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·专家风采·

孙莹璞教授

主任医师、医学博士、博士研究生导师; 郑州大学第一附属医院副院长兼生殖医学中心主任; 中华医学会生殖医学分会候任主任委员、中华医学会生殖医学分会实验室学组副组长; 河南省医学会生殖医学分会主任委员; 河南省医学会妇产科学分会副主任委员; 1997年创建了郑州大学第一附属医院生殖医学中心暨河南省生殖医学中心。2011年带领项目组完成了中国首例应用 SNP 微阵列技术进行胚胎植入前遗传学诊断试管婴儿并获临床妊娠和分娩, 带领的团队在卵子冷冻技术、胚胎植入前遗传学诊断技术及中期妊娠选择性减胎技术方面走在国内前列。承担国家自然科学基金项目 3 项, 卫生部科研基金、教育部 211 工程三期重点学科建设项目及省厅级重大课题 20 多项, 发表论文 150 余篇。

黄国宁教授

主任医师, 硕士生导师, 专业方向: 妇产科学、生殖医学。享受国务院特殊津贴, 卫生部中青年突出贡献专家, 现任中华医学会第三届生殖医学分会副主任委员、秘书长, 实验室学组组长, 重庆市妇幼保健院生殖中心主任。在国内外刊物发表论文 80 余篇, SCI 论文 10 多篇。主编两部专著: 《体外受精-胚胎移植实验室技术》(人民卫生出版社), 《辅助生殖技术系列规范化培训教材——辅助生殖实验室技术》(人民卫生出版社), 副主编参编一部专著: 《生殖医学临床诊疗常规》(人民卫生出版社)。参与编写《临床诊疗手册——辅助生殖技术与精子库分册》(人民卫生出版社)等。目前担任《生殖与避孕》、《生殖医学杂志》、《实用妇产科杂志》、《国际生殖健康/计划生育杂志》和《重庆医学》等杂志的编委。

·述 评·

重视辅助生殖技术相关的遗传学检测及筛查

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辅助生殖技术(assisted reproductive technology, ART)经过 36 年的发展, 已经取得了长足的进步。近年来 ART 的妊娠率得到了很大的提高, 但抱婴回家率却一直徘徊在 20%~30%。胚胎着床失败及妊娠丢失是其中的重要原因。目前认为胚胎着床失败及妊娠丢失的原因复杂, 可能与胚胎的体外培养环境和子宫内膜环境、胚胎发育潜能、内分泌因素、免疫学及遗传学等诸多因素相关。但越来越多的研究显示遗传学因素在反复胚胎种植失败及早期妊娠丢失中扮演了重要的角色, 而辅助生殖实验室的工作是整个 ART 的重要一环。因此重

视 ART 相关的实验室工作及遗传学检测和筛查对提高临床妊娠率, 改善 ART 预后有着重要的意义。

1 重视助孕前的遗传学检测和咨询

对于不孕不育夫妇而言, 其遗传学检测尤为必要。统计数据显示不孕不育夫妇占已婚夫妇的 10% 左右。普通人群中染色体异常所占比例为 0.37%~1.86%, 而在不孕不育症人群中则高达 3.95%~14.30%。我们对 2004.01~2011.12 期间因不孕不育就诊于本中心的 14 965 对夫妇进行了外周血淋巴细胞 G 显带核型分析, 这也是目前全球已知的最大样本量的数据, 结果显示染色体异常的发生率为 3.84%(1 150/29 930), 是正常人群中的 3 倍左右; 男方异常染色体的发生率为 6.84%(1 024/14 965), 女方异常染色体的发生率为 0.84%(126/14 965)。

染色体异常与不孕不育密切相关。染色体数目和结构异常, 不仅导致夫妇复发性自然流产, 同时还会导致女方卵巢功能异常和男方睾丸生精功能异常。另外, 对于重度少弱精子症男性, 无精子相关因子(AZF)的检测也是有必要的。因此必须重视对助孕前不孕夫妇的遗传学检测及不孕夫妇遗传学异常后的遗传咨询, 采取必要的手段如胚胎植入前遗传学诊断/筛查植入前遗传学诊断/筛查(preimplantation genetic diagnosis/screening, PGD/PGS), 以降低流产风险, 改善临床助孕的预后。

2 重视助孕中的胚胎 PGD/PGS

对于复发性自然流产、反复种植失败及染色体异常等的不孕不育夫妇, 必须重视胚胎 PGD 和 PGS。PGD 是在体外受精过程中, 对具有遗传风险夫妇的卵裂期胚胎或囊胚进行细胞活检和遗传学诊断, 以选择正常的胚胎移植, 从而获得健康后代的方法, 因此PGD可以避免孕妇在诊断出胎儿异常或有严重遗传学疾病的情况下面临选择流产或引产的难题, 减少患者生理及精神上的伤害及伦理问题。PGD 的目的不仅可避免遗传性疾病, 还可使因有遗传问题而不能生育的夫妇顺利生育健康的婴儿。因此它是 ART 的一个重要的、不可或缺的组成部分。

PGD/PGS 活检取材主要是极体、卵裂球和滋养外胚层细胞。目前越来越多的研究显示滋养外胚层细胞活检有更多的优势, 如获得的检测标本量更多, 诊断的误差更小及对胚胎的损伤更小。另外对于单细胞诊断技术而言, 传统的诊断方法如聚合酶链反应(PCR)和荧光原位杂交(FISH)因为其局限性, 逐渐被新的高通量的诊断方法如比较基因组杂交(CGH)技术、单核苷酸多态性微阵列(SNP array)技术及二代测序等新方法所替代。越来越多的研究显示新的高通量的诊断方法有明显的优势, 如降低诊断误差, 提高临床妊娠率及改善临床结局。因此, 随着诊断技术的不断改进, 必须重视胚胎 PGD/PGS 在 ART 中的临床应用。

