠率 (49.1%)、临床妊娠率 (45.1%)、胚胎种植率 (31.4%) 均显著优于对照组 (36.7%、33.5%、22.4%;  $P=0.032$ 、0.037、0.018)。**结论** 曼月乐治疗子宫腺肌症, 可提高 IVF-ET 治疗周期的临床妊娠率和胚胎种植率, 是一种新的简单安全、高效的、针对子宫腺肌症的辅助生殖方案。

**【关键词】** 曼月乐; 子宫腺肌症; 超促排卵; 冻融胚胎移植 (FET)

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· 临床研究 ·

**Effect of mirena on the outcome of frozen embryo transplantation in the treatment of adenomyosis** Liang Zhou, Yin Mingru, Ma Meng, Zhu Jing, Kuang Yanping

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**【Abstract】 Objective** To investigate the effect of levonorgestrel-releasing intrauterine system (LNG-IUS, Mirena) on adenomyosis and its effect on frozen embryo transfer outcomes. **Methods** A total of 122 oocytes pick up cycles treated with progestin primed ovarian stimulation (PPOS) + LNG-IUS regimen and 196 cycles treated with PPOS in control group were retrospectively analyzed. The general information, controlled ovary stimulation indexes and clinical outcomes were compared between treatment group and control group. **Results** There were no significant differences in the general information, number of follicles with diameter > 14 mm at the end of treatment, number of oocytes retrieved, number of mature eggs, the number of normal fertilized eggs, the number of high quality embryos, the total number of effective embryos between the groups ( $P>0.05$ ). The biochemical pregnancy rate (49.1%), the clinical pregnancy rate (45.1%) and the embryo implantation rate (31.4%) in the treatment group were significantly higher than those in control group (36.7%, 33.5%, 22.4%;  $P=0.032, 0.037, 0.018$ ). **Conclusion** The treatment of uterine adenomyosis with Mirena can improve the clinical pregnancy rate and embryo implantation rate of the IVF-ET treatment cycle. It is a new simple, safe and effective assisted reproductive program for adenomyosis.

**【Key words】** Adenomyosis; Levonorgestrel-releasing intrauterine system (LNG-IUS); Controlled ovarian stimulation; Frozen-thawed embryo transfer

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# 宫腔镜在不孕患者宫腔病变的诊断及治疗作用

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**【摘要】** 目的 探讨不孕症患者宫腔疾病的发生率及经宫腔镜下治疗后的妊娠结局。方法 回顾性分析 2015 年 1 月—2016 年 8 月期间因不孕症在本院就诊的 8 546 例经宫腔镜检查的初诊患者资料。根据患者年龄分为 <35 岁组 (6 786 例),  $\geq 35$  岁组 (1 760 例), 比较两组宫腔病变发生率。将其中移植成功的患者再根据宫腔镜诊疗结果将其分为 2 个亚组: 正常亚组及处理亚组。其中 <35 岁组中正常组共纳入 2 192 例, 处理亚组 531 例;  $\geq 35$  岁组中正常亚组共纳入 613 例, 处理亚组共 162 例。统计经宫腔镜下处理宫腔内病变并与宫腔正常者的妊娠结局进行比较。结果  $\geq 35$  岁组患者宫内病变发生率 (19.66%) 显著高于 <35 岁组 (16.92%,  $P=0.007$ ), 其中所占比例最高的宫腔内病变为子宫内膜息肉, 发生率分别为 11.36% 和 7.97%, 其次为子宫内膜单纯增生、宫腔粘连、宫腔畸形等, 最低的是子宫内膜结核; 经宫腔镜对宫腔内病变的进行处理后的不孕人群中, <35 岁女性处理亚组的临床妊娠率 (66.5%) 与正常亚组 (65.1%) 差异无统计学意义 ( $P=0.865$ ), 而  $\geq 35$  岁女性处理亚组临床妊娠率 (24.7%)、着床率 (16.5%) 显著低于正常亚组 (36.2%,  $P=0.006$ ; 23.6%,  $P=0.008$ )。结论 不孕者中发生宫腔病变者约占 16%~20%, 通过宫腔镜处理后, <35 岁者的妊娠率能与同龄宫腔正常者持平。

**【关键词】** 宫腔镜; 宫腔内病变; 妊娠结局

· 临床研究 ·

**The diagnosis and treatment outcome of hysteroscopy in infertility** Wang Mengying, Xie Rui, Hu Linli

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**【Abstract】 Objective** To explore the incidence of uterine cavity disease and the analysis of pregnancy outcome after hysteroscopic treatment. **Methods** Total 8 546 infertile patients who accepted hysteroscopy were analyzed retrospectively from January 2015 to August 2016. According to patients' age, they were divided into two groups: <35-year-old group (6 786 cases),  $\geq$  35-year-old group (1 760 cases), and the incidence of intrauterine lesions were compared between the two groups. Among the patients whose embryos were transferred successfully, they were divided into two subgroups according to hysteroscopy results: normal subgroup and treatment subgroup. Among the <35 years old group, 2 192 cases were included in the normal subgroup, and 531 cases were in treatment subgroup. Of  $\geq$  35-year-old group 613 cases were included in the normal subgroup and 162 cases were in treatment subgroup. The pregnancy outcomes were compared between the two subgroups.

**Results** The incidence of intrauterine lesions in advanced women  $\geq$  35-year-old (19.66%) was significantly higher than women <35-year-old (16.92%,  $P=0.007$ ). The highest proportion of intrauterine lesions was endometrial polyps in both groups, with the incidence rates of 11.36% and 7.97% respectively, followed by simple uterine hyperplasia, intrauterine adhesions and uterine malformations. The incidence of endometrial tuberculosis was rare. Among the infertile women who underwent hysteroscopy treatment for intrauterine lesions, the clinical pregnancy rate (66.5%) was not significantly different from that in uterine cavity non-lesioned patients (65.1%) in women <35-year-old ( $P=0.865$ ). However, the clinical pregnancy rate (24.7%) and implantation rate (16.5%) in the  $\geq$  35-year-old female treatment subgroup were significantly lower than those in the normal subgroup without uterine lesions (36.2%,  $P=0.006$ ; 23.6%,  $P=0.008$ ). **Conclusion** The incidence of uterine cavity disease is 16%~20%. Hysteroscopic treatment of uterine cavity lesions can significantly improve the pregnancy outcomes of infertile patients less than 35 years of age, but for the elderly infertility patients, the pregnancy outcomes after treatment was still inferior to the normal patients of the same age.

