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· 临床研究 ·

## 不同发育天数囊胚冻融移植后妊娠结局分析

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**【摘要】目的** 比较不同发育天数冻融囊胚移植后的妊娠结局。**方法** 回顾性分析 1 176 例行冻融囊胚移植患者的临床资料, 其中植入前遗传学诊断(preimplantation genetic diagnosis, PGD)周期 135 例, 比较第 5 日单囊胚移植(single embryo transfer, SET)组、双囊胚移植(double embryo transfer, DET)组与第 6 日 SET 组和 DET 组的妊娠结局。**结果** 同是优质囊胚级别的条件下, 第 5 日 DET 组的生化妊娠率(56.91%)、临床妊娠率(53.25%)以及多胎妊娠率(1.20%)显著高于其他组( $P<0.05$ ); 第 5 日 DET 组与 SET 组的胚胎着床率无统计学差异( $P>0.05$ ), 但均显著高于第 6 日 DET 组和 SET 组( $P<0.05$ ); 同级别以及 PGD 周期中第 5 日和第 6 日 SET 组相比较, 第 5 日组的生化妊娠率、胚胎着床率均显著高于第 6 日组( $P<0.05$ )。**结论** 在同是优质囊胚的条件下, 第 5 日 SET、DET 及经 PGD 诊断的 SET 妊娠结局均优于第 6 日。

**【关键词】** 冻融囊胚移植; 第 5 日囊胚; 第 6 日囊胚; 妊娠结局; 植入前遗传学诊断(PGD)

**基金项目:** 安徽省自然科学基金(1608085QH201)

· 临床研究 ·

**Pregnancy outcome of frozen-thawed blastocyst transfers on different developmental days** Wu Longmei,

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**【Abstract】Objective** To compare the pregnancy outcomes of frozen-thawed blastocyst transfer on different developmental days. **Methods** Retrospective analysis was performed in the clinical data of 1 176 patients accepting frozen-thawed blastocyst transfer, including 135 cases in preimplantation genetic diagnosis (PGD) cycle. Those patients were separated into two groups, single embryo transfer (SET) group and double embryo transfer (DET) group. The pregnancy outcomes in the two groups were compared on day 5 (D5) and D6. **Results** Biochemical pregnancy rate (56.91%), clinical pregnancy rate (53.25%) and multiple pregnancy rate (1.20%) in D5 DET were significantly higher than those in SET group ( $P<0.05$ ). There was no statistical difference in embryo implantation rate between D5 DET and D5 SET, while they were significantly higher than those in D6 DET group and SET group ( $P<0.05$ ). With the same level blastocysts and the blastocysts in PGD cycle between D5 and D6 SET in comparison, biochemical pregnancy rate, clinical pregnancy rate and embryo implantation rate in D5 group were significantly higher than those in D6 group ( $P<0.05$ ). **Conclusion** In frozen-thawed blastocyst transfer cycle, on the condition of all top-scoring blastocysts, pregnancy outcomes in D5 blastocyst transfer were better than those in D6 blastocyst transfer.

**【Key words】** Frozen-thawed blastocyst transfer; Day 5 blastocyst; Day 6 blastocyst; Pregnancy outcome; Preimplantation genetic diagnosis (PGD)

**Fund program:** Anhui Provincial Natural Science Research Project (1608085QH201)

· 临床研究 ·

# 生长分化因子 -9 和骨形成蛋白 -15 对多囊卵巢综合征患者卵丘细胞凋亡的影响

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**【摘要】目的** 探讨控制性超促排卵(COH)周期多囊卵巢综合征(PCOS)患者生长分化因子-9(GDF-9)、骨形成蛋白-15(BMP-15)的表达对卵丘细胞凋亡的影响。**方法** 收集本院行卵胞质内单精子注射(ICSI)治疗的PCOS组( $n=30$ )和对照组( $n=60$ )患者的卵丘细胞。TUNEL法及流式细胞术检测卵丘细胞凋亡;免疫组织化学方法检测卵丘细胞GDF-9、BMP-15蛋白表达,运用Motic Med 6.0数码医学图像分析系统对染色强度定量分析;Real-time PCR技术检测卵丘细胞GDF-9、BMP-15、B细胞淋巴瘤/白血病-2(BCL)-2、BCL-2相关X蛋白(BAX)mRNA表达。**结果** PCOS组穿刺卵泡数、获卵数高于对照组( $P<0.01$ );PCOS组卵丘细胞凋亡率高于对照组( $P<0.05$ );GDF-9、BMP-15蛋白在PCOS组和对照组卵丘细胞胞质中均呈阳性表达;PCOS患者卵丘细胞GDF-9、BMP-15、BCL-2、BAX mRNA的表达低于对照组( $P<0.05$ ),BAX/BCL-2比值高于对照组( $P<0.05$ )。Pearson相关分析结果显示PCOS患者GDF-9、BMP-15与BCL-2 mRNA表达呈正相关,与BAX mRNA的表达呈负相关。**结论** PCOS患者卵丘细胞GDF-9、BMP-15异常表达可能是卵丘细胞凋亡增加的原因之一。

**【关键词】** 生长分化因子-9(GDF-9);骨形成蛋白-15(BMP-15);卵丘细胞;细胞凋亡;多囊卵巢综合征(PCOS);控制性超促排卵(COH)

· 临床研究 ·

**Effects of growth differentiation factor-9 and bone morphogenetic protein-15 on the apoptosis of cumulus cells in patients with polycystic ovary syndrome**

