

• 实验研究 •

# 子宫内膜细胞诱导胚胎干细胞修复 小鼠受损子宫内膜

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**【摘要】** 目的: 探讨小鼠胚胎干细胞(ESCs)经体外与子宫内膜细胞共培养后移植于内膜损伤小鼠的子宫腔是否有助于损伤的修复并降低其成瘤性。方法: 制备新鲜子宫内膜损伤的小鼠模型, 利用带EGFP基因标记的小鼠胚胎干细胞(ESC<sup>-EGFP</sup>)与同种子宫内膜共培养后移植至模型鼠宫腔; 观察ESC<sup>-EGFP</sup>在模型鼠宫腔内滞留情况、对损伤内膜的修复影响以及对干细胞移植后成瘤性的影响。结果: 将与子宫内膜共培养后的ESC<sup>-EGFP</sup>移植到新鲜损伤的模型鼠宫腔内, 可使损伤子宫的外形较PBS对照组保持更好, 移植后1~4周的损伤子宫大体标本均可见荧光; 组织病理可见新生子宫内膜腺体样组织, 并显示GFP免疫组织化学标记; 且在有限观察时间内无肿瘤形成。结论: ESCs与子宫内膜细胞共培养方式可能诱导ESCs分化的方向, 而在体子宫腔损伤的局部环境有利于胚胎干细胞定植与进一步向子宫内膜分化。

**关键词:** 胚胎干细胞(ESCs); 增强型绿色荧光蛋白(EGFP); 子宫内膜; 子宫内膜损伤模型

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## Endometrial Cells Inducing Embryonic Stem Cells to Repair the Injured Mouse Endometrium

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**【ABSTRACT】 Objective:** To investigate whether the embryonic stem cells (ESCs) co-cultured with endometrial cells could help the endometrium reparation and reduce the neoplasia of ESCs. **Methods:** The mouse model with freshly injured endometrium was established. ESCs derived from EGFP transgenic mouse (ESC<sup>-EGFP</sup>) were transplanted to endometrium-injured mouse after cultured with endometrial cells. The retention and the effects of ESCs on the reparation of injured endometrium and the tumorigenicity of post-transplanted stem cells were observed. **Results:** The co-cultured ESC<sup>-EGFP</sup> could survive in the freshly endometrium-injured mouse's uterine cavities and keep the injured uterus in better shape compared with PBS group. The fluorescent light could be observed on the injured uterus in the first 4 weeks after the transplantation, with the new generated endometrial gland-like tissue observed by histopathology and GFP immunohistochemical staining positive. The evidence of endometrium neoplasia was not found during the limited observing period. **Conclusion:** Co-culture with endometrial cells may induce the differentiation of ESCs. And the environment of injured uterus cavity may avail to the implantation and differentiation of the ESC.

**Key words:** embryonic stem cells (ESC); enhanced green fluorescent protein (EGFP); endometrium; endometrium injured model

# VEGF基因多态性与广西壮族妇女复发性流产的相关性研究

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**【摘要】** 目的: 探讨血管内皮生长因子(vascular endothelial growth factor, VEGF)-2578C/A、-1154G/A、-634G/C、-460C/T和+936C/T位点单核苷酸多态性(single nucleotide polymorphisms, SNPs)与广西壮族妇女复发性流产(RSA)发病的关联。方法: 应用 PCR-限制性片段长度多态性技术(PCR-RFLP)检测 RSA 组(120 例, 病例组)和健康对照组(110 例)的 VEGF 5 个 SNPs 位点基因型频率分布情况。结果: VEGF -2578C/A、-1154G/A、-634G/C、-460C/T和+936C/T的 SNPs 位点基因型和等位基因频率分布在病例组和对照组间均无统计学差异( $P>0.05$ )。结论: VEGF -2578C/A、-1154G/A、-634G/C、-460C/T和+936C/T位点的基因多态性可能与广西壮族妇女 RSA 发病风险不相关。

**关键词:** 复发性流产(RSA); 血管内皮生长因子(VEGF); 基因多态性

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## Association of VEGF Single Nucleotide Polymorphisms and Patients with Recurrent Spontaneous Abortion in Guangxi Zhuang Women