**【Key words】** Hysteroscopy; Intrauterine lesions; Pregnancy outcome

# 既往自然流产胚胎染色体异常者的囊胚染色体异常发生率

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**【摘要】** 目的 分析既往自然流产胚胎染色体异常 (previous chromosome abnormality miscarriage, PCAM) 患者囊胚的染色体异常率及其影响因素。方法 回顾性研究比较因 PCAM(PCAM 组) 和因单基因遗传性疾病 (对照组) 进行植入前胚胎非整倍体遗传学筛查 (preimplantation genetic testing for aneuploid, PGT-A) 患者的活检囊胚染色体异常率, 并分析其与双方年龄、基础促卵泡激素 (FSH)、FSH/黄体生成素 (LH)、体质量指数 (BMI)、既往自然流产次数、新鲜取卵周期数、M<sub>II</sub> 卵子率、受精率、囊胚形成率、活检囊胚数和有无 PCAM 的关系。结果 多重线性回归分析显示, 仅女方年龄和有无 PCAM 对活检囊胚的染色体异常率有影响。女方年龄 ≤ 30 岁、31~34 岁和 35~38 岁, PCMA 组和对照组的囊胚染色体异常率分别为 25.29%、27.43%、45.76% 和 18.22%、19.85%、31.55% ( $P=0.034$ 、 $P=0.044$ 、 $P=0.011$ ); >38 岁时, PCMA 组和对照组的囊胚染色体异常率分别为 63.64% 和 46.15% ( $P=0.227$ )。结论 > 38 岁 PCAM 患者的囊胚染色体异常率超过 60%, 建议行 PGT-A 以降低胚胎染色体异常导致的再次流产风险。35~38 岁 PCAM 患者的囊胚染色体异常率明显高于对照组, 可考虑行 PGT-A。

**【关键词】** 自然流产; 胚胎; 染色体; 囊胚; 植入前胚胎非整倍体遗传学筛查 (PGT-A)

**基金项目:** 国家自然科学基金 (81170568); 广东省自然科学基金 (2015A030313192)

· 临床研究 ·

**The incidence of chromosomal abnormality in the blastocysts from patients with previous chromosome abnormality miscarriage**

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**【Abstract】 Objective** To explore the chromosomal abnormality rate of the blastocysts of patients with previous chromosome abnormality miscarriage (PCAM) undergoing preimplantation genetic testing for aneuploidies (PGT-A), and investigate the factors affecting the blastocyst abnormal rate. **Methods** In this retrospective study, the incidence of chromosomal abnormality in the blastocysts from patients undergoing PGT-A with PCAM were compared to the single gene defect patient with PGT-A (control). The relationship between parental age, basal follicle-stimulating hormone (FSH), FSH/luteinizing hormone (LH), body mass index (BMI), the frequency of spontaneous abortions, No. of cycles, M<sub>II</sub> egg rate, fertilization rate, blastocyst formation rate, the biopsy blastocyst count, the presence of PCAM and the chromosomal abnormality rate of blastocyst were also analyzed by multiple linear regression analysis. **Results** Multivariate linear regression analysis showed that female age and the presence of PCAM affected the rate of chromosomal abnormalities in biopsies. The chromosomal abnormality rate of blastocyst in PCMA group and control group were 25.29%, 27.42%, 45.76% and 18.22%, 19.85%, 31.55% ( $P=0.034$ ,  $P=0.044$ ,  $P=0.011$ ) for women aged  $\leq 30$  years, 31–34 years and 35–38 years respectively. For women aged  $>38$  years, the chromosomal abnormality rate in PCMA group and control group were 63.64% and 46.15% ( $P=0.227$ ). **Conclusion**  $>38$ -year-old PCAM patients have a high rate (over 60%) of chromosomal abnormality in blastocysts and PGT-A treatment should be recommend to reduce the risk of next miscarriage caused by fetal chromosomal abnormalities. The chromosomal abnormalities of blastocysts in 35–38-year-old patients with PCAM were significantly higher than those in the control group. PGT-A treatment may be considered.

**【Key words】** Spontaneous abortion; Embryo; Chromosome; Blastocyst; Preimplantation genetic testing for aneuploidies (PGT-A)

**Fund program:** National Natural Science Foundation of China (81170568); Natural Science Foundation of Guangdong Province (2015A030313192)

# 卵巢恶性生殖细胞肿瘤患者的预后分析： 一项基于数据库的回顾性研究

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**【摘要】** 目的 分析不同临床病理特征的卵巢恶性生殖细胞肿瘤 (MOGCTs) 患者预后。方法 选取监测、流行病学和结果数据库 (SEER) 中 MOGCTs 的患者的临床病理数据共 2 801 例进行分析。用 Kaplan-Meier 法绘出生存曲线，log-rank 检验单因素分析预后影响因素，Cox 回归模型进行多因素分析。结果 单因素分析显示：MOGCTs 预后与年龄 ( $\chi^2=93.119$ ,  $P=0.000$ )、种族 ( $\chi^2=12.894$ ,  $P=0.002$ )、病理类型 ( $\chi^2=316.287$ ,  $P=0.000$ )、肿瘤分化 ( $\chi^2=27.476$ ,  $P=0.000$ )、国际妇产科联盟 (FIGO) 分期 ( $\chi^2=187.837$ ,  $P=0.000$ )、肿瘤位置 ( $\chi^2=36.959$ ,  $P=0.000$ )、肿瘤大小 ( $\chi^2=319.981$ ,  $P=0.000$ )、淋巴结转移 ( $\chi^2=20.849$ ,  $P=0.000$ ) 和手术方式 ( $\chi^2=170.370$ ,  $P=0.000$ ) 等有关。多因素分析显示 MOGCTs 预后与 FIGO 分期 ( $P=0.004$ , 95%  $CI=1.204\sim 2.603$ )、病理类型 ( $P=0.010$ , 95%  $CI=1.109\sim 2.144$ )、发病年龄 ( $P=0.009$ , 95%  $CI=1.340\sim 7.584$ ) 有关。结论 FIGO 分期、病理类型和发病年龄高是 MOGCTs 其预后的独立危险因素。