3 重视妊娠后的遗传学诊断

与自然妊娠一样, ART 妊娠成功后必须重视产前诊断及妊娠丢失物的遗传学检测。自然妊娠后产前诊断的重要性毋容置疑, 对于 ART 妊娠后的产前诊断更要受到重视。尤其对于高龄夫妇、PGD 成功妊娠的夫妇尤为必要。

另外需重视流产组织的遗传学检测。高比例的妊娠丢失率是影响 ART 成功率的重要原因之一。目前普遍认为自然妊娠后的自然流产与胚胎染色体异常密切相关, 50%以上自然妊娠后的自然流产胚胎有不同程度和类型的染色体异常。而对于 ART 治疗获得的妊娠, 妊娠丢失率为 22%~63%, 其中 58% 发生在妊娠 6 周以前, 妊娠 6 周的妊娠丢失率达 10%~45%。ART 自然流产的原因复杂, 目前尚不清楚, 但通过对绒毛标本的核型分析提示胚胎染色体异常仍然是其重要的原因之一。我们中心截止目前采用 SNP 基因芯片对 455 例流产组织进行了分子核型分析, 结果显示异常比例为 72.7%(331/455)。因此必须重视妊娠后流产组织的遗传学检测, 这对指导下次助孕治疗、获得良好的临床结局有重要的作用。

4 重视辅助生殖实验室工作及过程的安全性

经过近 30 多年的发展, 辅助生殖实验室不但开展日常体外受精、胚胎培养工作, 还开展了生物化学和细胞生物学等的研究, 人们不断地研究和改善体外受精、胚胎培养的技术, 同时也越来越关注实验室的质量控制和管理体系, 以达到安全和高效的目的, 最大限度地保障 ART 能够安全、有效。

总之, 生殖与遗传密切相关, 必须重视 ART 相关的遗传学检测及筛查, 以降低流产风险, 提高临床妊娠率以改善临床结局。毋庸置疑, 辅助生殖实验室技术是整个 ART 的一个重要组成部分, 随着实验室技术, 包括遗传学诊断方法和技术的不断改进, ART 的安全性和有效性将不断提高。ART 相关的遗传学检测及筛查对提高人口素质、降低人口出生缺陷及改善辅助生殖的临床结局都有重要意义。

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胚胎发育与表观遗传修饰

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随着辅助生殖技术(assitsted reproductive technology, ART)的发展, 目前关于胚胎发育的研究已经获得长足的进步, ART治疗的临床妊娠率不断提高, 伴随胚胎植入前遗传学诊断技术(preimplantation genetic diagnosis, PGD)的发展, 遗传学在人类胚胎选择过程中扮演着越来越重要的角色, 由最初的荧光原位杂交法(florescence *in situ* hybridization, FISH)-PGD 历经比较基因组杂交技术(comparative genomic hybridization, CGH)、微阵列比较基因组杂交技术(array comparative genomic hybridization, aCGH)、单核苷酸多肽性分析技术(single-nucleotide polymorphism, SNP)至第二代 DNA 测序技术。新技术的出现使得遗传学由最初的只检测有限几条染色体数目异常, 历经检测染色体整倍性、大片段碱基缺失 / 突变, 至现在检测单基因疾病的发展, 使得遗传学在胚胎诊断及选择发面发挥着越来越重要的作用。同时, 遗传学诊断技术也验证了新兴胚胎选择技术, 如胚胎时差成像培养系统和胚胎呼吸率等在胚胎培养及发育过程中的积极作用。

但是, 表观遗传学在胚胎发育过程中的作用及调控研究较少。表观遗传修饰是指DNA序列不发生变化, 但基因表达却发生了可遗传性的改变, 主要包括 DNA 甲基化和组蛋白修饰, DNA 甲基化通过 DNA 甲基化转移酶(DNA methyltransferases, DNMT)完成, 催化甲基结合到 DNA 碱基的胞嘧啶 5’ 端位置, 引起基因沉默。组蛋白修饰包括(不仅限于)丝氨酸残基的磷酸化, 赖氨酸残基的乙酰化, 赖氨酸 / 精氨酸残基的甲基化等, 组蛋白修饰可以改变染色质的疏松程度, 进而改变基因转录活性。

DNA 甲基化在生殖细胞和早期胚胎发育阶段经历了基因组范围内重编程。基因的 2 次 DNA 甲基化重编程发生在配子形成和早期胚胎发育阶段, 在这两个阶段会发生全基因组范围的DNA去甲基化后再重新甲基化。第一阶段的 DNA 甲基化重编程是亲代印迹基因去除和重新确立所必需的, 第二阶段的 DNA 甲基化重编程是受精卵获得全能性并产生新个体所必需的。DNA 甲基化对胚胎发育主要具有抑制基因表达、使雌性 X 染色体失活、调控印迹基因表达、沉默转座原件和调控组织特异性基因表达的作用。DNA 甲基化修饰异常会对胚胎发育产生影响。DNMT 的缺失会引起胚胎发育异常甚至死亡, 其原因可能与 DNA 甲基化水平降低, 甲基化模式紊乱以及等位基因丢失有关。人类胚胎染色体主要包括 5 种组蛋白, 即核心组蛋白 H2A、H2B、H3、H4 和连接组蛋白, 通过与染色质的结合，改变染色质的结构, 进而参与卵母细胞的成熟, 也可重塑受精卵中精子染色质。