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**【Abstract】 Objective** To investigate the effects of abnormal expression of growth differentiation factor-9 (GDF-9) and bone morphogenetic protein-15 (BMP-15) on the apoptosis of cumulus cells in patients with polycystic ovary syndrome (PCOS) undergoing controlled ovarian hyperstimulation (COH). **Methods** Cumulus cells were collected from PCOS patients ( $n=30$ ) and control group ( $n=60$ ) who underwent intracytoplasmic sperm injection (ICSI) in our hospital. Cumulus cells were collected and purified after oocyte retrieval. The apoptosis of cumulus cells was tested by terminal deoxynucleotidyl transferase-mediated dUTP nick-End labeling (TUNEL) and flow cytometry. Immunocytochemistry was used to detect the expression of GDF-9, BMP-15 protein in cumulus cells and Motic Med 6.0 system was used to analyze average optical density of cumulus cells. The mRNA levels of *GDF-9*, *BMP-15*, B-cell lymphoma-2 (*BCL-2*) and Bcl-2 associated X (*BAX*) in cumulus cells were analyzed by real-time PCR. **Results** The number of punctured follicles, retrieved oocytes in PCOS group were higher than those in control group. The apoptosis rate of cumulus cells in PCOS group was higher than that in control group. GDF-9 and BMP-15 proteins were positively stained in cytoplasm of cumulus cell in both groups. *GDF-9*, *BMP-15*, *BCL-2* and *BAX* mRNA levels in PCOS group were significantly lower, while *BAX/BCL-2* ratio was significantly higher than that in control group. According to Pearson linear correlation, *GDF-9* and *BMP-15* mRNA levels were significantly positively correlated with *BCL-2* mRNA level, and negatively correlated with *BAX* mRNA in PCOS patients. **Conclusion** The abnormal expression levels of GDF-9 and BMP-15 in cumulus cell of PCOS patients may be one of the reasons that lead to higher cells apoptosis.

**【Key words】** Growth differentiation factor-9 (GDF-9); Bone morphogenetic protein-15 (BMP-15); Cumulus cell; Apoptosis; Polycystic ovary syndrome (PCOS); Controlled ovarian hyperstimulation (COH)

· 临床研究 ·

# 绒毛中表皮生长因子受体和血管内皮生长因子的表达对早孕绒毛血管生成的影响及与稽留流产的关系

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**【摘要】目的** 探讨表皮生长因子受体(EGFR)、血管内皮生长因子(VEGF)的表达对早孕绒毛血管生成的影响及与早孕稽留流产的关系。**方法** 应用免疫组织化学方法检测 30 例稽留流产(稽留流产组)及 30 例早孕人工流产(早孕人工流产组)绒毛 EGFR、VEGF 的表达及绒毛的微血管密度(MVD), 并分析相关因子的相关性。**结果** 稽留流产组绒毛的 MVD( $7.03 \pm 1.72$ )比早孕人工流产组( $14.74 \pm 1.66$ )显著降低( $P < 0.01$ )。稽留流产组绒毛的 EGFR 表达水平( $0.42 \pm 0.14$ )表达比早孕人工流产组( $0.49 \pm 0.07$ )低( $P < 0.05$ ), 稽留流产组绒毛的 VEGF 表达水平( $0.47 \pm 0.12$ )表达比早孕人工流产组( $0.60 \pm 0.12$ )低( $P < 0.01$ )。Pearson 相关分析显示在早孕人工流产绒毛及稽留流产绒毛中 EGFR 与 VEGF 的表达呈正相关, EGFR 的表达与 MVD 呈正相关, VEGF 表达与 MVD 呈正相关。**结论** 绒毛组织中 EGFR 和 VEGF 的表达与绒毛血管生成状况密切相关, EGFR 和 VEGF 低表达参与了稽留流产的绒毛血管的形成障碍。

**【关键词】** 表皮生长因子受体(EGFR); 血管内皮生长因子(VEGF); 微血管密度(MVD); 稽留流产

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· 临床研究 ·

**Influence of epidermal growth factor receptor and vascular endothelial growth factor expression on angiogenesis in chorionic villi and its relationship with missed abortion**

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**【Abstract】 Objective** To investigate the potential roles of epidermal growth factor receptor (EGFR) and vascular endothelial growth factor (VEGF) in villous angiogenesis in the first trimester and its relationship with missed abortion. **Methods** We detected the expression of EGFR, VEGF and micro vessel density (MVD) by immunohistochemistry in the villi from women with missed abortion group ( $n=30$ ) and from women with requested induced abortion in the first trimester group (control group) ( $n=30$ ). We also analyzed their correlations between the two groups. **Results** Missed abortion patients were detected significantly lower MVD than control group. Compared with control group, the expressions of EGFR and VEGF were statistically reduced in missed abortion. Correlation analysis showed that the expressions of EGFR and VEGF were positively correlated with MVD in the two groups. **Conclusion** The expressions of EGFR and VEGF were closely related to villous angiogenesis. EGFR and VEGF were closely involved in abnormal angiogenesis etiology of missed abortion.

**【Key words】** Epidermal growth factor receptor (EGFR); Vascular endothelial growth factor (VEGF); Microvessel density (MVD); Missed abortion

**Fund program:** Guangxi Natural Science Foundation (2016GXNSFAA380250); Guangxi “139” Program (2014); New Century Excellent of Guangxi Ten Hundred and Thousand Talent Project (2013)



· 临床研究 ·

# 男性染色体多态性对精子质量及体外受精 / 卵胞质内单精子显微注射结局的影响

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**【摘要】目的** 研究男方染色体多态性对精子质量及体外受精 - 胚胎移植(IVF-ET)结局的影响。**方法** 回顾性比较 IVF/ 卵胞质内单精子显微注射(ICSI)-ET 助孕治疗的男方染色体多态( $n=131$ )和正常对照夫妇( $n=160$ )的妊娠结局, 观察男方的精子质量和受精情况、临床妊娠率、早期流产率。**结果** 男方染色体多态组中严重少/弱精子症(19.85%)比例显著高于染色体正常组(5.00%,  $P<0.001$ ), Yqh+ 在严重少/弱精子症(38.46%)中的比例最高; Yqh- 也高达 15.38%, 1qh+ 在严重少/弱精子症组是最常见的常染色体多态类型(19.23%); 染色体多态组的女方年龄、体质量指数(BMI)、基础性激素水平均无统计学差异( $P>0.05$ ), 男方前向精子率(PR%)、精子正常率以及获卵数、移植胚胎数均无统计学差异( $P>0.05$ )。染色体多态组行 IVF-ET 助孕治疗后, 其着床率(17.42%)、临床妊娠率(28.17%)均显著低于正常对照组(32.26%, 59.38%)( $P<0.05$ ); 并且早期流产率(11.11%)高于对照组(2.04%), 但差异无统计学意义( $P>0.05$ )。染色体多态组行 ICSI-ET 助孕治疗后与正常对照组妊娠结局无统计学差异( $P>0.05$ ), 优质胚胎率(75.24% ± 23.68%)还高于正常对照组(49.97% ± 29.31%)( $P<0.05$ )。行 ICSI-ET 助孕的男方染色体多态患者其着床率(34.78%)以及临床妊娠率(52.00%)显著高于行 IVF-ET 助孕的男方染色体多态患者(17.42%, 28.17%)( $P<0.05$ )。**结论** 男性染色体多态性患者中严重少/弱精子的比例增加, 男性染色体多态不利于 IVF 妊娠结局, 对 ICSI 影响较小。