**【关键词】** 卵巢；卵巢恶性生殖细胞肿瘤 (MOGCTs)；预后

基金项目：国家自然科学基金项目 (81272213)2213)

· 临床研究 ·

**Prognostic analysis of malignant germ cell tumor of ovary: a retrospective study based on database**

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**【Abstract】 Objective** To analyse the prognosis of malignant germ cell tumor of ovary (MOGCTs) with different clinicopathological features. **Methods** The clinical and pathological data of 2 801 patients with MOGCTs in SEER database were analyzed. Survival curve was plotted by Kaplan-Meier method. Univariate analysis was performed by log-rank test. Cox regression model was used for multivariate analysis. **Results** Univariate analysis showed that the prognosis was associated with the age of diagnosis ( $\chi^2=93.119$ ,  $P=0.000$ ), race ( $\chi^2=12.894$ ,  $P=0.002$ ), pathological types ( $\chi^2=316.287$ ,  $P=0.000$ ), pathological differentiation ( $\chi^2=27.476$ ,  $P=0.000$ ), International Federation of Gynecology and Obstetrics (FIGO) stage ( $\chi^2=187.837$ ,  $P=0.000$ ), tumor location ( $\chi^2=36.959$ ,  $P=0.000$ ), tumor size ( $\chi^2=319.981$ ,  $P=0.000$ ), lymphatic metastasis ( $\chi^2=20.849$ ,  $P=0.000$ ) and scope of operation ( $\chi^2=170.370$ ,  $P=0.000$ ). Multivariate analysis showed that the prognosis was associated with FIGO stage ( $P=0.004$ , 95%  $CI=1.204-2.603$ ), pathological types ( $P=0.010$ , 95%  $CI=1.109-2.144$ ), and the age of diagnosis ( $P=0.009$ , 95%  $CI=1.340-7.584$ ). **Conclusion** FIGO stage, pathological type and age are independent risk factors for prognosis of MOGCTs. Therefore, it is feasible for young women to perform the operation of preserving reproductive function.

**【Key words】** Ovary; Malignant germ cell tumor of ovary (MOGCTs); Prognosis

**Fund program:** National Natural Science Foundation of China (81272213)

# 染色体多态性对男性生精能力及生育结局的研究

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**【摘要】**目的 探讨染色体多态性对男性生精能力和生育结局的影响。方法 选择 3 203 例男性不育者(不育组)和 4 893 例捐精初筛合格者(捐精组)进行回顾性队列研究, 其中根据精液精子数量将不孕组患者分为精子正常组、少精子症组、无精子症组。检查并比较各组的精液常规、染色体核型、Y 染色体微缺失。对有多态性的捐精者和患者进行随访, 了解他们的生育结局。结果 不育组和捐精组多态性发生率分别为 4.62% 和 3.78%, 差异无统计学意义 ( $P>0.05$ )。不育组的 Y 异染色质长度减少(Yqh-)发生率(0.59%) 高于捐精组(0.27%), 差异有统计学意义 ( $P=0.022$ ), 且随着精子数量减少 Yqh- 发生率明显增加(精子数量正常组为 0.15%, 少精子症组为 0.22%, 无精子症组为 0.99%), 差异有统计学意义(精子正常组与无精子症组  $P=0.033$ ; 少精子症组与无精子症组  $P=0.027$ )。携带有 Yqh- 的患者 Y 染色体微缺失检出率为 56.25%(9/16), 显著高于其它类型人群 ( $P<0.001$ )。不育组中弱精子者和畸形精子者的多态性发生率分别为 3.92%、3.96%, 同捐精组(3.78%) 相比, 差异无统计学意义 ( $P>0.05$ )。随访捐精组和不育组有多态性人群的配偶, 结果其自然流产率分别为 6.25%(3/48) 和 6.67%(2/30), 差异无统计学意义 ( $P>0.05$ ), 且无 1 例发生子代出生缺陷。结论 除 Yqh- 部分伴随无精子因子(AZF) 缺失可导致精子发生障碍, 使男性生育力下降, 其它类型多态对男性生育无明显影响。

**【关键词】** 染色体多态性; 男性生育力; 辅助生殖技术; 出生缺陷; 生育结局

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· 临床研究 ·

**The research of chromosomal polymorphisms on male spermatogenesis and reproductive outcomes**

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**【Abstract】 Objective** To investigate the effect of chromosome polymorphism on the male spermatogenesis and reproductive outcomes. **Methods** Totally 3 203 cases of male (infertile group), who were divided into normozoospermia group, oligozoospermia group, azoospermia group according to the sperm count of semen analysis, and 4 893 cases of donor (donor group) were involved the study. Semen analysis, karyotype analysis, and Y chromosome microdeletion test were compared between the groups. The reproductive outcomes of sperm donors and infertile patients were investigated. **Results** The incidence of polymorphism in infertile group and donor group was 4.62% and 3.78% respectively, and the difference was not statistically significant. The incidence of Yqh<sup>-</sup> in infertile patients increased significantly with the decrease of sperm count (0.15% in normozoospermia group, 0.22% in oligozoospermia group, 0.99% in azoospermia group), and the difference was statistically significant ( $P=0.033$ , compared between normozoospermia group and azoospermia group;  $P=0.027$ , compared between oligozoospermia group and azoospermia group), the rate of Y chromosome microdeletion in group C with Yqh<sup>-</sup> was 56.25% (9/16), significantly higher than that of other groups ( $P<0.05$ ). The incidence of polymorphism in the asthenozoospermia group and teratozoospermia group was 3.92% and 3.96%, respectively, and the difference was not statistically significant ( $P>0.05$ ). Follow-up investigation found that the spontaneous abortion rate was 6.25% (3/48) and 6.67% (2/30) in people with polymorphic of donor group and infertile group respectively, no statistical significance ( $P>0.05$ ), and no child birth defects were observed. **Conclusion** Part with azoospermia factor (AZF) microdeletion in Yqh<sup>-</sup> may lead to spermatogenesis, and other types of polymorphism have no obvious effect on male fertility.