表观遗传修饰变化引起的疾病总称为印记错乱, 主要包括: X 染色体失活、Beckwit-Wiedemann综合征、Angelman 综合征、Prader-Willi 综合征、Angelman 综合征、眼部遗传癌症及肾脏遗传癌症等。试管婴儿奠基人 Edwards 早在 2003 年就表达了超促排卵、取卵操作、胚胎培养等非生理环境对胚胎及子代的表观遗传学改变(印记错乱)的担忧, Shawn等2014的研究表明, 与正常人相比不孕患者胚胎表观遗传学调控因子的表达存在差异, 可能是由于胚胎长时间体外培养过程中选择性添加生长因子阻止了表观遗传学修饰。2014 年 Lazaraviciute 等研究提示, 接受 ART 助孕所产子代相比于正常受孕子代, 总印记错乱的发生几率增加。

综上, 通过对早期胚胎发育过程中的遗传学修饰研究, 不仅仅可以提高胚胎发育潜能, 也可以为由表观遗传学异常引起的患先天性缺陷疾病预防, 提供理论基础。ART 技术带来的大量非生理性操作, 是否会导致胚胎表观遗传学修饰的异常, 以及是否会增加胎儿的安全性风险, 也是亟待需要深入研究的重要课题。

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· 专 题 讨 论 ·

一种基于微流控芯片的胚胎动态培养方法

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【摘要】目的: 建立一种接近生理状态的胚胎动态培养方法。**方法**: 按功能设计和构建微流控芯片, 使小鼠体外受精卵在微流控芯片微孔中接受持续的灌注培养, 同时模拟输卵管收缩和纤毛运动引起的流体机械刺激和生化刺激, 并与常规微滴培养法比较, 监测胚胎发育情况和囊胚形成率。**结果**: 微流控芯片动态培养方法可显著改善胚胎的质量。与常规微滴培养法相比, 微流控动态培养获得的 4- 细胞胚胎、桑椹胚和囊胚形成率均有显著提高(68.4 ± 1.2% *vs* 53.2 ± 2.5%; 55.3 ± 2.6% *vs* 45.5 ± 3.3%; 40.5 ± 2.7% *vs* 35.5 ± 2.3%)(P<0.05)。而 2 种方法获得的卵裂率无统计学差异(75.5 ± 3.2% *vs* 73.9 ± 4.2%, P>0.05)。**结论**: 在微流控芯片上实现了小鼠近生理状态的胚胎培养, 显著改善了胚胎质量, 有希望成为一种胚胎培养的有力工具。

关键词: 微流控芯片; 动态培养; 胚胎发育

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A Dynamic Method of Embryo Culture Based on A Microfluidic Chip

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【**ABSTRACT**】**Objective**: To develop a microfluidic chip for embryo dynamic culture method nearly physiological status. **Methods**: A microfluidic chip was designed and fabricated for testing the influence of continual fluid flow on embryo development. This gave rise to design of a microfluidics system using microchannels as conduits for fluid flow through a 16-microcellular where mouse embryos resided by mimicking the fluid-mechanical and biochemical stimulation embryos experience *in vivo* from ciliary currents and oviductal contractions. And compared with conventional droplet culture method, monitoring of the embryonic development conditions and blastocyst formation rate. **Results**: The microfluidic chip dynamic culture method can significantly improve the embryo development. The microfluidic dynamic method was superior to the microdrop-static method in *terms of 4-cell embryo rate (68.4* ± 1.2% *vs* 53.2 ± 2.5%), morula rate (55.3 ± 2.6% *vs* 45.5 ± 3.3%) and blastocyst rate (45.5 ± 2.7% *vs* 35.5 ± 2.3%)(P<0.05). These two methods didn't show significant difference in the rate of 2-cell embryos (75.5 ± 3.2% *vs* 73.9 ± 4.2%, P>0.05). **Conclusion**: Physiological embryo culture was achieved on a microfluidic chip. This microfluidic method was able to improve embryo development and showed advantage over the conventional method, which was expected to serve as a powerful tool for embryo culture in the future.

Key words: microfluidic chip; dynamic culture; embryo development

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可溶性人类白细胞抗原G与胚胎发育关系的初步研究

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【摘要】目的: 探讨卵裂期胚胎可溶性人类白细胞抗原G(sHLA-G)表达与胚胎发育和种植的关系。**方法:** 收集受精后第2日和第3日的单胚胎培养液300份, 应用流式微球技术(CBA)检测其中sHLA-G的含量, 并设置阴性对照(不含有胚胎的胚胎培养上清液)。妊娠组和未妊娠组移植胚胎各100枚。A组移植胚胎均为sHLA-G阳性, B组移植胚胎至少1枚为sHLA-G阴性, C组移植胚胎均为sHLA-G阴性。分析单胚胎培养液sHLA-G的表达与临床妊娠率和种植率的关系。**结果:** ①妊娠组第3日胚胎培养液中平均sHLA-G水平明显高于未妊娠组(P<0.05)。②妊娠组第3日平均sHLA-G水平高于第2日(P<0.05), 但未妊娠组第3日平均sHLA-G水平升高不明显(P>0.05)。③ A组种植率最高, 其次是B组, C组最低(P<0.05)。④优质胚胎(≥6-细胞Ⅱ级)的平均sHLA-G水平妊娠组明显高于未妊娠组(P<0.05)。**结论:** 胚胎培养液中sHLA-G的表达水平与胚胎的发育潜能及其种植能力间存在正相关关系。若将第3日sHLA-G浓度(尤其是第2日及第3日sHLA-G浓度变化情况)和胚胎形态学参数评估联合作为选择最优移植胚胎的标准, 有望为单胚胎移植提供参考数据。