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**【ABSTRACT】 Objective:** To investigate the association of single nucleotide polymorphisms (SNPs) in vascular endothelial growth factor (VEGF) gene with the risk of recurrent spontaneous abortion (RSA) in Guangxi Zhuang women. **Methods:** Totally 120 patients suffering RSA and 110 controls were enrolled in this study. Genotypes of VEGF were measured by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method. **Results:** No significant difference was observed in allele and genotype distributions of the VEGF -2578C/A, -1154G/A, -634G/C, -460C/T and +936C/T polymorphisms between patients and controls ( $P>0.05$ ). **Conclusion:** The SNP of VEGF -2578C/A, -1154G/A, -634G/C, -460C/T and +936C/T may have no association with RSA in Guangxi Zhuang women.

**Key words:** recurrent spontaneous abortion (RSA); vascular endothelial growth factor (VEGF); genetic polymorphism

# 辅助生殖和自然妊娠中早期自然流产 胚胎染色体数目异常的研究

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**【摘要】**目的: 探讨辅助生殖技术(ART)与早期流产胚胎染色体数目异常的关系。方法: 通过多重连接依赖探针扩增技术对 145 例 ART 妊娠和 36 例自然妊娠孕早期自然流产的绒毛组织进行染色体数目检测, 分析流产胚胎的染色体异常情况, 比较不同受孕方式、受精方式、移植新鲜/冷冻胚胎妊娠后自然流产绒毛染色体异常率。结果: 所有早期自然流产绒毛标本染色体总异常率为 66.85% (121/181), 以常染色体三体为主, 非整倍体涉及除 1 号染色体以外所有染色体, 以 16 号染色体最多见。流产胚胎非整倍体发生率在自然妊娠组与 ART 组间 (66.67% vs 66.90%,  $P=1.000$ )、新鲜胚胎移植组与冷冻胚胎移植组间 (65.91% vs 68.42%,  $P=0.857$ ) 均无统计学差异, 体外受精(IVF)组略高于卵胞质内单精子注射(ICSI)组, 但无统计学差异 (73.26% vs 57.63%,  $P=0.072$ )。结论: 胚胎染色体数目异常是自然流产的主要病因, ART 包括 ICSI 和冻融胚胎均没有增加胎儿非整倍体发生率。

关键词: 非整倍体; 自然流产; 辅助生殖技术(ART); 绒毛

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## Study on Fetal Chromosome Numerical Abnormalities in Spontaneous Abortion during the First Trimester following Assisted Reproductive Technology and Natural Conception

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**【ABSTRACT】 Objective:** To explore the relationship between the numerical abnormalities of fetal chromosomes and spontaneous abortion during the first trimester following assisted reproductive technology (ART). **Methods:** A total of 145 cases of ART and 36 cases of natural conception (NC) suffered from spontaneous abortion during the first trimester were included in this study. Chorionic villus specimens were tested for the chromosome number by multiplex ligation-dependent probe amplification (MLPA) method, and then the incidence and types of aberrations were assessed. Comparisons were performed between different conception ways, different fertilization ways and the fresh or frozen-thawed embryo transfer. **Results:** The overall chromosomal abnormality's rate of early spontaneous abortion was 66.85% (121/181), and the most prevalent abnormality was autosomal trisomy. Aberration for each chromosome, with the exception of chromosome 1, was identified and the most common trisomy was chromosomes 16. No difference in the prevalence of chromosomal aberrations was found by comparing NC to ART (66.67% vs 66.90%,  $P=1.000$ ), or between the fresh embryo transfer (fresh-ET subgroup) and the frozen-thawed embryo transfer (FET subgroup) (65.91% vs 68.42%,  $P=0.857$ ). The aneuploidy rate of the IVF subgroup was higher than that of the ICSI subgroup but with no statistical difference (73.26% vs 57.63%,  $P=0.072$ ). **Conclusion:** Fetal chromosomal abnormality is the most important reason of spontaneous abortion during the first trimester. ART, ICSI or the cryopreservation of embryo does not increase the risk of aneuploidy.