**【Key words】** Chromosomal polymorphism; Male fertility; Assisted reproductive technology (ART); Birth defect; Reproductive outcome

**Fund programs:** Frontier Technology Project of Shanghai (SHDC12015122); National High-tech Research and Development Program (863) of China (2015AA020404); Key Program of Science and Technology(2013FY110500)



# 探索蛋白酶体抑制剂 MG-132 对小鼠早期胚胎发育的影响

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**【摘要】** 目的 探讨泛素-蛋白酶体抑制剂 MG-132 对小鼠早期胚胎发育细胞周期的影响。方法 通过体外受精的方法, 分别收集受精后 12 h、24 h、36 h、48 h、60 h、72 h、84 h、96 h 的胚胎 (12 hpi、24 hpi、36 hpi、48 hpi、60 hpi、72 hpi、84 hpi、96 hpi), 通过 Western Blotting 验证在检测 12 hpi 时总蛋白泛素化水平最高, 以此为基准设置不同浓度以及时间梯度, 确定 MG-132 引起 2- 细胞发育阻滞和延迟的最适浓度和处理时间, 最终确定 MG-132 浓度 1  $\mu\text{mol/L}$ , 在 14~18 hpi 作用 4 h 可以引起 2- 细胞发育阻滞和延迟。通过 Edu 检测、免疫荧光实验, 观察分析 MG-132 是否会引起早期胚胎发育细胞周期改变。**结果** 用 1  $\mu\text{mol/L}$  MG-132, 在 14~18 hpi 处理 4 h 可以引起早期胚胎发育细胞周期延迟。**结论** MG-132 作为泛素-蛋白酶体抑制剂, 可以抑制胚胎发育中蛋白质的降解, 引起早期胚胎发育细胞周期进程受抑, 致使胚胎发育阻滞在 G2/M 期。

**【关键词】** 泛素-蛋白酶体; MG-132; 胚胎发育周期

**基金项目:** 国家自然科学基金项目 (31471107)

· 实验研究 ·

**Effects of ubiquitin proteasome inhibitor MG-132 on early embryonic development in mice** Lei Yangyang,

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**【Abstract】 Objective** To investigate the effects of ubiquitin proteasome inhibitor MG-132 on early embryonic development. **Methods** We collected the embryos of 12 hpi, 24 hpi, 36 hpi, 48 hpi, 60 hpi, 72 hpi, 84 hpi and 96 hpi through *in vitro* fertilization, the result of Western Blotting showed that polyubiquitinated proteins were mainly accumulated in the embryos of 12 hpi. Based on the above, different concentrations and time gradients were set to determine the optimal concentration and processing time of MG-132 induced cell retardation and delayed in two cell development. Ultimately, we found that treatment of embryos with 1  $\mu\text{mol/L}$  MG-132 from 14 hpi to 18 hpi could lead to retardation and delay in two cell development mostly. Edu assay and immunofluorescence assay were used to observe whether MG-132 could influence the cell cycle of embryos. **Results** Treatment of embryos with 1  $\mu\text{mol/L}$  MG-132 from 14 hpi to 18 hpi could lead to retardation and delay in two-cell stage development. **Conclusion** The ubiquitin proteasome inhibitor MG-132 could inhibit the degradation of proteins during embryonic development and it could lead to cell cycle of embryonic development arrested in G2/M phase.

**【Key words】** Ubiquitin proteasome; MG-132; Cell cycle of embryonic development

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# 辅助生殖技术对小鼠胎盘氨基酸转运通道载体蛋白表达的影响

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**【摘要】**目的 探讨辅助生殖技术 (ART) 对胎盘氨基酸转运通道载体蛋白表达水平的影响。方法 分别选取体外受精 (IVF)18.5 d 昆明仔鼠胎盘组织 (IVF 组) 和自然妊娠 18.5 d 昆明仔鼠的胎盘组织 (对照组), 对两组出生体质量、胎盘相对重量及胎盘效率 (出生体质量与胎盘相对重量比值) 进行比较和统计分析, 采用实时定量聚合酶链反应 (RT-qPCR) 及蛋白质印迹 (Western blotting) 方法检测两组胎盘组织中氨基酸转运体 A 系统 (Snat1、Snat2、Snat4) 及 L 系统 (Lat1、Lat2) 的 mRNA 和蛋白表达水平。结果 ① IVF 组新生仔鼠体质量 [(1 609.14±128.23) mg] 与对照组 [(1 640.20±148.13) mg] 间差异无统计学意义 ( $P>0.05$ ); IVF 组小鼠胎盘相对重量 [(192.86±28.87) mg] 显著高于对照组 [(126.20±21.50) mg] ( $P=0.000$ ); IVF 组小鼠胎盘效率 [(8.52±1.54)%] 显著低于对照组胎盘效率 [(13.38±2.73)%] ( $P=0.000$ )。②与对照组相比, IVF 组 A 系统氨基酸转运体 Snat1、Snat2、Snat4 mRNA 和其蛋白表达水平显著下调 (mRNA:  $P=0.000$ 、 $P=0.008$ 、 $P=0.005$ ; 蛋白:  $P=0.008$ 、 $P=0.006$ 、 $P=0.000$ )。③与对照组相比, IVF 组 L 系统氨基酸转运体 Lat1 mRNA 和蛋白表达水平差异无统计学意义 ( $P>0.05$ ); Lat2 mRNA 和蛋白表达水平显著下调 ( $P=0.011$ 、 $P=0.000$ )。结论 ART 导致小鼠足月胎盘氨基酸转运体 Snat1、Snat2、Snat4 及 Lat2 的表达水平显著下调, 提示 ART 会影响妊娠末期胎盘氨基酸的转运能力。