关键词: 可溶性人类白细胞抗原G(sHLA-G); IVF-ET; 胚胎发育潜能; 流式微球(CBA); 胚胎培养液

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Preliminary Study on the Relationship of Soluble Human Leukocyte Antigen-G (sHLA-G) with Embryonic Development

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【**ABSTRACT**】**Objective**: To investigate the relationship of soluble human leukocyte antigen-G (sHLA-G) expression with embryo development and implantation by qualitative and quantitative analysis of this molecule in culture medium from single human embryo at different cleavage stages. **Methods**: The single embryo culture medium on day 2 and day 3 after fertilization was collected, and the values of sHLA-G in the media were detected by the flow cytometry microsphere array (CBA). The media without embryo kept under the same condition as media with embryos, served as negative controls. A total of 300 copies of culture media from single embryo were detected for the expression of sHLA-G. The patients who received embryo transfer divided into pregnancy and non-pregnancy groups. In each group, a total of 100 embryos cultured in media being checked for the expression of sHLA-G were transferred. Ninty-four patients received embryo transfer and were divided into three groups according to the values of sHLA-G detected in culture media from transferred embryos. Patients with all the transferred embryos cultured in media being tested positive for HLA-G were classified as group A, for those patients with at least one transferred embryo cultured in media being tested negative for HLA-G were classified as group B, and patients with all the transferred embryos cultured in media being tested negative for HLA-G were classified as group C. The relationship between the expression of sHLA-G in single-embryo culture medium and clinical pregnancy rate and implantation rate was analyzed. **Results**: 1) The mean levels of sHLA-G on day 3 of embryo culture media in pregnancy group were significantly higher than those in non-pregnancy group (P<0.05). 2) The mean levels of sHLA-G on day 3 in pregnancy group were higher than those on day 2 (P<0.05), but in non-pregnancy group, there were no significant differences of mean sHLA-G levels between day 2 and day 3 (P>0.05). 3) The implantation rate of group A was the highest, followed by group B, and that of group C was the lowest (P<0.05). 4) In pregnancy group, the mean sHLA-G levels in culture media from high-quality embryos (≥ class **II /6-cell stage) were significantly higher than those in non-pregnancy group (**P<0.05). **Conclusion**: There was a positive relationship between the sHLA-G expression levels in embryo culture medium and the developmental potential and implantation capability of embryos. sHLA-G levels on day 3 (in particular the changes of sHLA-G during day 2 and 3) in combination with embryo morphology parameters may be as a standard for seclecting the best embryos for transfer and may provide a reference data for single embryo transfer.

Key words: soluble human leukocyte antigen-G (sHLA-G); IVF-ET; embryonic developmental potential; flow cytometric bead array; embryo culture medium

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自然流产患者绒毛与复发性流产患者胚胎植入前遗传学筛查微阵列比较基因组杂交结果对比分析

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【摘要】 目的: 探讨植入前遗传学筛查(PGS)降低复发性流产(RSA)患者早期流产率的可能原因及临床意义。**方法:** 通过微阵列比较基因组杂交(aCGH)检测, 统计自然流产(SA)患者绒毛染色体非整倍性异常高发核型, 分析该高发核型在RSA患者胚胎中的发生几率。**结果:** SA患者绒毛中16、X、15号3条染色体的非整倍性占绒毛染色体非整倍性异常的52.27%; 在RSA患者胚胎中, 该3条染色体非整倍性占胚胎染色体非整倍性异常的50.50%。**结论:** SA患者绒毛染色体异常类型相对集中, 具有明显的高发核型; RSA患者胚胎染色体非整倍性高发核型与流产绒毛相一致, 提示对RSA患者行PGS助孕, 可规避染色体异常胚胎的着床, 从而降低早期流产率。

关键词: 植入前遗传学筛查(PGS); 微阵列比较基因组杂交(aCGH); 复发性流产(RSA); 自然流产(SA); 染色体非整倍性

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Comparative Analysis by aCGH in Patients with Spontaneous Abortion Villus and PGS Embryos with Recurrent Spontaneous Abortion

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【**ABSTRACT**】**Objective**: To investigate the possible mechanism and clinical worth of preimplantation genetic screening (PGS) in reducing early abortion rate in patients with recurrent spontaneous abortion (RSA). **Methods**: By the microarray comparative genomic hybridization (aCGH) detection, the aneuploidy karyotypes which had the high frequency appeared in the villus from patients with spontaneous abortion (SA) were explored. And then, the occurrence probability of these aneuploidy karyotypes in embryos from patients with RSA were detected. **Results**: The percent of villus with aneuploidy of 16, X or 15 was 52.27% in all aneuploidy anomalies villus from the patients with SA. And the percent of such aneuploidy was 50.50% in all aneuploidy anomalies embryos from the patients with RSA. **Conclusion**: The abnormal chromosome types which appear with high frequency in villus from the patients with SA also present a high frequency in embryos from the patients with RSA. It suggests that applying PGS in RSA patients is helpful to avoid implantation of chromosome abnormality embryos and reduce the early abortion rate.