**Key words:** aneuploidy; spontaneous abortion; assisted reproductive technology (ART); chorionic villus

• 临床研究 •

## 比较短时受精联合早期补救ICSI与常规IVF 在不明原因性不孕治疗的结局

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**【摘要】** 目的: 探讨短时受精联合早期补救 ICSI 在不明原因性不孕治疗中的应用价值。方法: 对 118 例不明原因不孕患者(A 组)行短时受精, 于 IVF 受精后 4~6 h 去颗粒细胞, 观察第二极体(Pb2)排出情况; 若所有成熟卵细胞均未排出 Pb2 或大部分成熟卵细胞(>70%)无 Pb2 则及时行补救 ICSI (A2 组), 未行补救 ICSI 的则归为 A1 组。同时选择 85 例行常规 IVF 的不明原因不孕患者作为对照组(B 组), 比较 2 种受精方法的结局。结果: A 组 118 个周期中有 72 个周期(A1 组)未行补救 ICSI; 46 个周期(A2 组)行早期补救 ICSI。A1 组共 763 个成熟卵中 490 个卵受精后 6~8 h 观察到 Pb2, 24 h 过夜后观察到 2 原核(2PN)。A 组未发生受精完全失败, 但其中 2 例(A2 组)因受精卵有多个明显的 PN 而放弃胚胎移植。B 组 85 个周期中有 17 个周期因完全受精失败无可移植胚胎放弃移植, 完全受精失败率为 20.0%, 明显高于 A 组(0%)( $P < 0.01$ )。A 组总受精率明显高于 B 组(74.6% vs 56.2%) ( $P < 0.05$ ); 卵裂率、可用胚胎率、胚胎种植率、移植周期妊娠率、流产率、多胎率 A、B 组间均无统计学差异( $P > 0.05$ )。A2 组的多精受精率较其它各组(A1 组、B 组)未见明显增高( $P > 0.05$ )。A 组的起始周期妊娠率(32.2%)略高于 B 组(25.0%), 但无统计学差异( $P > 0.05$ )。结论: 短时受精联合早期补救 ICSI 作为预防不明原因性不孕患者中可能发生受精失败的策略, 可以获得较高的受精率、胚胎种植率以及临床妊娠率。

**关键词:** 短时受精; IVF; 早期补救 ICSI; 不明原因不孕

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## Comparison of Early Rescue ICSI of Oocytes that Failed to Extrude the Second Polar Body with Routine IVF in Couples with Unexplained Infertility

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**【ABSTRACT】 Objective:** To explore the clinical application of early rescue ICSI of oocytes that failed to extrude the second polar body (Pb2) in couples with unexplained infertility. **Methods:** A total of 118 couples with unexplained infertility (group A) were recruited, granular cells were denuded after 4–6 h sperms and oocytes incubation, and Pb2 was observed whether was extruded or not. The early rescue ICSI was applied if most or more than 70% of matured oocytes failed to extrude Pb2. Totally 85 patients were also recruited to take routine IVF as control group (group B). The pregnancy outcomes were compared between the two groups. **Results:** In group A, 72 cycles (group A1) were not taken rescue ICSI, whereas 46 cycles (group A2) were taken rescue ICSI. The total fertilization failure (TFF) did not happen in group A, but 2 cycles were given up due to 3PN formation. In group B, 17 cycles were given up due to TFF, the TFF rate was much higher than that in group A ( $P<0.01$ ). The fertilization rate in group A was higher than that in group B (74.6% vs 56.2%)( $P<0.05$ ). The cleavage rate, the number of transferable embryos, the pregnancy rate per transfer cycle, the implantation rate, the abortion rate were comparable between the two groups ( $P>0.05$ ). The rate of >2PN in group A2 was not increased compared with group A1 and group B. **Conclusion:** Early rescue ICSI of oocytes that failed to extrude Pb2 can be used to prevent fertilization failure, it can obtain higher fertilization rate, implantation rate and pregnancy rate.