**【关键词】** 男方染色体多态性; 精子质量; 体外受精 / 卵胞质内单精子显微注射(IVF/ICSI); 妊娠结局; Yqh+; 1qh+

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· 临床研究 ·

**Effects of male chromosomal polymorphism on spermatozoa quality and the outcome of *in vitro* fertilization/intracytoplasmic sperm injection treatment** Zhou Danni, Li Saijiao, Yang Jing, Sun Liping

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**【Abstract】 Objective** To explore the effect of male chromosomal polymorphism on spermatozoa quality and *in vitro* fertilization/intracytoplasmic sperm injection-embryo transfer (IVF/ICSI-ET) outcomes. **Methods** A retrospective analysis was performed in 131 couples with male chromosomal polymorphism as study group, and 160 couples with normal chromosomes as control group. **Results** There was a statistically significant difference about the ratio of severe oligozoospermia/asthenospermia between study group (19.85%) and control group (5.00%,  $P < 0.001$ ). Yqh<sup>+</sup> was the most frequently occurring in patients with severe oligozoospermia/asthenospermia (38.46%). The secondary was Yqh<sup>-</sup> (15.38%). 1qh<sup>+</sup> was the most frequently occurring in men with autosomal polymorphism with severe oligozoospermia/asthenospermia (19.23%). There were no significant differences in the female age, female body mass index (BMI), female basic sex hormone level, PR% and the proportion of normal spermatozoa, number of oocytes retrieved and transplantation between study group and control group. When undergoing IVF-ET treatment, the implantation rate (17.42%), the clinical pregnancy rate (28.17%) in study group were significantly lower than those in control group (32.26%, 59.38%) ( $P < 0.05$ ). There was no significant increase in early abortion rate between the two groups. There was no significant difference in clinical outcomes between the two groups when undergoing ICSI-ET treatment. In addition, the good-quality embryo rate was higher in study group ( $75.24\% \pm 23.68\%$ ) than in control group ( $49.97\% \pm 29.31\%$ ) ( $P < 0.05$ ). In study group, the implantation rate (34.78%) and the clinical pregnancy rate (52.00%) were significantly higher among the patients undergoing ICSI-ET treatment than those undergoing IVF-ET treatment (17.42%, 28.17%) ( $P < 0.05$ ). **Conclusion** It suggests that male chromosome polymorphism can increase the ratio of severe oligozoospermia/asthenospermia. Male chromosome polymorphism has an adverse effect on IVF reproductive outcome and has no obvious effect on ICSI reproductive outcome.

**【Key words】** Male chromosomal polymorphism; Spermatozoa quality; *In vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI); Pregnancy outcome; Yqh<sup>+</sup>; 1qh<sup>+</sup>

**Fund program:** National Natural Science Foundation of China (81571513); The Young Teachers in Colleges and Universities Funded Projects (2042016kf0086); Merck Serono Reproductive Medicine Fund (MerckSerono\_CREATE-2016141)

· 实验研究 ·

## 体外受精子代小鼠性成熟期心血管功能的评估

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**【摘要】目的** 探讨体外受精(IVF)子代心血管系统的安全性。**方法** 利用 C57BL/6J 小鼠建立 IVF 子代小鼠模型(IVF 组,  $n=12$ ), 以 C57BL/6J 自然妊娠子代小鼠为对照组( $n=12$ ), 观察比较小鼠性成熟期的体质量、血压, 并利用彩色超声评估其心脏结构及功能。**结果** 12 周龄 IVF 组子代小鼠的体质量[(26.13 ± 4.58) g]高于对照组[(22.50 ± 2.37) g], 差异有统计学意义( $P<0.05$ ); 仔鼠的血压组间无统计学差异( $P>0.05$ )。彩色超声显示仔鼠心血管功能的主要指标(对照组, IVF 组), 左心室射血分数(65.41% ± 5.26%, 65.77% ± 6.71%)、左室短轴缩短率(35.41% ± 4.05%, 35.81% ± 4.84%)、颈动脉中内膜厚度[(0.05 ± 0.01) mm, (0.05 ± 0.01) mm]等无统计学差异( $P>0.05$ ); 左房内径[(2.13 ± 0.12) mm, (2.25 ± 0.10) mm]、左心室质量指数[(8.24 ± 0.46) g/m<sup>2</sup>, (11.87 ± 2.03) g/m<sup>2</sup>]、主动脉内径[(1.33 ± 0.06) mm, (1.45 ± 0.11) mm]3 项指标 IVF 组显著高于对照组( $P<0.05$ )。**结论** IVF 子代小鼠与自然妊娠小鼠相比, 部分心血管指标存在差异, 提示 IVF 对性成熟期子代小鼠的心血管结构与功能可能存在潜在的影响, 需要更多的远期随访。