**【关键词】** 辅助生殖技术 (ART); 胎盘; 氨基酸转运体

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· 实验研究 ·

**Research on the protein expression of amino acid transport channel of mice placenta from assisted reproductive technology** Jia Qingge, Chen Shuqiang, Guo Xiangyu, Dong Jie, Wang Xin, Wang Xiaohong

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**【Abstract】 Objective** To study the effect of assisted reproductive technology (ART) on the protein expression of amino acid transport channel in placenta. **Methods** We chose the placenta tissue of mice by *in vitro* fertilization (IVF) in 18.5 d (IVF group) and by natural pregnancy in 18.5 d (control group) to compare the birth weight, placental relative weight and ratio of the fetal/placental weight. We then detected the mRNA and protein expressions of placental amino acid transporter (Snat1, Snat2, Snat4, Lat1 and Lat2) by real-time quantitative polymerase chain reaction (RT-qPCR) and Western blotting. **Results** 1) There were no statistical differences in new birth weight between IVF group [(1 609.14±128.23) mg] and control group [(1 640.20±148.13) mg] ( $P>0.05$ ). Compared with control group [(126.20±21.50) mg, (13.38±2.73)%], the placenta relative weight of mice was significantly higher in IVF group [(192.86±28.87) mg,  $P=0.000$ ] and ratio of the fetal/placental weight was significantly lower in IVF group [(8.52±1.54)%] ( $P=0.000$ ). 2) Compared with control group, the mRNA and protein expression of A system amino acid transporter Snat1, Snat2 and Snat4 in placenta were significantly down-regulated in IVF group (mRNA:  $P=0.000$ ,  $P=0.008$ ,  $P=0.005$ ; protein:  $P=0.008$ ,  $P=0.006$ ,  $P=0.000$ ). 3) There were no statistical differences of the mRNA and protein expression of L system amino acid transporter Lat1 between these two groups ( $P>0.05$ ), but the mRNA and protein expression of amino acid transporter Lat2 in placenta was significantly down-regulated in IVF group ( $P=0.011$ ,  $P=0.000$ ). **Conclusion** ART leads to the expressions of amino acid transporter Snat1, Snat2, Snat4 and Lat2 significantly down-regulated in placenta, which suggests that ART may affect the function of placenta amino acid transporter during the late pregnancy.

**【Key words】** Assisted reproductive technology (ART); Placenta; Amino acid transporter

**Fund program:** Key Research and Development Plan of Shanxi Province Key Industry Innovation Chain (2017SF-084); Key Research and Development Plan General Project of Shanxi Province (2017ZDCXL-SF-02-03)

## 拮抗剂方案在卵巢高反应人群中的应用

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**【摘要】目的** 探讨促性腺激素释放激素拮抗剂 (GnRH-A) 方案在卵巢高反应患者中的应用价值。**方法** 回顾性分析 2014 年 6 月—2016 年 9 月期间在本院生殖中心行体外受精 / 卵胞质内单精子显微注射 (IVF/ICSI) 的卵巢高反应患者共 1 916 个周期, 分成两大组: A 组为采取 GnRH-A 方案的共 480 个周期; B 组为采取黄体中期促性腺激素释放激素激动剂 (GnRH-a) 长方案的共 1 436 个周期。再按获卵数进行分组, 获卵数 <15 个时为 A1、B1 组, 获卵数  $\geq 15$  个时为 A2、B2 组。分别比较患者的一般情况和助孕结局。**结果** ① A 组平均 Gn 启动剂量、hCG 注射日平均雌二醇 ( $E_2$ ) 值、获卵数、种植率、临床妊娠率、早期流产率及活产率与 B 组相比差异无统计学意义 ( $P>0.05$ )。A 组 Gn 用量 [(1 561.89 $\pm$ 695.38) IU] 及使用时间 [(10.8 $\pm$ 2.6) d] 均少于 B 组 [(1 949.33 $\pm$ 795.72) IU, (12.4 $\pm$ 2.4) d], A 组中重度卵巢过度刺激综合征 (OHSS) 发生率 (10.0%) 低于 B 组 (14.42%), 差异均有统计学意义 ( $P$  分别为 0.00、0.00、0.01)。② A1 组的平均 Gn 启动剂量 [(134.18 $\pm$ 44.08) IU]、Gn 用量 [(1 499.99 $\pm$ 633.93) IU] 及使用时间 [(10.6 $\pm$ 2.9) d]、获卵数 (9.8 $\pm$ 3.2) 均少于 B1 组 [(148.45 $\pm$ 82.98) IU, (2 091.19 $\pm$ 991.81) IU], (12.6 $\pm$ 2.8) d, 10.4 $\pm$ 2.9], 中重度 OHSS 发生率 (2.81%) 低于 B1 组 (7.08%), 差异均有统计学意义 ( $P$  分别为 0.03、0.00、0.00、0.02、0.04); A1 组胚胎种植率、临床妊娠率及活产率与 B1 组相比差异无统计学意义 ( $P>0.05$ )。A2 组 Gn 用量 [(1 598.62 $\pm$ 727.94) IU] 及使用时间 [(10.9 $\pm$ 2.5) d] 均少于 B2 组 [(1 886.82 $\pm$ 683.2) IU, (12.4 $\pm$ 2.1) d], 差异均有统计学意义 ( $P$  均为 0.00); 中重度 OHSS 发生率、临床妊娠率及活产率低于 B2 组, 差异无统计学意义 ( $P>0.05$ )。**结论** GnRH-A 方案能减少卵巢高反应患者的 Gn 用量及使用时间, 控制卵巢高反应人群的获卵数, 并获得较好的临床妊娠, 同时降低 OHSS 发生率, 可作为有发生中重度 OHSS 风险患者的首选促排卵方案。