**Key words:** short-time fertilization; IVF; early rescue ICSI; unexplained infertility



# 超长方案用于子宫内膜异位症合并不孕者的体外受精-胚胎移植

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**【摘要】** 目的: 比较不同分期的子宫内膜异位症(EMs)合并不孕妇女采用超长 GnRH-a 降调节方案进行体外受精-胚胎移植(IVF-ET)助孕治疗的结局。方法: 回顾性分析以超长方案降调节行IVF-ET助孕卵巢储备功能正常的233例EMs合并不孕患者不同EMs分期的治疗结局, 按EMs分期分为A组(I~II期, 102例)和B组(III~IV期, 131例)。结果: ①患者年龄、平均手术次数、基础FSH(bFSH)等组间无统计学差异( $P>0.05$ )。B组有卵巢内膜异位囊肿手术史的比例明显高于A组( $P<0.01$ )。②促性腺激素(Gn)启动日及hCG注射日性激素、Gn使用剂量及天数、获卵数、受精率、卵裂率、可移植胚胎数等组间均无统计学差异( $P>0.05$ )。③周期取消率、临床妊娠率、种植率、流产率等组间无统计学差异( $P>0.05$ ), 移植周期活产率组间相似(60.64% vs 62.18%)( $P>0.05$ )。结论: 在卵巢储备功能正常的前提下, EMs合并不孕者采用超长方案降调节实施IVF-ET助孕的结局不受EMs分期的影响。

**关键词:** 子宫内膜异位症(EMs); 体外受精-胚胎移植(IVF-ET); 控制性卵巢刺激(COS); 超长方案

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## Outcome of IVF-ET Conducted with Prolonged GnRH-a Protocol on Infertility Patients with Different Stages of Endometriosis

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**【ABSTRACT】 Objective:** To compare the outcome of *in vitro* fertilization-embryo transfer (IVF-ET) conducted with prolonged GnRH-a down-regulation protocol on infertile patients with different stages of endometriosis (EMs). **Methods:** A retrospective analysis was performed on infertile patients with EMs regarding the IVF-ET cycles used prolonged protocol in our center. Totally, 233 patients who fulfilled all the including criteria were divided into group A (stage I-II,  $n=102$ ) and group B (stage III-IV,  $n=131$ ). The characteristics of patients, data of controlled ovarian stimulation cycles, IVF-ET outcomes of two groups were compared. **Results:** 1) Patients in the two groups were comparable in terms of age, surgery times and basal FSH ( $P>0.05$ ). The proportion of patients with previous surgery of ovarian endometrioma was higher in group B than that in group A ( $P<0.01$ ). 2) The hormone levels on gonadotropins (Gn) launch day and hCG injection day, doses and days of gonadotropins, the number of retrieved oocytes, the fertilization rate, the cleavage rate, the number of embryos transferred were comparable in two groups ( $P>0.05$ ). 3) There was no obvious difference in the cycle cancellation rate, the clinical pregnancy rate, the implantation rate and the abortion rate between the two groups ( $P>0.05$ ). The live birth rates of two groups were 60.64% and 62.18%, respectively ( $P>0.05$ ). **Conclusion:** The outcomes of IVF-ET conducted with prolonged GnRH-a protocol on women with EMs-related infertility were not affected by the stages of EMs if they had normal ovarian reserve.

**Key words:** endometriosis (EMs); *in vitro* fertilization-embryo transfer (IVF-ET); controlled ovarian stimulation (COS); prolonged protocol

# 不育门诊男性体质量指数与精液质量的相关性研究

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**【摘要】** 目的: 探讨不育男性体质量指数(body mass index, BMI)与精液质量间的相关性。方法: 选择就诊于本院不育门诊的男性共803名, 以中国成人BMI标准将其分为低体质量组(BMI<18.5 kg/m<sup>2</sup>)、正常组(BMI 18.5~23.9 kg/m<sup>2</sup>)、超重组(BMI 24.0~27.9 kg/m<sup>2</sup>)、肥胖组(BMI 28.0~29.9 kg/m<sup>2</sup>)、重度肥胖组(BMI ≥ 30.0 kg/m<sup>2</sup>), 并按照世界卫生组织第5版标准检测精液质量参数。统计分析不同BMI与性激素水平、精液质量参数之间的关系。结果: 肥胖组的E<sub>2</sub>明显高于非肥胖组( $P<0.001$ ); 随着BMI等级上升, T水平及T/LH值均逐渐降低( $P<0.001$ )。正常组精液体积显著大于其他各组( $P<0.001$ )。低体质量、正常组与超重组相比, 精子总数明显较多( $P<0.05$ )。其余精液质量参数各组间无统计学差异。BMI大小与E<sub>2</sub>水平呈显著正相关( $P<0.001$ ), 与T水平、T/LH及精子总数呈显著负相关(均 $P<0.01$ )。T/LH与精子总数间也呈显著正相关( $P<0.01$ )。结论: 超重及肥胖可能对男性生育能力带来不良影响。