**【关键词】** 辅助生殖技术(ART); 子代; 心血管; 安全性; 小鼠

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· 实验研究 ·

**Effects of *in vitro* fertilization on the cardiovascular function of adult offspring mice** Zhang Ting,

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**【Abstract】Objective** To evaluate cardiovascular health in adult mice derived from an *in vitro* fertilization (IVF) procedure. **Methods** We examined the body weight and blood pressure in adult C57BL/6J mice (12 weeks) that were conceived by IVF and natural conception (NC). Cardiovascular structure and function was evaluated by Doppler echocardiography. **Results** The body weight was significantly higher in IVF mice than NC mice [(26.13 ± 4.58) g, (22.50 ± 2.37) g] ( $P < 0.05$ ). The blood pressure was similar in the two groups. The main parameters on cardiovascular structure and function were similar between NC and IVF groups ( $P > 0.05$ ), including left ventricular ejection fraction (65.41% ± 5.26%, 65.77% ± 6.71%), left ventricular fractional shortening (35.41% ± 4.05%, 35.81% ± 4.84%), and carotid intima-media thickness [(0.05 ± 0.01) mm, (0.05 ± 0.01) mm], whereas several other parameters, such as left atrial dimension [(2.13 ± 0.12) mm, (2.25 ± 0.10) mm], left ventricular mass index [(8.24 ± 0.46) g/m<sup>2</sup>, (11.87 ± 2.03) g/m<sup>2</sup>] and aortic dimension [(1.33 ± 0.06) mm, (1.45 ± 0.11) mm], were significantly increased in IVF group compared with NC group ( $P < 0.05$ ). **Conclusion** Mice conceived by IVF manifested a statistically significant increase in several cardiovascular structure parameters. Our findings indicate that IVF procedure may make a potential effect on cardiovascular structure and function among IVF offspring, which calls for further investigation and longer-term follow-ups.

**【Key words】** Assisted reproductive technology (ART); Offspring; Cardiovascular function; Safety; Mouse

**Fund program:** National Natural Science Foundation of China (81401267); National Program on Key Basic Research Project (973 Program) (2012CB944902); Research Fund of National Health and Family Planning Commission of China (201402004)

· 实验研究 ·

## 二补助育汤对胚胎着床障碍小鼠子宫内膜的形态学影响

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**【摘要】目的** 从形态学角度探讨二补助育汤对胚胎着床障碍模型小鼠子宫内膜的影响。**方法** 将 56 只 C57 小鼠随机分为空白组、模型组、补佳乐组、阿司匹林组、二补助育汤低、中、高剂量组, 每组 8 只。用吲哚美辛建立胚胎着床障碍动物模型, 小鼠妊娠第 5 日下午脱颈椎处死, 计算各组小鼠妊娠率及胚胎着床位点数; 光学显微镜下观察各组小鼠子宫内膜形态结构; 透射电子显微镜下观察超微结构、胞饮突表达情况, 并计算胞饮突评分。**结果** ① 模型组平均着床位点数( $1.8 \pm 2.1$ )明显低于空白组( $8.1 \pm 4.2$ )( $P < 0.05$ ); 中药中、高剂量组平均着床位点数(分别为 62.5%, 75.0%)明显高于模型组( $P < 0.05$ ); 与补佳乐组和阿司匹林组间无统计学差异。② 光学显微镜下形态学观察: 正常组内膜间质疏松、腺体和血管丰富、腺体扩张; 模型组内膜变薄或消失、腺体和血管减少; 二补助育汤各剂量组、补佳乐组、阿司匹林组内膜均有改善, 以二补助育汤中剂量组与正常组最接近。③ 电子显微镜下超微结构观察: 空白组子宫内膜上皮细胞及细胞器结构清晰; 模型组细胞破坏严重甚至局灶性坏死, 线粒体膜不完整、嵴结构消失, 胞质中较多空泡样变, 核糖体和内质网明显减少; 二补助育汤各剂量组、补佳乐组、阿司匹林组细胞及细胞器有不同程度破坏, 与模型组相比有明显改善。④ 胞饮突: 空白组胞饮突丰富, 绒毛较少; 模型组绒毛丰富, 但胞饮突很少; 二补助育汤各剂量组胞饮突较模型组丰富, 见少量绒毛; 补佳乐组和阿司匹林组可见少量胞饮突, 较模型组增加, 绒毛表达稀疏。⑤ 胞饮突评分: 模型组胞饮突评分( $1.1 \pm 0.3$ )较空白组低( $2.5 \pm 0.7$ )( $P < 0.05$ ); 中药中剂量组( $2.3 \pm 0.9$ )、阿司匹林组( $2.0 \pm 0.7$ )评分高于模型组( $P < 0.05$ ), 亦高于补佳乐组( $1.3 \pm 0.5$ )( $P < 0.05$ )。**结论** 二补助育汤能够促进子宫内膜发育及胞饮突, 从而提高子宫内膜容受性, 有利于胚胎着床。

**【关键词】** 二补助育汤; 胚胎着床障碍; 子宫内膜容受性; 形态学; 胞饮突

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· 实验研究 ·

**Experimental research of Erbu Zhuyu decoction on the endometrial morphology in mouse model of embryo implantation dysfunction**

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**【Abstract】 Objective** To explore the effects of Erbu Zhuyu decoction on endometrial morphology in mouse model of embryo implantation dysfunction. **Methods** A total of 56 C57 mice were randomly divided into seven groups: blank group, model group, progynova group, aspirin group, and low-dose group, middle-dose group, high-dose group of Erbu Zhuyu decoction before built into embryo implantation dysfunction model by indometacin, 8 mice in each group. Indomethacin was used to build the mouse of embryo implantation dysfunction. The mice were killed at day 5 of pregnancy, and the pregnancy rate and the number of embryo implantation sites were calculated. Endometrial morphology was observed by light microscope, ultrastructure of endometrial cells and pinopodes was observed by transmission electron microscope (TEM), and pinopodes expression was scored. **Results** The number of implantation sites in model group ( $1.8 \pm 2.1$ ) was less than that in blank group ( $8.1 \pm 4.2$ ) ( $P < 0.05$ ), which was more in middle-dose group ( $7.0 \pm 6.2$ ) and high-dose group ( $7.9 \pm 5.2$ ) than that in model group ( $P < 0.05$ ), but were not significantly different from western medicine groups (progynova group, aspirin group). For morphologic study: in blank group, there were loose endometrial stroma, abundant glands and vessels, which were opposite in model group, and were better in other groups than in model group, especially in the middle-dose of Erbu Zhuyu decoction group. For ultrastructure study: endometrial epithelial cell structure and organelle structure were clear in blank group. The cells were severely damaged and even focally necrosed in model group, organelle structure was also damaged, such as integrated mitochondrial membrane and disappeared cristae structure, decreased ribosome. They were better in others groups than in model group. For pinopodes expression: in blank group, pinopodes expression was rich, while pinopodes expression was much less and more villi were expressed in model group. Pinopodes expression was abundant in Erbu Zhuyu decoction groups, more than model group. In western medicine groups, pinopodes expression was not as good as that in Erbu Zhuyu decoction groups, but better than model group. The pinopodes scores in model group ( $1.1 \pm 0.3$ ) was lower than those in blank group ( $2.5 \pm 0.7$ ) ( $P < 0.05$ ), which were higher in middle-dose group ( $2.3 \pm 0.9$ ) and aspirin group ( $2.0 \pm 0.7$ ) than that in model group and progynova group ( $1.3 \pm 0.5$ ) ( $P < 0.05$ ). **Conclusion** Erbu Zhuyu decoction could improve endometrial receptivity by the way of regulating endometrial development and pinopodes expression.