**【关键词】** 拮抗剂方案 (GnRH-A); 长方案; 卵巢高反应; 临床结局; 卵巢过度刺激综合征 (OHSS)

**基金项目:** 人类辅助生殖技术质量控制体系建立的相关研究 (201402004)

· 临床报道 ·

**Roles of gonadotropin-releasing hormone antagonist in patients with high ovarian response** Huang Qianwen,

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**【Abstract】 Objective** To explore the clinical outcomes of *in vitro* fertilization/intracytoplasmic sperm injection and embryo transfer (IVF/ICSI-ET) in high responders using long gonadotropin-releasing hormone agonist (GnRH-a) protocol or GnRH antagonist (GnRH-A) protocol. **Methods** The retrospective analysis was performed based on 1 916 IVF-ET/ICSI cycles, including 480 cycles of GnRH-A protocol (group A) and 1 436 cycles of GnRH-a long protocol (group B), from June 2014 to September 2016. Then all cycles were divided into two groups by oocyte numbers, respectively: group A1 and group B1 (No. of oocyte <15) and groups A2 and B2 (No. of oocyte  $\geq$  15). **Results** No statistical differences were noticed in group A and group B in terms of starting dose, estradiol ( $E_2$ ) level on the day of human chorionic gonadotropin (hCG) injection, No. of retrieved oocytes, implantation rate, clinical pregnancy rate, ectopic pregnancy rate, live birth rate. Compared with group B [(1 949.33  $\pm$  795.72) IU, (12.4  $\pm$  2.4) d, 14.42%], the total gonadotropin (Gn) dosage [(1 561.89  $\pm$  695.38) IU] and duration [(10.8  $\pm$  2.6) d], ovarian hyperstimulation syndrome (OHSS) incidence (10.0%) were significantly lower in group A ( $P=0.00$ ,  $P=0.00$ ,  $P=0.01$ ). The total Gn used dosage [(1 499.99  $\pm$  633.93) IU] and duration [(10.6  $\pm$  2.9) d], OHSS incidence (2.81%), No. of retrieved oocytes (9.8  $\pm$  3.2) were significantly lower in group A1 than group B1 [(2 091.19  $\pm$  991.81) IU, (12.6  $\pm$  2.8) d, 7.08%, 10.4  $\pm$  2.9] ( $P=0.00$ ,  $P=0.00$ ,  $P=0.02$ ,  $P=0.04$ ). The implantation rate, clinical pregnancy rate and live birth rate were significantly higher in group A1 than group B1, but no statistical difference was noticed ( $P>0.05$ ). The total Gn used dosage [(1 598.62  $\pm$  727.94) IU] and duration [(10.9  $\pm$  2.5) d] were significantly lower in group A2 than group B2 [(1 886.82  $\pm$  683.2) IU, (12.4  $\pm$  2.1) d] ( $P=0.00$ ,  $P=0.00$ ). OHSS incidence, implantation rate, clinical pregnancy rate and live birth rate between group A1 and group B1 showed no statistical differences ( $P>0.05$ ). **Conclusion** GnRH-A protocol can reduce Gn used dosage and control the OHSS rate of high responders, which can be used in patients with OHSS risk as the first choice.

**【Key words】** Gonadotropin-releasing hormone antagonist (GnRH-a) protocol; GnRH agonist long protocol; High responder; Clinical outcomes; Ovarian hyperstimulation syndrome (OHSS)

**Fund program:** Research on the Establishment of Human Assisted Reproductive Technology Quality Control System (201402004)

## 定坤丹治疗卵巢储备功能下降致月经后期肾虚证的临床观察

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**【摘要】** 目的 观察定坤丹对卵巢储备功能下降 (DOR) 导致月经后期肾虚证的临床疗效。方法 62 例患者, 按随机数字表法随机分为治疗组和对照组, 每组 31 例, 治疗组用中成药定坤丹, 对照组用西药克龄蒙, 均治疗 3 个月, 比较患者治疗前后的中医临床证候积分、卵泡刺激素 (FSH)、FSH/ 黄体生成激素 (LH)、抗苗勒管激素 (AMH)、平均卵巢体积 (MOV)、窦卵泡计数 (AFC) 等改善情况。结果 治疗组总有效率为 93.55%, 对照组为 83.87%, 治疗后组间中医临床证候的疗效分布差异有统计学意义 ( $P=0.0068$ )。激素水平和 MOV 改善方面, 治疗组与对照组的疗效基本相当, 但定坤丹在改善 AMH 及 AFC 方面优于克龄蒙。结论 定坤丹对肾虚型月经后期卵 DOR 患者治疗效果好, 能有效改善患者性激素水平, 增大平均卵巢体积, 增加窦卵泡计数, 促进月经来潮, 进而恢复和改善卵巢储备功能。

**【关键词】** 卵巢储备功能下降 (DOR); 肾虚证; 定坤丹; 月经后期

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· 临床报道 ·

**Clinical observation of Ding Kudan on kidney-deficiency syndrome of delayed menorrhoea due to decreasing ovarian reservation** Tan Zhenyu, You Hui, You Zhaoling

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**【Abstract】 Objective** To evaluate curative effect of Ding Kudan (DKD) on kidney-deficiency syndrome of delayed menorrhoea due to decreasing ovarian reservation (DOR). **Methods** Sixty-two patients were divided into treatment group and control group randomly, 31 patients for each group, the treatment group applied DKD and the latter applied climen for three months. The clinical syndrome scores, follicle-stimulating hormone (FSH), FSH/luteinizing hormone (LH), anti-Müllerian hormone (AMH), mean ovary volume (MOV) and antral follicle count (AFC) scores of the patients before and after treatment were compared. **Result** The total effective rates of treatment group and control group were 93.55% and 83.87%, respectively. After treatment, there were significant differences between the two groups in the distribution of Traditional Chinese Medicine syndromes ( $P=0.0068$ ). Treatment group and control group had the same curative effect for improvement of hormone level and MOV, but DKD in the improvement of AMH and AFC was better than Climen. **Conclusion** DKD for kidney patients with late menstrual ovarian reserve function has a good treatment effect. It can effectively improve patient sex hormone levels, increase the average ovarian volume and the sinus follicle count, promote the menstrual flow, and improve the ovarian reserve function.