Key words: preimplantation genetic screening (PGS); array comparative genomic hybridization (aCGH); recurrent spontaneous abortion (RSA); spontaneous abortion (SA); aneuploidy

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透明带激光削薄法在玻璃化冻融胚胎移植中的作用

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【摘要】 目的: 为探讨激光削薄法对冻融胚胎移植结局的影响。**方法**: 选取分裂期胚胎移植组 372 个周期、囊胚期胚胎移植组 81 个周期以及反复种植失败(既往移植失败≥2 次)移植组 128 个周期, 分别按解冻单、双日将周期解冻胚胎分为激光削薄组和对照组, 激光削薄组胚胎于移植前行卵透明带激光削薄处理, 对照组胚胎不进行削薄处理, 分析比较各组间的实验室和临床效果。**结果**: 移植分裂期胚胎组患者的生化妊娠率、临床妊娠率及胚胎种植率激光削薄组与对照组相*比无统计学差异*(49.11% *vs* 48.28%, 42.01% *vs* 42.36%, 28.66% *vs* 28.35%, $P>0.05$); 囊胚期胚*胎激光削薄组患者的上述移植结局与对照组比较亦无统计学差异*(60.47% *vs* 63.16%, 48.84% *vs* 55.26%, 37.88% *vs* 38.57%, $P>0.05$); 反复种植失败患者的冻融胚胎经激光削薄法处理后没有改*善其妊娠结局*(43.33% *vs* 45.59%, 36.67% *vs* 39.71%, 25.23% *vs* 26.15%, $P>0.05$), 但是在囊胚期胚*胎和反复种植失败患者中*, 患者移植后的流产率激光削薄组较对照组有增高的趋势(19.05% *vs* 4.76%, $P=0.153$; 36.36% *vs* 11.11%, $P=0.035$), 其中反复种植失败激光削薄组显著高于对照组($P<0.05$)。**结论**: 透明带激光削薄辅助孵化技术并不能有效改善冻融胚胎移植患者的妊娠结局, 其远期安全性有待于进一步研究。

关键词: 激光; 辅助孵化(AH); 玻璃化冷冻; 胚胎移植(ET)

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Effect of Laser Thinning Assisted Hatching on Vitrified-warmed Embryo Transfer

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【**ABSTRACT**】 **Objective**: To explore the effect of laser thinning assisted hatching on frozen-thawed embryo transfer outcome. **Methods**: Selected embryos from 372 cleavage stage embryo transfer cycles, 81 blastocyst transfer cycles and 128 repeated implantation failure cycles were processed, and divided into laser thinning group and control group respectively according to odd-numbered days and even-numbered days of embryo thawed day. The embryos in laser thinning group received laser thinning assisted hatching (AH) treatment before fertilization, and which in control group did not. The laboratory and clinical outcomes were compared between the two groups. **Results**: The biochemical pregnancy rate, the clinical pregnancy rate and the implantation rate in the assisted hatching cleavage stage embryo group showed no significant differences with those of the control (49.11% *vs* 48.28%, 42.01% *vs* 42.36%, 28.66% *vs* 28.35%, $P>0.05$); There was no statistical difference of biochemical pregnancy rate, clinical pregnancy rate and implantation rate between the assisted hatching blastocyst group and the control group (60.47% *vs* 63.16%, 48.84% *vs* 55.26%, 37.88% *vs* 38.57%, $P>0.05$); the application of laser assisted hatching did not improve the pregnancy outcomes of repeated implantation failure patients (43.33% *vs* 45.59%, 36.67% *vs* 39.71%, 25.23% *vs* 26.15%, $P>0.05$). However, in the blastocyst transfer patients and repeated implantation failure patients, there was an increasing trend of abortion rate in laser assisted hatching **group (19.05%** *vs* 4.76%, $P=0.153$; 36.36% *vs* 11.11%, $P=0.035$). **Conclusion**: The laser assisted hatching technique does not improve pregnancy outcomes of frozen-thawed embryo transfer patients, and its long-term safety needs further study. The clinical application of this method should be cautious.

Key words: laser; assisted hatching (AH); vitrification freezing; embryo transfer (ET)

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人类不同时期未成熟卵母细胞玻璃化冷冻后发育潜能的比较

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【摘要】目的: 探索未成熟卵子的最佳冷冻时期。 **方法**: 收集卵胞质内单精子显微注射 - 胚胎移植(ICSI-ET)周期中未成熟的卵母细胞, 按其成熟度分为生发泡期(GV组)卵子179枚和第一次减数分裂中期(M_I组)卵子 323 枚, 所有卵子均经玻璃化冷冻, 解冻后行体外成熟(IVM)培养, ICSI 受精, 观察比较 GV 组和 M_I 组解冻后存活、体外成熟、受精及胚胎发育情况。**结果**: GV 组复苏存活率显著高于 M_I 组(83.24% *vs* 75.54%, *P*=0.045), M_I 组体外成熟率、受精率、卵裂率、优质胚胎率均略均高于 GV 组, 但无统计学差异(*P*>0.05), M_I 组可利用胚胎率显著高于 GV 组(78.67% *vs* 60.53%, *P*=0.041)。**结论**: 超促排卵周期中未成熟卵母细胞先玻璃化冷冻保存, 再行体外培养是可行的。GV 期卵母细胞复苏存活率高于M_I期卵母细胞, 但M_I期卵母细胞冻融后发育潜能优于GV组卵母细胞。

关键词: 未成熟卵母细胞; 玻璃化冷冻; 体外成熟; 发育潜能

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Study on Developmental Potential of Human Immature Oocytes at Different Developmental Stages after Vitrification