**【Key words】** Erbu Zhuyu Decoction; Model of embryo implantation dysfunction; Endometrial receptivity; Morphology; Pinopode

**Fund program:** National Natural Science Foundation of China (81473721); Graduate Program of Beijing University of Chinese Medicine (2017-JYB-XS-098)

# 阴道分娩产后出血发病率及影响因素的队列研究

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**【摘要】目的** 探讨上海市孕产妇阴道分娩产后出血相关的影响因素。**方法** 将 2015 年 6 月—2016 年 5 月期间在上海市 4 家医院首次建卡产检的孕妇纳入队列, 随访至分娩, 收集其建卡、初次产检和分娩的资料。计算阴道分娩产后出血的发生率, 并用独立样本 *t* 检验或方差分析进行单因素分析, 用多元线性回归分析探讨阴道分娩产后出血量的影响因素。**结果** 共收集到阴道分娩孕产妇资料 3 495 份, 产后出血(>500 mL) 发生率为 1.5%(53/3 495), 产后出血量平均为(255.6 ± 156.4) mL。多元线性回归分析显示, 产次每增加 1 次, 产后出血量下降 13.3 mL; 合并妊娠期高血压疾病和分娩巨大儿分别可使产后出血量升高 42.3 mL 和 22.3 mL。**结论** 上海市孕产妇阴道分娩产后出血发生率较低, 提倡孕期的合理增重有利于控制产后出血量, 对于初产妇和合并妊娠期高血压疾病的孕妇应积极防范产后出血的发生。

**【关键词】** 阴道分娩; 产后出血(PPH); 发生率; 影响因素; 前瞻性队列研究

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· 流行病学研究 ·

**Incidence and risk factors of postpartum hemorrhage among vaginal delivery: a perspective cohort study**

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**【Abstract】 Objective** To investigate the incidence of postpartum hemorrhage (PPH) among women with vaginal delivery in Shanghai, as well as the influencing factors. **Methods** Pregnant women (12–16 weeks of gestation) who had their first prenatal health examinations at 4 hospitals in Shanghai from June 2015 to May 2016 were recruited and followed up until delivery in this study. Data of their background information, clinical and lab examination results and delivery outcomes were collected. The incidence of vaginal delivery PPH was calculated. *T*-test, analysis of variance and multivariate linear regression model were applied to identify the determinants. **Results** A total of 3 495 vaginal delivery women were included in the study. The incidence of PPH (>500 mL) was 1.5% (53/3 495), and the average amount of bleeding was (255.6 ± 156.4) mL. Multivariate linear regression analysis showed that compared with primipara, the blood loss of women delivered second baby was 13.3 mL lower. The amount of PPH in vaginal delivery could be increased by 42.3 mL due to hypertensive disorder complicating pregnancy (HDP) and 22.3 mL due to macrosomia. **Conclusion** The incidence of PPH among vaginal delivery in Shanghai is relatively low. Progestational weight control should be advocated, and maternity hospitals should pay high attention to the primipara or maternal with hypertensive disorder.

**【Key words】** Vaginal delivery; Postpartum hemorrhage (PPH); Incidence; Influencing factors; Prospective cohort study

**Fund program:** National Natural Science Foundation of China (81472990)



· 临床报道 ·

## 一项有关中国女性子宫动静脉畸形(AVM)危险因素的回 性研究

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**【摘要】目的** 研究中国女性子宫动静脉畸形(AVM)的相关危险因素,为临床诊断、处理子宫AVM提供依据。**方法** 对本院治疗子宫AVM的28例患者进行分析,分析术后出血天数、流产次数及手术方式等因素与AVM的关系。**结果** 年龄、手术方式、术后出血天数、手术医院、流产次数以及孕周与AVM在统计学上均显著相关。术后出血天数、流产次数及手术方式是AVM的独立危险因素。**结论** AVM的发生与术后出血天数、流产次数及手术方式等因素有关,可以通过分析相关风险因素,判断AVM发生的可能性,为临床诊断、处理子宫AVM提供理论与数据指导。

**【关键词】** 子宫动静脉畸形; 危险因素; 子宫动脉栓塞术

**基金项目:** 国家自然科学基金(81202042); 南京市医学科技发展资金(QRX11212)

· 临床报道 ·

**Risk factors for uterine arteriovenous malformation in Chinese women: a retrospective study** Xu Qing,

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**【Abstract】Objective** To determine the risk factors for uterine arteriovenous malformation (AVM) in Chinese women, providing basis for clinical diagnosis and management. **Methods** A total of 28 cases with uterine AVM were retrospectively analyzed to investigate the relationship of duration of postoperative bleeding, abortion frequency, history of intrauterine operation and other factors with AVM. **Results** Age, method of intrauterine surgery, days of postoperative bleeding, hospitalization for surgery, abortion frequency as well as gestational age were significantly correlated with AVM. Days of postoperative bleeding, abortion frequency and method of intrauterine operation were independent risk factors for AVM. **Conclusion** Occurrence of AVM was associated with the duration of postoperative bleeding, abortion frequency, method of intrauterine surgery and other factors. Predicting the possibility of AVM based on relevant risk factors facilitates clinical diagnosis and management.