**关键词:** 体质量指数(BMI); 肥胖; 不育; 男性; 精液质量

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## Relationship between Body Mass Index and Semen Quality Parameters in Males Attending An Infertility Clinic

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**【ABSTRACT】 Objective:** To explore the relationship between body mass index (BMI) and semen quality parameters in males attending an infertility clinic. **Methods:** A total of 803 men who came for preconception examination or help for infertility were recruited, and divided into 5 groups as underweight group (BMI<18.5 kg/m<sup>2</sup>), normal group (BMI 18.5–23.9 kg/m<sup>2</sup>), overweight group (BMI 24.0–27.9 kg/m<sup>2</sup>), obesity group (BMI 28.0–29.9 kg/m<sup>2</sup>) and extreme obesity group (BMI ≥ 30.0 kg/m<sup>2</sup>), according to the BMI criteria of Chinese adults. Semen quality parameters were measured according to the fifth World Health Organization criteria. Then the association between BMI and sex hormone levels, and semen parameters were examined. **Results:** Obesity males had significantly higher E<sub>2</sub> level than non-obesity ones ( $P<0.001$ ). As the BMI leveled up, the values of T and T to LH ratio decreased significantly ( $P<0.001$ ). Semen volume was higher in normal group than in others ( $P<0.001$ ), and total sperm count was higher in two non-overweight groups than three overweight ones ( $P<0.05$ ). Other parameters had non-significant differences among groups. The level of BMI had a significant positive relationship with E<sub>2</sub>, and negative relationship with T and T/LH ( $P<0.001$ ). T/LH was positively associated with total sperm count ( $P<0.01$ ). **Conclusion:** Overweight and obesity may have adverse effects on male reproductive potential.

**Key words:** body mass index (BMI); obesity; infertility; male; semen quality

# 晚卵泡期孕酮水平升高增加卵裂期胚胎移植异位妊娠风险

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**【摘要】** 目的: 探索晚卵泡期孕酮(P)水平升高与体外受精(IVF)卵裂期胚胎移植异位妊娠风险的关系。方法: 回顾性分析行IVF卵裂期胚胎移植或囊胚移植并获得妊娠的1508个周期异位妊娠发生情况。根据hCG注射日P水平分为P正常组( $P \leq 1.5$  ng/ml)与P升高组( $P > 1.5$  ng/ml), 比较组间的异位妊娠发生率。结果: 卵裂期胚胎移植P正常组、P升高组异位妊娠率分别为2.8%(32/1132)和7.9%(11/140), 差异有统计学意义( $P=0.005$ )。囊胚移植P正常组、P升高组异位妊娠率分别为1.5%(3/199)和5.4%(2/37), 组间差异无统计学意义( $P>0.05$ )。结论: 晚卵泡期P升高可增加IVF卵裂期胚胎移植异位妊娠风险。

**关键词:** 体外受精 - 胚胎移植(IVF-ET); 异位妊娠; 孕酮(P); 卵裂期胚胎; 囊胚

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## Elevated Progesterone Level at the End of the Follicular Phase Increased Ectopic Pregnancy Risk in Day 3 Embryo Transfer

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**【ABSTRACT】Objective:** To explore the association of elevated progesterone (P) level in late-follicle phase and ectopic pregnancy after *in vitro* fertilization (IVF). **Methods:** A total of 1 508 cycles of ectopic pregnancy after d 3 embryo transfer or blastocyst transfer were retrospectively analyzed. All patients were divided into normal P group ( $P \leq 1.5$  ng/ml) and elevated P group ( $P > 1.5$  ng/ml) according to the P level on the day of hCG injection. The ectopic pregnancy rate was compared between the two groups. **Results:** Elevated P level at the end of the follicular phase significantly increased ectopic pregnancy rate in d 3 embryo transfer compared with normal P group (2.8% vs 7.9%,  $P=0.005$ ). No significant difference was observed in ectopic pregnancy rate of blastocyst transfer between the two groups (1.5% vs 5.4%,  $P=0.14$ ). **Conclusion:** Elevated P level at the end of the follicular phase increases ectopic pregnancy risk in d 3 embryo transfer but has no effect on blastocyst transfer.