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【**ABSTRACT**】**Objective**: To explore the best vitrification stage of human immature oocytes. **Methods**: A total of 502 suplurs immature oocytes (GV group, *n*=179 and M_I group, *n*=323) were obtained from patients who underwent intracytoplamic sperm injection (ICSI) cycles. Frozen-thawed immature oocytes treated with *in vitro* maturation (IVM) in both groups were inseminated by ICSI. The injected oocytes were cultured in cleavage medium. The rates of survival, maturation, fertilization and early embryonic development were observed in these two groups. **Results**: Survival rate was significantly higher in GV group than in M_I group (83.24% *vs* 75.54%, *P*=0.045). The available embryo rate was significantly lower in GV group than in M_I group (60.53% *vs* 78.67%, *P*=0.041). There were no significant differences in the rates of maturation, fertilization, cleavage, day 3 good-quality embryos and blastocyst between the two groups (*P*>0.05). **Conclusion**: 1) The human immature oocytes derived from controlled ovarian hyperstimulation (COH) cycles can be well cryopreserved by using vitrification method because of high survival rate, fertilization rate, cleavage rate and available embryo rate. So these immature oocytes should be fully utilized. 2) The immature oocytes at GV stage can be more effectively vitrified than that at the M_I stages. But developmental potential of immature oocytes in M_I group was superior to that in GV group.

Key words: immature oocytes; vitrification; *in vitro* maturation (IVM); developmental potential

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IVF-ET后胚胎停育患者绒毛染色体异常的影响因素

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【摘要】 目的: 探讨常规体外受精 - 胚胎移植(IVF-ET)后胚胎停育患者绒毛染色体异常的相关影响因素。**方法**: 回顾性分析 IVF-ET 后胚胎停育的 61 个周期, 按绒毛染色体单核苷酸多态性(SNP)分子核型检测结果分为分子核型正常组(A 组)和分子核型异常组(B 组), 分析比较 A、B 组间对象的临床特征及实验室指标等。**结果**: 未限制年龄时, 女方 BMI、流产次数、COH 次数、不孕年限、*女方基础*FSH、Gn 用量及获卵数 A、B 组间差异均无统计学意义(P>0.05), A 组男方年龄、女方年*龄*、*移植胚胎数小于*B 组, 差异均有统计学意义(P<0.05), 正常形态精子比率、头部缺陷精子比率、颈部和中段缺陷精子比率、尾部缺陷精子比率、胞质水滴缺陷精子比率、畸形精子症比例组间均无统计学差异(P>0.05)。女方年龄<35 岁时, A、B 组间上述各指标差异均无统计学意义(P>0.05)。**结论**: 女方年龄与 IVF-ET 后绒毛染色体异常有关, 精子形态学指标对 IVF-ET 后胚胎停育患者绒毛染色体分子核型检测结果无预测价值。

关键词: 精子形态; 体外受精(IVF); 胚胎停育; 绒毛染色体; 异常

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Influencing Factors for Abnormal Molecular Karyotype of Villi Chromosome for Embryonic Arrest after IVF-ET

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【**ABSTRACT**】**Objective**: To study the influencing factors which result in abnormal molecular karyotype of villi **chromosome for embryonic arrest after** *in vitro* fertilization and embryo transfer (IVF-ET). **Methods**: A total of 61 cycles of embryonic arrest after IVF-ET were retrospectively surveyed. They were divided into two groups based on the outcomes of single nucleotide polymorphism microarray (SNP array) in molecular karyotype analysis for villi chromosome: group A with normal molecular karyotype, group B with abnormal molecular karyotype. The paternal age, woman's body mass index (BMI), infertility duration, the times of abortion, woman's basal FSH level, the number of controlled ovarian hyperstimulation, total gonadotropin dose, the number of oocytes retrieved, the number of embryo transfer and sperm morphology were compared between group A and group B. **Results**: Before controlling the woman's age, there was a significant difference bewteen the two groups in the woman's age, man's age and the number of embryos transferred ($P<0.05$), but there was no difference in the normal form rate, head defect rate, neck and midpiece defect rate, principal piece defect rate, excess residual cytoplasm (ERC) rate and teratozoospermia rate ($P>0.05$). After controlling the woman's age, there was no significant **difference between the two groups in these indexes for the women less than 35 years old (**$P>0.05$). **Conclusion**: There is a significant influence of woman's age on the outcomes of SNP array in molecular karyotype analysis of villi chromosome for embryonic arrest after IVF but not sperm morphology.

Key words: sperm morphology; *in vitro* fertilization (IVF); embryonic arrest; villi chromosome; abnormal

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女性年龄与早期自然流产胚胎染色体数目异常的关系

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【摘要】目的: 探讨辅助生殖和自然妊娠中女性年龄与早期自然流产绒毛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(MLPA)对 55 例自然妊娠(NC)、147 例体外受精(IVF)妊娠和 85 例卵胞质内单精子注射(ICSI)妊娠孕早期自然流产的绒毛组织进行染色体数目检测, 比较不同妊娠方式、不同染色体、不同异常染色体个数间女性年龄和非整倍体的关系。 **结果**: NC 组和 IVF 组中非整倍体的孕妇年龄显著高于绒毛染色体正常的孕妇年龄(NC 组: 35.0 ± 5.0 岁 *vs* 31.6 ± 4.1 岁, *P*=0.014; IVF 组: 35.2 ± 4.5 岁 *vs* 32.1 ± 4.6 岁, *P*=0.000), 而 ICSI 组中无统计学差异(34.4 ± 5.1 岁 *vs* 33.5 ± 4.1 岁, *P*=0.391); NC 组和 IVF 组随孕妇年龄的增长流产儿非整倍体率递增, IVF 组有统计学差异(*P*=0.002), 但 ICSI 组未观察到该现象。15、20、21 和 22 号染色体异常率随孕妇年龄的增长递增, 其中 20、21 号染色体有统计学差异(*P*<0.05); 13 号染色体异常率在 40~47 岁亚组中显著增高(*P*=0.027); 16 号染色体在各孕母年龄段的异常率相近; 性染色体异常率在 40~47 岁亚组中降低。多重非整倍体组的孕妇年龄显著高于单一非整倍体组(37.4 ± 5.3 岁 *vs* 34.9 ± 4.6 岁, *P*=0.039), 40¯47 岁亚组中多重非整倍体发生率显著增高(*P*<0.05)。 **结论**: 女性高龄是 NC 和 IVF 妊娠非整倍体胎儿的高危因素, 而 ICSI 可能还存在其他机制导致胎儿染色体异常。多重非整倍体及大部分小染色体非整倍体的流产儿多见于高龄孕妇, 而性染色体单体流产儿则多见于较年轻孕妇, 16-三体不存在母亲年龄效应。