**【Key words】** Uterine arteriovenous malformation; Risk factor; Uterine artery embolization

**Fund program:** Natural Science Foundation of China (81202042); Nanjing Medical Science and Technology Development Fund (QRX11212)

## 同被引聚类分析方法挖掘妇产科学研究热点的初步探讨

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**【摘要】**目的 从大量文献中挖掘妇产科研究热点。方法 收集 2016—2017 年科学引文索引(SCI)妇产科领域高影响因子期刊全部文献共 5 800 篇, 使用书目共现分析系统统计出高频被引论文 38 篇, 形成被引用 - 引用矩阵, 在聚类分析软件 gCluto 中进行高频被引论文的同被引聚类分析。结果 可视化图像清晰显示目前国际妇产科领域五大研究热点。结论 同被引聚类分析方法可从大量文献中有效挖掘出研究热点。

**【关键词】** 妇产科学; 研究热点; 高频被引论文; 聚类分析; 文献计量学分析

· 科研方法 ·

**Active research fields of gynecology and obstetrics: a document co-citation clustering analysis of literatures**

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**【Abstract】 Objective** To explore active research fields of gynecology and obstetrics from a large amount of literatures. **Methods** Document co-citation clustering analysis method was used in this article. ISI web of knowledge-SCI-EXPANDED was used to retrieve all the 5 800 documents published in 2016–2017 from journals with higher impact factor. Then the occurrence of cited literatures was compared and ranked. A reference co-occurrence matrix of selected 38 cited literatures can be created using Bibliographic Item Co-Occurrence Matrix Builder (BICOMB). This co-occurrence matrix was then transformed into gCluto (gCluTo -Graphical Clustering Toolkit) for further analysis within co-citation clusters. **Results** A co-occurrence matrix was formed based on these findings, and ultimately co-citation clustering indicators, i.e., information trees, data matrix were formed and provided direct visualization as hot spots on five active gynecology and obstetrics categories. **Conclusion** The active categories of gynecology and obstetrics research were identified by using the co-citation cluster analysis.

**【Key words】** Gynecology and obstetrics; Hot spots; High-frequency cited papers; Clustering analysis; Bibliometric analysis

## 更年期女性胆固醇水平调查与影响因素分析

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**【摘要】目的** 研究胆固醇代谢与绝经的关联和可能的影响因素。**方法** 对杭州市拱墅区 963 例 40~60 岁女性进行横断面调查, 收集其月经史及其他临床资料, 填写改良 Kupperman 更年期症状量表(mKMI), 检测血清总胆固醇(TC)、低密度脂蛋白胆固醇(LDL-C)、卵泡刺激素(FSH)、黄体生成素(LH)、雌二醇(E<sub>2</sub>)水平。收集参与者教育程度、婚姻状态、职业状态、收入、居住地等社会人口资料。研究不同绝经状态女性胆固醇水平及高胆固醇血症、LDL-C 升高的发生率, 并分析年龄、绝经状态、FSH、E<sub>2</sub>、社会人口等因素对血清胆固醇的影响。**结果** 963 例参与者平均年龄(51.0 ± 5.6)岁, 其中绝经前期 302 例(31.4%), 围绝经期 197 例(20.5%), 绝经后期 464 例(48.2%), 绝经后参与者的平均绝经年龄(49.9 ± 3.8)岁。在所有参与者中, 绝经前期 mKMI 总分(6.36 ± 6.43)显著低于围绝经期(10.30 ± 7.88)和绝经后期(10.35 ± 7.97)(*P*<0.001)。绝经前后平均 TC、LDL-C 水平呈显著上升趋势, FSH、LH 水平呈上升趋势, E<sub>2</sub> 水平呈下降趋势(*P*<0.001)。所有参与者中高胆固醇血症比例为 13.3%, LDL-C 升高比例为 15.0%, 从绝经前期过渡到围绝经期、绝经后期的过程中, 高胆固醇血症及 LDL-C 升高的发生率显著上升(*P*<0.001)。Logistic 多元回归分析表明 FSH ≥ 40 IU/L 是发生高胆固醇血症和 LDL-C 升高的危险因素(*OR*=2.821, 95% *CI*=1.429~5.569, *P*=0.003; *OR*=2.587, 95% *CI*=1.356~4.937, *P*=0.004), 调整 FSH 水平后, 年龄、绝经状态、E<sub>2</sub> 水平、社会人口因素与发生高胆固醇血症和 LDL-C 升高均无显著关联(*P*>0.05)。**结论** 相比绝经前期, 围绝经期和绝经后女性平均 TC、LDL-C 上升, 胆固醇水平升高的发生率增加, FSH 水平升高可能是胆固醇代谢紊乱的内在机制, 降低 FSH 水平可作为绝经激素补充治疗的目标和疗效指标。

**【关键词】** 绝经; 总胆固醇(TC); 低密度脂蛋白胆固醇(LDL-C); 性激素; 影响因素

**基金项目:** 国家自然科学基金(81370685); 浙江省教育厅一般科研项目(Y201738349)

· 现场调查 ·

**Investigation of serum cholesterol level of women in different menopausal stages and its influencing factors**

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**【Abstract】 Objective** To investigate serum cholesterol level and prevalence of hypercholesterolemia and to analyze influencing factors of women in different menopausal stages. **Methods** A cross-sectional study was carried out involving 963 participants aged 40–60 years in Gongshu District, Hangzhou. Clinical data including menstrual history were collected. The menopausal symptom was evaluated by having the participants complete modified Kupperman Menopausal Index (mKMI) questionnaire. Serum levels of total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), follicle-stimulating hormone (FSH), luteinizing hormone (LH) and estradiol (E<sub>2</sub>) were measured. Sociodemographic characteristics including education, occupation, place of residence and income were collected. TC, LDL-C level and the percentage of hypercholesterolemia of women were compared in different menopausal stages. Statistical analysis was performed to identify factors associated with the occurrence of hypercholesterolemia. **Results** The mean age of all participants was (51.0 ± 5.6) years. Among 963 participants, 31.4% (302/963) were premenopausal, 20.5% (197/963) were perimenopausal, and 48.2% (464/963) were postmenopausal. The mean age of menopause was (49.8 ± 3.8) years. The total mKMI scores of premenopausal women (6.36 ± 6.43) were significantly lower than that of peri- and postmenopausal women (10.30 ± 7.88, 10.35 ± 7.97) ( $P < 0.001$ ). The mean TC and LDL-C level increased significantly from premenopausal to postmenopausal stage ( $P < 0.001$  for both). The FSH, LH level displayed an increasing trend while the E<sub>2</sub> level displayed a downward trend from premenopausal to postmenopausal stage ( $P < 0.001$  for all). In all participants, the prevalence of hypercholesterolemia was 13.3% and 15.0% participants had high LDL-C. The prevalence of hypercholesterolemia and high LDL-C increased significantly during menopausal transition ( $P < 0.001$  for both). The Logistic regression model revealed that FSH ≥ 40 IU/L were significantly associated with the occurrence of hypercholesterolemia and high LDL-C ( $OR = 2.821$ , 95%  $CI = 1.429-5.569$ ,  $P = 0.003$ ;  $OR = 2.587$ , 95%  $CI = 1.356-4.937$ ,  $P = 0.004$ ; respectively). **Conclusion** Compared with premenopausal women, peri- and postmenopausal women had higher serum TC, LDL-C levels and higher prevalence of hypercholesterolemia. The increased FSH level may be the internal mechanism of cholesterol metabolic disorder. Reduction of FSH level is expected to be the aim and therapeutic index of menopause hormone therapy.