**Key words:** IVF-ET; ectopic pregnancy; progesterone (P); cleavage stage embryo; blastocyst

# 冻融卵裂期胚胎单个卵裂球 体外发育潜能的初步探讨

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**【摘要】** 目的: 探讨体外受精-胚胎移植(IVF-ET)治疗周期中冻融胚胎来源的单卵裂球体外发育潜能。方法: 20例IVF-ET术生育成功后捐赠的91枚多余冷冻的胚胎, 解冻后分为<6-细胞组、6~8-细胞组和>8-细胞组, 将每枚胚胎中的卵裂球分离、取出, 每个单卵裂球单独培养于一个液滴中, 每24 h观察并比较各组间单卵裂球发育情况的差异。结果: 6~8-细胞组单卵裂球的卵裂率、紧密化率和囊胚形成率显著高于其它各组。结论: 单卵裂球体外培养发育能力及时序与其来源的胚胎发育潜力及发育阶段密切相关; 辅助生殖 FET 周期应优先选择 6~8-细胞的胚胎进行移植。

**关键词:** 冻融胚胎; 单卵裂球; 体外培养; 发育潜能

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## Preliminary Investigation on the *in vitro* Developmental Potential of Single Blastomeres Derived from Frozen-thawed Cleavage-stage Embryos

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**【ABSTRACT】 Objective:** To investigate the developmental potentiality of single isolated blastomeres of human frozen-thawed embryos *in vitro* during *in vitro* fertilization and embryo transfer (IVF-ET). **Methods:** Ninety-one frozen embryos from 20 patients who accepted IVF-ET and were successfully pregnant were divided into three groups: <6-cell, 6–8-cell and >8-cell. Single isolated blastomere was separated with the technology of biopsy and continued culturing in one single culture drop *in vitro*. During this period, the development characteristics of blastomeres were observed every 24 h. **Results:** The rates of cleavage, compaction and blastocyst of single isolated blastomere from the 6–8-cell group were significantly higher than those in other two groups. **Conclusion:** The developmental capacity and timing of single isolated blastomere were closely related to developmental potential and developmental stage of its embryos. Embryos of 6–8-cell should be a priority for the frozen-thawed embryo transfer (FET) cycle of assisted reproduction technology (ART).

**Key words:** frozen-thawed embryo; single blastomere; *in vitro* culture; development potential



• 综述 •

## 胚胎培养体系研究进展

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**【摘要】** 以往人们对体外胚胎发育的研究大多集中在培养液中的化学成分上, 而培养体系中的物理微环境对胚胎发育的影响往往易被忽略。近年来, 胚胎培养体系已从静置的微滴、微穴培养逐渐发展到动态的微流体培养。静置培养体系因培养效果稳定, 且易操作, 一直占据主导地位。动态培养体系不但能为胚胎补充新鲜的培养液, 并还能及时清除胚胎产生的代谢产物, 但其操作更复杂, 限制了其在临床的广泛应用。本文就各种培养体系在体外胚胎培养中的研究进展综述如下。

**关键词:** 胚胎培养; 培养装置; 微流体; 静置培养体系; 动态培养体系; 辅助生殖技术(ART)

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## Advances in Embryo Culture System

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**【ABSTRACT】** Over the last two decades, the immense amount of data aiming at improving embryo development *in vitro* has involved the chemical composition of the culture media, however, physical requirements for embryos development *in vitro* have been largely neglected. Recently, the culture system has been developed from simple static microdrop and microwell culture to dynamic microfluid culture. Static embryo culture has been the predominate method employed to date for its stable culture effect and easy operation. Dynamic embryo culture system will not only be able to add fresh culture medium, and also the timely removal of metabolites produced by the embryo. As theoretically promising as dynamic culture appears, one of the limitations of these systems is their relative complexity in comparison to static culture devices. The current progress in embryo culture platforms on the development of embryo would be reviewed in this article.