**【Key words】** Decreasing ovarian reservation (DOR); Nephraesthesia syndrome; Ding Kudan; Delayed menorrhoea

**Fund program:** National Natural Science Foundation of China (81403427); Hunan Provincial Administration of Traditional Chinese Medicine (2014117)



## 内窥可视宫腔组织吸引系统用于早孕人工流产的临床观察

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**【摘要】** 目的 观察内窥可视宫腔组织吸引系统临床应用效果。方法 本研究共纳入 60 例非意愿妊娠而要求终止者, 随机分配到试验组 (内窥可视宫腔组织吸引系统人工流产术) 和对照组 (常规负压吸引术), 每组各 30 例, 观察 2 种手术方式的应用效果。结果 两组均未发生不全流产、子宫穿孔、人工流产综合征、大出血及感染等并发症。试验组手术时间  $[(6.9 \pm 1.9) \text{ min}]$  较对照组显著增加  $[(4.6 \pm 1.0) \text{ min}]$ ,  $P=0.000$ ; 术中疼痛、手术出血量及术后出血时间等组间差异均无统计学意义 ( $P>0.05$ )。结论 内窥可视宫腔组织吸引系统安全性较好, 可试用于帮助减少人工流产手术对于手术者经验的过度依赖, 以降低人工流产并发症的发生。但本试验样本量较小, 可扩大样本进一步研究。

**【关键词】** 早孕; 人工流产; 并发症; 内窥可视宫腔组织吸引系统

· 临床报道 ·

**Termination of early pregnancy by visualized vacuum aspiration system** Qian Jinfeng, Yao Xiaoying,

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**【Abstract】 Objective** To observe the effect of visualized vacuum aspiration system in termination of early pregnancy. **Methods** Sixty subjects were randomized to the experimental group and control group to evaluate the clinical effect. **Results** There were no complications for both groups such as incomplete abortion, perforation of the uterus, abortion syndrome, haemorrhage and infection. The operation time was significant longer in the experimental group [(6.9±1.9) min] than that in the control [(4.6±1.0) min,  $P=0.000$ ]. There were no differences in pain, bleeding amount during the operation and bleeding time after operation between the two groups. **Conclusion** The visualized vacuum aspiration system may reduce the reliance on the experience of gynecologists and reduce the incidence of complications of induced abortion. Larger sample size and further exploration are needed to prove the effectiveness and safety of the visualized vacuum aspiration system.

**【Key words】** Early pregnancy; Induced abortion; Complication; Visualized vacuum aspiration system

## 剩余胚胎处置方法的随访调查和伦理法律思考

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**【摘要】** 目的 调查接受体外受精-胚胎移植 (IVF-ET) 技术助孕夫妇在结束治疗后对剩余冷冻胚胎的处置意愿, 寻求剩余冷冻胚胎的适宜处置办法。方法 对 IVF-ET 技术治疗后 1~6 年未返院处置剩余冷冻胚胎的 672 对夫妇, 进行电话随访调查。结果 129 对 (19.2%) 夫妇未能配合电话随访, 543 对 (80.8%) 夫妇接受电话随访调查。接受随访的夫妇中, 38.1%(207/543) 未明确是否来院办理相关手续, 3.0%(16/543) 拒绝来院办理相关手续; 58.9%(320/543) 承诺来院办理相关手续, 截止发稿仅 11.6%(63/543) 夫妇返院。胚胎冻存时间 <3 年和 3~6 年被弃存的概率分别为 43.8% 和 61.1%( $P=0.000$ )。结论 对于有剩余冷冻胚胎的患者再次随访确认是有必要的, 呼吁各个生殖中心讨论生殖伦理相关问题, 并形成专家共识来规范剩余冷冻胚胎的处置。

**【关键词】** 体外受精-胚胎移植 (IVF-ET); 剩余胚胎; 胚胎处置; 伦理法律

**Surplus embryo disposition follow-up investigation and ethical legal thinking** Yao Chenxi, Xia Hong, Zhang Jing, Bai Xiaohong

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**【Abstract】 Objective** To investigate the willingness of couples to dispose of remaining surplus embryos after treatment with *In vitro* fertilization-embryo transfer (IVF-ET). **Methods** Within 1–6 years, 672 couples who did not return to the hospital for the disposition of the surplus embryos after the treatment of IVF-ET were followed up by telephone. **Results** After 672 telephone follow-up visits, 543 couples (80.8%) participated in the telephone follow-up survey, with 129 couples (19.2%) not participating in the survey. Of the couples who were followed up, 38.1% (207/543) did not specify whether come to the hospital for relevant procedures and 3.0% (16/543) refused to come to the hospital for relevant procedures; 58.9% (320/543) promised to come to the hospital for relevant procedures, and at present only 11.6% (63/543) of them returned to the hospital. The probability of embryo freezing in the period <3 years and 3–6 years was 43.8% and 61.1% ( $P=0.000$ ). **Conclusion** It is necessary for patients with residual surplus embryos to be followed up again, calling for the reproductive center to discuss related reproductive ethics and form the expert consensus to regulate the disposal of surplus frozen embryos.

**【Key words】** *In vitro* fertilization-embryo transfer (IVF-ET); Surplus embryos; Embryo disposition; Ethics laws

## 早发性卵巢功能不全的遗传学最新研究进展

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**【摘要】** 早发性卵巢功能不全 (premature ovarian insufficiency, POI) 是指女性 40 岁以下发生绝经至少 4 个月, 且卵泡刺激素 (FSH) 数值在 >4 周的两次检测中均高于 25 IU/L。该病在 40 岁以下女性中发病率约为 1%, 是导致女性不孕的重要因素之一。近年来随着我国女性婚育年龄的提高, POI 引起的不孕问题更加突出。遗传学致病因素是 POI 发病的原因之一, 近年来高通量测序技术及精准医学的发展使研究者更加准确并快速的定位并确定 POI 致病基因及突变。本文将综述近期 POI 遗传学领域新的重要研究进展, 并对相关进展进行评述。这些研究进展对育龄女性的遗传咨询、生育风险评估和遗传诊断等方面将发挥重大作用。