**【Key words】** Menopause; Total cholesterol (TC); Low-density lipoprotein cholesterol (LDL-C); Sex hormones; Influencing factors

**Fund program:** National Natural Science Foundation of China (81370685); Programs Foundation of Ministry of Education of Zhejiang Province (Y201534797)

## 体外受精治疗非典型 21-羟化酶缺乏症患者成功妊娠 1 例

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**【摘要】目的** 21-羟化酶缺乏症(21-OHD)、17 $\alpha$ -羟化酶缺乏症(17-OHD)为先天性肾上腺皮质增生的 2 种类型, 因酶缺乏程度不同, 临床表现不一又分为多种亚型, 其中非典型 21-OHD 与不完全型 17-OHD 皆症状轻微, 临床不易发现, 目前此类患者妊娠率较正常者低下, 如何鉴别疾病, 改善临床预后并提高生育能力是临床诊治及随访的重点。**方法** 对本院生殖中心 1 例罕见的非典型 21-OHD 合并人细胞色素 P450c17A1 (CYP17A1)、卵泡刺激素受体(FSHR)、黄体生成素受体(LHCGR)基因多态性病例的诊断、治疗及促排卵的过程进行回顾性分析。**结果** 该患者经基因型检测获得明确诊断, 高孕酮血症及时得到治疗, 并予以个体化促排卵方案, 最终获得良好妊娠结局。**结论** 生殖科临床医生应提高对先天性肾上腺皮质增生的认识, 适当利用基因型分析协助诊断, 在助孕过程中灵活制定个体化促排卵方案。

**【关键词】** 非典型 21-羟化酶缺乏症(21-OHD); 基因多态性; 促排卵; 妊娠

· 个案报道 ·

**Pregnancy received *in vitro* fertilization treatment associated with non-classical 21-hydroxylase deficiency: 1 case report**

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**【Abstract】 Objective** 21-hydroxylase deficiency (21-OHD) and 17 $\alpha$ -hydroxylase deficiency (17-OHD) are two types of congenital adrenal hyperplasia (CAH). There are different subtypes according to the degree of hydroxylase deficiency and various clinical characteristics, which non-classical 21-hydroxylase deficiency and incomplete 17 $\alpha$ -hydroxylase deficiency show mild characteristics. The rate of pregnancy with non-classical 21-OHD and incomplete 17-OHD are moderately reduced when compared with normal adult women. How to improve clinical outcome and the fertility are our key points. **Methods** This paper attached with a report of a client in our reproductive center who suffered from non-classical 21-OHD with cytochrome P450 family 17 subfamily A member 1 (CYP17A1), follicle stimulating hormone receptor (FSHR), luteinizing hormone receptor (LHCGR) gene polymorphism, analyzed the diagnoses and ovarian stimulation treatment. **Result** The patient had a good pregnancy outcome after a definite diagnosis by genotype test, treatment of high progesterone and individualized ovarian stimulation. **Conclusion** We aim to understand CAH and figure out the proper treatment which assists in achieving a pregnancy.

**【Key words】** Non-classical 21-hydroxylase deficiency (21-OHD); Gene polymorphism; Ovarian stimulation; Pregnancy



## 代谢重编程调控巨噬细胞极化及其在母 - 胎界面的作用

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**【摘要】** 母 - 胎界面的免疫反应在妊娠建立、维持以及分娩发动中起至关重要的作用。正常的巨噬细胞极化及其功能是维持母 - 胎界面正常免疫微环境的基础, 若异常, 会导致子痫前期、早产等妊娠相关重大疾病的发生。代谢重编程是细胞对所处环境关键改变的反应统称, 可以调控巨噬细胞的不同极化状态。本文对代谢重编程与巨噬细胞极化、母 - 胎界面巨噬细胞代谢以及代谢重编程对其极化类型的影响在正常妊娠和病理性妊娠中可能发挥的作用进行综述。

**【关键词】** 代谢重编程; 巨噬细胞极化; 母 - 胎界面; 炎症; 妊娠

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· 综述 ·

**Metabolic reprogramming regulates macrophage polarization and its roles at the maternal-fetal interface**

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**【Abstract】** Immune responses at the maternal-fetal interface play a vital role in the establishment, maintenance and delivery of normal pregnancy. Appropriate macrophage polarization and its biological function are the basis of maintaining normal immune microenvironment of the maternal-fetal interface. On the contrary, the abnormal polarization both spatially and temporally will lead to a series of pregnancy-related major diseases, such as pre-eclampsia, premature birth. Metabolic reprogramming is the responses of cells to key changes in the environment, which can regulate macrophage polarization, and make them exhibit diverse biological functions. In this review, we focus on the metabolic characteristic of macrophages, and how metabolic reprogramming regulates their polarization at the maternal-fetal interface and what the roles of the process have in normal and pathological pregnancies.