**Key words:** embryo culture; culture device; microfluidic; static culture platforms; dynamic culture platforms; assisted reproductive technology (ART)

# 双酚A在日常生活接触及其 对人类生殖内分泌的干扰

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**【摘要】** 双酚A(BPA)是一种工业原料,广泛存在于日常用品。BPA可通过多种途径进入体内,从而干扰哺乳动物的内分泌,被认为是一种拟雌激素作用。目前,BPA暴露引起的疾病包括肿瘤的形成、代谢疾病、脑部发育障碍、心血管疾病、血糖增高等。本文将具体介绍BPA在胎儿、新生儿及成人时期的剂量与疾病发生的关系。

**关键词:** 双酚A(BPA); 内分泌干扰物; 拟雌激素

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## **Bisphenol A's Application in Life and Its Interference about Reproductive Endocrinology**

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**【ABSTRACT】** Bisphenol A (BPA) is a kind of the industrial raw materials and exists in life products widely. BPA can enter the body by many ways, leading to disturb mammal endocrine. BPA is a known endocrine disruptor. At present, exposed BPA can induce many diseases, including neoplasia, developmental disabilities of brain, cardiovascular disease and hyperglycemia increased. This article will introduce the relationship between dosage and diseases during the period of fetus, newborn and adult.

**Key words:** bisphenol A (BPA); endocrine disruptor; xenoestrogen

# 复发性自然流产的病因学研究进展

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**【摘要】** 复发性自然流产病因繁杂, 目前已知的病因主要包括遗传因素(染色体数量和结构异常、单基因活性改变或突变等)、解剖因素(先天性子宫发育异常、子宫获得性异常、子宫血管异常等)、免疫因素(自身免疫抗体形成、封闭抗体减少、辅助性T淋巴细胞因子失衡、NK细胞活性增强等)、内分泌因素、感染因素、母亲躯体及心理健康和环境因素等。然而, 仍有50%的复发性自然流产病因不明。

**关键词:** 复发性自然流产(RSA); 病因; 研究进展

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## Study of Etiology in Recurrent Spontaneous Abortion

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**【ABSTRACT】** The etiology of recurrent spontaneous abortion (RSA) is very complex. The known causes of RSA include genetics factors (the abnormalities of chromosome number and structure, copy number variation and the mutation of single-gene), anatomic factors (congenital and acquired morphological abnormalities of uterine, uterine vascular malformation), immunologic factors (auto-antibodies formation, the lack of blocking antibodies, the imbalance of T-helper lymphocyte cytokine, increased activity of natural killer cell), endocrinological dysfunction, infection, maternal physical and psychological health problems, environmental factors. However, the causes of about 50% RSA cases remain to be clarified.

**Key words:** recurrent spontaneous abortion (RSA); etiology; study progress

• 临床报道 •

## 重复控制性卵巢刺激(COS)-IVF/ICSI治疗对 卵巢储备功能及反应性的影响

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**【摘要】** 目的: 探讨年轻女性在接受反复控制性卵巢刺激(COS)-IVF/ICSI治疗对卵巢储备功能及其反应性的变化。方法: 回顾性分析连续3次接受COS-IVF/ICSI-ET治疗周期的<35周岁的不孕症患者, 分析比较其实验室指标和临床结局。结果: 共纳入129例不孕症患者的387个周期。患者3个COS-IVF/ICSI治疗周期期间月经第3日的基础卵泡刺激素(basal follicle-stimulating hormone, bFSH)、窦卵泡计数(antral follicle count, AFC)、促排卵天数、hCG注射日E<sub>2</sub>峰值、获卵数、正常受精率及优质胚胎率均无统计学差异( $P>0.05$ ); 第2次和第3次治疗周期使用促性腺激素(gonadotropin, Gn)剂量明显高于第1次治疗, 差异具有统计学意义( $P<0.05$ )。结论: <35周岁重复COS-IVF/ICSI周期对卵巢储备功能无影响, 对其卵巢反应性有一定影响。

**关键词:** 重复COS-IVF/ICSI; 卵巢反应性; 卵巢储备; 促性腺激素剂量

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## Effect of Repeated COS-IVF/ICSI Treatment on Ovarian Reaction and Ovarian Reserve