**【关键词】** 早发性卵巢功能不全 (POI); 卵巢早衰 (POF); 遗传; 基因突变; 高通量测序

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**Recent advances in the genetics of premature ovarian insufficiency** Li Lin, Yan Lun, Yan Huihui, Ma Yanmin, Dai Yinmei, Yue Wentao, Yin Chenghong

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**【Abstract】** Premature ovarian insufficiency (POI) is characterized as premature menopause before the age of 40 years, with elevated follicle-stimulating hormone (FSH) levels ( $>25$  IU/L) on two occasions more than four weeks apart. POI is one of the main factors causing female infertility, with the prevalence of 1% in women under 40 year-old. The infertility matter caused by POI become more predominant due to the elevated childbearing age in recent China. Genetic factor is an important cause of POI, recent years clinical geneticists and researchers efficiently find more and more pathogenic genes and mutations using high-throughput sequencing such as whole-exome and whole-genome sequencing technologies. This review will summarize and comment the recent new advances in the genetic field of POI. These genetic advances will paly critical roles in genetic counseling, fertility evaluation and genetic diagnosis.

**【Key words】** Premature ovarian insufficiency (POI); Premature ovarian failure (POF); Genetics; Genetic mutation; High through-put sequencing

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## 反复植入失败与胚胎及内膜同步化关系的研究进展

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**【摘要】** 胚胎反复植入失败 (repeated implantation failure, RIF) 作为辅助生殖技术实践中一个给患者带来经济和情绪负担的问题, 始终吸引着生殖科医生及研究人员的密切关注。近年来有研究提出, RIF 与发育胚胎和容受性内膜的同步化失败相关, 通过现代分子基因诊断技术确定 RIF 患者的个性化植入窗 (personalized window of implantation, pWOI) 对改善其 IVF 结局有重要的意义。本文介绍了 RIF 的概念、原因, 并从理论机制、评估方法、临床效果等方面对胚胎与内膜同步化的相关研究进展作一综述。

**【关键词】** 反复植入失败 (RIF); 内膜容受性; 同步化; 植入窗; 个体化胚胎移植

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**Advance of the relationship of repeated implantation failure with the synchronization between embryo and endometrium** Li Na, Zhang Yunshan

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**【Abstract】** Repeated implantation failure (RIF) has always been a grave concern of fertility specialists and researchers as a problem that brings financial and emotional burden to the patients in assisted reproductive technology. In recent years, it has been suggested that RIF is related to the desynchronization between the developing embryo and the receptive endometrium. It is of great importance to identify the personalized window of implantation (pWOI) in patients with RIF by modern molecular genetic diagnosis techniques for improving the outcome of IVF. In this review we introduce the concept of RIF and the causes of RIF, while the advance of synchronization between the embryo and endometrium in terms of theoretical mechanisms, assessment methods, clinical effects are discussed.

**【Key words】** Repeated implantation failure (RIF); Endometrial receptivity; Synchronization; Window of implantation; Personalized embryo transfer



## 甾体激素预处理在辅助生殖技术中的应用

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**【摘要】** 卵巢储备功能下降 (DOR) 及卵巢低反应 (POR) 是辅助生殖中常遇到的棘手问题, 常导致不良的助孕结局。人们尝试探索不同的方法改善卵巢储备功能及卵巢的反应性, 甾体激素最为常用。本文就常用的雄激素、口服避孕药及雌激素的预处理在辅助生殖技术中的应用做一综述。

**【关键词】** 辅助生殖; 预处理; 雄激素; 口服避孕药; 雌激素

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**Steroid hormone pretreatments in assisted reproductive technology**     *Zhang Qiaoli, Jia Chanwei, Li Ying, Liang Yu, Ma Yanmin, Zhang Jun, Wang Shuyu*

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**【Abstract】** The diminished ovarian reserve (DOR) and poor ovarian response (POR) are the thorny issues in the assisted reproductive technology (ART), which often lead to adverse assisted reproduction outcome. Many different ways are explored to improve ovarian function and promote the controlled ovarian stimulation. The pretreatment of steroid hormones is the most commonly used. The article reviewed the pretreatment including androgens, oral contraceptive and estradiol in ART.

**【Key words】** Assisted reproduction; Pretreatment; Androgen; Oral contraceptive; Estradiol

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## 屏障法和药物干预男性避孕的研究进展

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**【摘要】** 男性避孕可分为屏障法、药物干预法和其他三类。屏障法包括避孕套、输精管结扎术、可逆性抑精剂(RISUG)、Vasalgel等, 药物干预分为激素类和非激素类。激素类男性避孕药基于下丘脑-垂体-性腺轴的负反馈调节影响精子发生达到避孕目的。大多数非激素类避孕药因其具有特异性高、毒副作用低和可逆性恢复等优点而成为开发热点。其他有应用射线、微波、纳米物质、高温封闭等研究开发避孕的方法。本文主要对屏障法和药物干预法进行系统综述。

**【关键词】** 避孕方法; 屏障法; 激素类避孕药; 非激素避孕药; 靶点

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**Research advances of barrier methods and pharmaceutical intervention methods in male contraception**

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**【Abstract】** Male contraceptive methods can be divided into barrier methods, pharmaceutical intervention methods and the other. Barrier methods include condoms, vasoligation, reversible inhibition sperm under guidance (RISUG) and Vasalgel, etc. Pharmaceutical intervention methods can be further classified as hormonal and non-hormonal male contraceptive. Hormone-based male contraceptives based on negative feedback regulation of the hypothalamic-pituitary-gonadal axis affect spermatogenesis for contraceptive purposes. Development of non-hormonal male contraceptive is a trend because of the advantages of high specificity, hypotoxicity and reversibility. In addition, there are some contraceptive researches by the use of radiation, microwaves, nanomaterials, and high-temperature sealing. Herein we focus on a systematic review of barrier methods and pharmaceutical intervention methods.

**【Key words】** Contraceptive method; Barriers methods; Hormonal contraceptive; Nonhormonal contraceptive; Target

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