关键词: 非整倍体; 高龄孕妇(AMA); 自然流产; 辅助生殖技术(ART); 绒毛

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Relationship between Maternal Age and Numerical Abnormalities of Fetal Chromosomes in Spontaneous Abortion during the First Trimester

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【**ABSTRACT**】**Objective**: To explore the relationship between maternal age and numerical abnormalities of chorionic villus chromosomes in spontaneous abortion during the first trimester following assisted reproductive *technology (ART) and natural conception (NC)*. **Methods**: A total of 55 cases of NC, 147 cases of *in vitro* fertilization (IVF) and 85 cases of intracytoplasmic sperm injection (ICSI) suffered from spontaneous abortion during the first trimester were enrolled in this study. Chorionic villus specimens were tested for the chromosome number by multiplex ligation-dependent probe amplification (MLPA) method. The relationship between maternal age and aneuploidy was compared among different pregnancy ways, different chromosomes and different numbers of abnormal chromosome. **Results**: Maternal age of abortuses with aneuploidy was significantly higher than that of abortuses without aneuploidy in NC and IVF groups (NC group: 35.0 ± 5.0 years *vs* 31.6 ± 4.1 years, *P*=0.014; IVF group: 35.2 ± 4.5 years *vs* 32.1 ± 4.6 years, *P*=0.000), but not in ICSI group (34.4 ± 5.1 years *vs* 33.5 ± 4.1 years, *P*=0.391). Abortus' aneuploidy rate increased with maternal age in NC and IVF groups but not in ICSI group, while statistical difference was observed in IVF group (*P*=0.002). An increase in abnormal rates of chromosomes 15, 20, 21 and 22 was noted with increasing maternal age and this tendency of chromosomes 20 and 21 demonstrated statistical differences (*P*<0.05). Abnormal rate of chromosome 13 was significantly increased in ≥ 40-year subgroup (*P*=0.027). Abnormal rates of chromosome 16 were similar in different maternal age subgroups. Sex chromosome's abnormal rate of 40–49-year subgroup decreased. Maternal age of abortuses with multiple aneuploidy was significantly higher than that with single aneuploidy (37.4 ± 5.3 years *vs* 34.9 ± 4.6 years, *P*=0.039), as well as the incidence of multiple aneuploidy in ≥ 40-year subgroup was **significantly higher than that in other three subgroups (***P*<0.05). **Conclusion**: Advanced maternal age is a high risk factor to conceive aneuploidy fetuses in NC and IVF groups, but additional mechanisms may be also involved in causing the foetal chromosome abnormality in ICSI group. Abortuses with multiple aneuploidy and with most of small chromosomes' aneuploidy occur predominantly in advanced maternal age, whereas abortuses with Turner syndrome are more common in the young gravidas. Effect of maternal age on trisomy 16 does not exist.

Key words: aneuploidy; advanced maternal age (AMA); spontaneous abortion; assisted reproductive technology (ART); chorionic villus

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石家庄地区生育障碍者的细胞遗传学分析

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【摘要】目的: 探讨石家庄地区生育障碍者的染色体异常状况, 了解不同疾病与异常核型间的关系。**方法**: 收集石家庄地区生育障碍者的外周血淋巴细胞进行培养, 制片, G显带, 行染色体核型分析。**结果**: 收集到的 3 558 例生殖障碍者中, 共检出染色体核型异常 327 例, 包括数目和结构异常 166 例, 染色体多态 161 例, 异常率为 9.19%。其中 1 347 对(2 694 例)不良孕产史夫妇的染色体异常检出率为 6.27%, 769 例男性不育患者的染色体异常检出率为 19.12%, 95 例闭经 / 性腺发育不良患者的染色体异常检出率为 11.58%。**结论**: 染色体异常是导致反复流产、生育畸形儿、原发闭经、性腺发育异常等生育障碍的重要原因之一, 进行染色体检查有助于患者的临床诊断与治疗。

关键词: 不良孕产史; 自然流产; 不育; 闭经; 染色体

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Cytogenetic Analysis of Reproductive Disorder Patients in Shijiazhuang Area

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【**ABSTRACT**】 **Objective**: To investigate the relationship between chromosome abnormality and patients with different reproductive disorders. **Methods**: Patients with reproductive disorders in Shijiazhuang area were collected. G banding techniques were used by regular culturing lymphocytes of peripheral blood, then the chromosome karyotypes were analyzed. **Results**: There were 327 cases of abnormal karyotypes in 3 558 patients with reproductive disorder. The abnormality rate was 9.19%. The abnormality rates of abnormal pregnancy history group (1 347 couples), male infertility group (769 cases) and amenorrhea/abnormal gonadal development group (95 cases) were 6.27%, 19.12% and 11.58%, respectively. **Conclusion**: Chromosomal abnormality is one of the important reasons for the habitual abortion, child deformity, primary amenorrhea and infertility, etc. Chromosome karyotyping is necessary for clinical diagnosis and treatment of such patients. It can provide an important basis for fertility guidance, which will decrease the birth defect rate and improve population quality.