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**【ABSTRACT】 Objective:** To investigate the possible effect of repeated control ovarian stimulation (COS)-IVF/ICSI treatment on ovarian reserve and reaction. **Methods:** Patients who were underwent three IVF/ICSI treatments and with female age <35 years old were retrospectively analyzed. The effect of repeated COS-IVF/ICSI treatment on the basal follicle-stimulating hormone (bFSH), the antral follicle count (AFC), the dosage required of gonadotropin (Gn), the number of oocytes retrieved, the fertilization rate and the high-quality embryo rate were compared. **Results:** A total of 129 infertile couples (387 cycles) were included. The dosage of Gn used was significantly higher in the second and third cycles than in the first cycle ( $P<0.05$ ). The results showed no statistically significant differences in all three cycles ( $P>0.05$ ) in terms of the number of oocytes retrieved, bFSH, AFC, the fertilization rate and the high-quality embryo rate. **Conclusion:** Repeated COS-IVF/ICSI treatment has no significantly adverse impact on the ovarian reserve of women aged <35 years old, but ovarian reaction is influenced in some degree.

**Key words:** repeated COS-IVF/ICSI treatment; ovarian reaction; ovarian reserve; the dosage required of gonadotropin (Gn)



## CD68、IL-6 和 IL-10 在子宫腺肌病患者 子宫内膜组织中的异常表达

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**【摘要】**目的: 探讨子宫腺肌病(AM)患者子宫内膜容受性下降的免疫学因素。方法: 分别收集AM患者( $n=18$ )、非AM患者( $n=17$ )在自然周期种植窗期和控制性超促排卵周期(COH)因故放弃移植的子宫内膜组织。再将AM患者分为自然周期组(A组,  $n=9$ )和COH周期组(B组,  $n=9$ ); 非AM患者也分为自然周期组(C组,  $n=7$ ), COH周期组(D组,  $n=10$ ), 采用免疫组织化学SP法检测内膜组织中CD68(巨噬细胞分子标志物)、IL-6、IL-10的表达。结果: CD68、IL-6在AM患者的内膜组织中表达较非AM患者增强( $P<0.05$ ); 而IL-10的表达则相反( $P<0.05$ ); 内膜组织中CD68、IL-6、IL-10的表达在A、B组间和C、D组间均无统计学差异( $P>0.05$ )。结论: AM患者在位内膜CD68、IL-6活性增强, 可能对胚胎产生毒性作用, 干扰局部免疫环境, 而具有妊娠保护作用的IL-10表达减低, 推测三者间的共同作用是导致AM患者内膜容受性下降的免疫学因素。

**关键词:** 子宫腺肌病(AM); 在位内膜; 免疫着床因子

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## Abnormal Expression of Immunity Factors CD68, IL-6 and IL-10 in Endometrial Tissues of Patients with Adenomyosis

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**【ABSTRACT】 Objective:** To investigate the immunological mechanism of decreasing endometrial receptivity of adenomyosis (AM). **Methods:** The eutopic endometrium was obtained from four groups of AM and non-AM patients during the window of implantation in natural cycle and controlled ovarian hyperstimulation (COH). Eighteen patients of AM were divided into group A of natural cycle ( $n=9$ ) and group B of COH ( $n=9$ ), 17 patients of non-AM were divided into group C of natural cycle ( $n=7$ ) and group D of COH ( $n=10$ ). CD68, IL-6 and IL-10 were detected by immunohistochemistry SP method. **Results:** The expressions of CD68 and IL-6 were stronger in the AM endometrium (groups A and B) than in the non-AM endometrium (groups C and D) with natural cycle and COH cycle ( $P<0.05$ ). While IL-10 was expressed more weakly in the AM endometrium than in the normal endometrium of non-AM ( $P<0.05$ ). There was no difference in the expression of CD68, IL-6 and IL-10 between groups A and B, the same between groups C and D ( $P>0.05$ ). **Conclusion:** There are increasing expressions of CD68 and IL-6 in the eutopic endometrium of AM, which may have toxicity effect on the embryo and interfere the local surroundings, while IL-10 which can protect the pregnancy was down-expressed. CD68, IL-6 and IL-10 may play an important role in the decreasing endometrium receptivity of AM.

**Key words:** adenomyosis (AM); eutopic endometrium; immunity factors on the window of implantation