**【Key words】** Metabolic reprogramming; Macrophage polarization; Maternal-fetal interface; Inflammation; Pregnancy

**Fund program:** National Natural Science Foundation of China (81671490); Integrated Innovative Team for Major Human Diseases Program of Tongji Medical College, HUST (5001519002)

## 自体外周血单个核细胞(PBMCs)治疗改善反复种植失败患者妊娠结局的免疫学机制

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**【摘要】** 辅助生殖技术飞速发展的同时, 仍有部分患者中遭受反复胚胎种植失败(RIF)。RIF 的治疗在不断更新和发展, RIF 的免疫学病因和免疫治疗是否有效仍存在争议, 相关的治疗是否有效尚未达成共识。目前有临床数据及动物实验显示, 自体外周血单个核细胞(PBMC)治疗能改善该类患者的妊娠结局。然而, 大多关于 PBMC 治疗均着重于临床现象, 关于其具体的免疫学机制文章甚少。故本文对反复种植失败进行了概述并对 PBMC 治疗改善体外受精-胚胎移植(IVF-ET)RIF 患者妊娠结局的免疫学机制进行了深入探讨与总结。

**【关键词】** 自体外周血单个核细胞(PBMC); 宫腔灌注; 反复种植失败(RIF); 免疫

· 综述 ·

**Immunological mechanism of autologous peripheral blood mononuclear cells (PBMCs) in improving pregnancy outcomes in patients with recurrent implantation failure during *in vitro* fertilization-embryo transfer**

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**【Abstract】** With the rapid development of assisted reproductive technology, there are still some patients suffering from recurrent implantation failure (RIF). Although treatments about RIF are in the constant updation and development, immunological etiology and immunotherapy of RIF is still controversial, whether the treatment is effective has not yet reached a consensus. Recently, there are clinical data and animal experiments showing that autologous peripheral blood mononuclear cells (PBMCs) treatment can improve the pregnancy outcome in patients with RIF. However, most of the treatment about autologous PBMCs are focused on clinical phenomena, there is few research on its specific immunological mechanisms. Therefore, in this article we will present an overview of RIF and have an in-depth discussion and summary on the immunological mechanism of autologous PBMCs intrauterine infusion in patients with RIF during *in vitro* fertilization-embryo transfer (IVF-ET).

**【Key words】** Peripheral blood mononuclear cells (PBMCs); Intrauterine infusion; Recurrent implantation failure (RIF)

## 雌、孕激素受体、生长激素受体、胰岛素样生长因子 1 受体与子宫内膜容受性的关系

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**【摘要】** 辅助生殖技术(ART)经过近 40 年的发展, 已取得突飞猛进的进展。但是临床妊娠率仍然徘徊在 30%~40%。决定能否成功妊娠的因素主要包括 2 个方面, 一是胚胎发育的质量, 二是子宫内膜对胚胎的容受性。而在临床工作中, 即使胚胎质量良好, 种植率仍然不能令人满意。因此, 如何提高子宫内膜容受性已经成为辅助生殖领域一个亟待解决的问题, 了解影响子宫内膜容受性的相关因素, 对于在种植窗期如何调节母体的内膜达到最佳的接纳胚胎的状态, 具有重要的指导性意义。本文着重阐述子宫内膜容受性与雌激素受体(ER)、孕激素受体(PR)、胰岛素样生长因子 1 受体(IGF-1R)、生长激素受体(GHR)之间的关系, 期望对临床判断子宫内膜容受性有所帮助。

**【关键词】** 雌、孕激素受体(ER、PR); 胰岛素样生长因子 1 受体(IGF-1R); 生长激素受体(GHR); 子宫内膜容受性; 不孕症

· 综述 ·

**Role of estrogen receptor, progesterone receptor, growth hormone receptor and receptor of insulin like growth factor-1 in the endometrial receptivity** Wang Qiaofeng, Yang Fan

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**【Abstract】** Even though the assisted reproductive technology (ART) has achieved a rapid progress nearly 40 years, the implantation rate is about 30%–40%. Successful embryonic implantation depends on high-quality embryo and the endometrial receptivity in the best situation. In clinical work, the embryo implantation rate is dissatisfaction, even though there is high-quality embryo. Therefore, how to improve the endometrial receptivity is a pressing problem. This article reviews the relationship between the receptors of endometrium [including estrogen receptor (ER), progesterone receptor (PR), the receptor of insulin like growth factor-1 (IGF-1R) and growth hormone receptor (GHR)] and the endometrial receptivity. We hope that it can help clinical doctors judging the situation of endometrial receptivity in the future.

**【Key words】** Estrogen receptor (ER); Progesterone receptor (PR); Receptor of insulin like growth factor-1 (IGF-1R); Growth hormone receptor (GHR); Endometrial receptivity; Infertility

## 抗苗勒管激素在高龄女性中检测的临床意义

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**【摘要】** 女性卵巢功能随年龄增加而下降, 高龄生育成为社会性问题。高龄女性妊娠率及活产率下降, 因此准确评估高龄女性的卵巢功能及妊娠结局非常重要。抗苗勒管激素(AMH)是评估卵巢功能的可靠指标, 在预测卵巢反应性、卵母细胞质量、获卵数、生殖结局以及指导促排卵方案等方面具有一定临床意义。高龄以及低或极低 AMH 水平女性仍然存在一定的生育机会, 不应作为辅助生殖技术(ART)排除的指征。

**【关键词】** 抗苗勒管激素(AMH); 高龄; 生育力; 卵巢低反应; 生殖结局

· 综述 ·

**Clinical significance of anti-Müllerian hormone in advanced age women** Sun Xiaoyan, Shi Xin,

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**【Abstract】** Female ovarian function decreased with age, so the fertility of advanced age women gradually becomes a social problem. It is important to accurately assess the ovarian function and pregnancy outcome of older women who have a low pregnancy rate and low live-birth rate. As a reliable indicator of ovarian function, anti-Müllerian hormone (AMH) can predict ovarian response, oocyte quality, the number of oocytes and reproductive outcomes, and guide the ovulation program. The women of advanced age and low or very low level of AMH still have some fertility opportunities and should not be excluded from assisted reproductive technology (ART).

**【Key words】** Anti-Müllerian hormone (AMH); Advanced age; Fertility; Poor ovary response; Reproductive outcome