Key words: abnormal pregnancy history; spontaneous abortion; infertility; amenorrhea; chromosome

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胚胎显微操作与妊娠早期人血清 β-hCG 值的关系

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【摘要】目的: 探讨辅助生殖技术(ART)中的胚胎显微操作与妊娠早期血清 β-hCG 值的关系。**方法**: 回顾性分析体外受精/卵胞质内单精子注射/胚胎植入前遗传学诊断(IVF/ICSI/PGD)新鲜囊胚移植的 259 个宫内妊娠周期, 根据移植胚胎数及不同周期类型分组, 比较移植 14 d、18 d 血清 β-hCG 水平的差异。**结果**: 单囊胚移植组中, 行 IVF 周期、ICSI 周期和 PGD 周期间妊娠早期的血清 β-hCG 有统计学差异, 其中常规移植 14 d IVF 周期血清 β-hCG 值为 877.31 ± 480.40 IU/L, 显著高于 ICSI 周期 711.86 ± 485.64 IU/L, P<0.05。移植 18 d 时, 两者血清 β-hCG 无统计学差异(4 198.32 ± 2 306.48 IU/L *vs* 3 763.75 ± 2 268.87 IU/L, P>0.05)。而 PGD 周期移植 14 d 血清 β-hCG 值为 556.22 ± 418.94 IU/L, 18 d 为 3 027.22 ± 2 455.80 IU/L, 与 IVF、ICSI 周期相比均有显著统计学差异(®P<0.05); 双囊胚移植组中, IVF 周期、ICSI 周期及 PGD 周期各组间 14 d、18 d 血清 β-hCG 比较差异均无统计学意义(P>0.05)。**结论**: 判断行 ICSI、PGD 周期患者妊娠与否时适度降低评估患者妊娠早期(移植 14 d、18 d)有效妊娠血清 β-hCG 值标准是可行且必要的。

关键词: 血清 β-hCG; 体外受精 - 胚胎移植(IVF-ET); 卵胞质内单精子显微注射(ICSI); 胚胎植入前遗传学诊断(PGD)

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Relationship between Micromanipulation upon Gametes or Embryos and Serum β-hCG Level in Early Pregnancy

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【**ABSTRACT**】**Objective**: To investigate the relationship between micromanipulation in reproductive medicine and serum β-hCG level in early pregnancy. **Methods**: In this retrospective study, a total number of 820 patients who underwent fresh blastocyst transferred and obtained clinical pregnancy were analyzed. Serum β-hCG level and the rising range on day 14 and day 18 after blastocysts transfer were compared among the groups, which were divided according to the number of the blastocysts they transferred as well as the different assisted reproductive technology (ART) techniques they accepted. **Results**: In single blastocyst transfer group, patients undergoing intracytoplasmic sperm injection (ICSI) had a lower β-hCG level than those undergoing IVF and patients undergoing preimplantation genetic diagnosis (PGD) had a much lower level than that in IVF subgroup as well as ICSI subgroup. Both of the differences were statistical significant. While in two blastocysts transfer group although the patients' β-hCG level in ICSI and PGD subgroups were lower, there was no statistically significant difference. **Conclusion**: PGD may adversely affect serum β-hCG levels in early pregnancy. Setting a lower cut-off value for predicting a successful pregnancy in PGD could be helpful in counseling pregnant patients following PGD.

Key words: serum β-hCG; *in vitro* fertilization (IVF); intracytoplasmic sperm injection (ICSI); preimplantation genetic diagnosis (PGD)

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代谢组学在胚胎评估中的应用前景

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【摘要】胚胎发育能力的评估在人类辅助生殖技术中起很重要的作用。代谢物组学作为一种非侵入性检测手段可以客观地评价胚胎质量, 有良好的重复性; 可通过碳水化合物、氨基酸等代谢物评估胚胎及卵母细胞的发育潜能, 从而使代谢组学在辅助生殖领域有广阔的应用前景。

关键词: 代谢物组学; 胚胎; 卵母细胞

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Application of Metabonomics in Embryos Evaluation

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【**ABSTRACT**】Embryo viability assessment plays a vital role in the human assisted reproductive technology. Currently, the embryo grade is mainly based on morphological observation index. Metabolomics study, which acts as a noninvasive detection method, is able to evaluate the embryo quality objectively. Using the metabolomics to estimate the relationship between metabolites, such as carbohydrates and amino acids, and embryo or oocyte developmental potential. Metabolomics has broaded application prospects in the field of assisted reproduction.

Key words: metabolomics; embryo; oocyte

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微阵列技术在植入前遗传学筛查领域中的应用

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【摘要】 胚胎植入前遗传学筛查(preimplantation genetic screening, PGS)是一种低风险的植入前遗传学诊断(preimplantation genetic diagnosis, PGD)。如今各种技术方法的不断涌现并应用于临床PGD中, 大大增加了诊断的准确性, 降低了误诊风险。而近几年微阵列技术如阵列比较基因组杂交(aCGH)和单核苷酸多态性阵列(SNP)已应用于临床PGS研究中, 该项技术突破了以往经典遗传学检测技术如FISH等的诸多限制, 能够在全基因组范围内同时检测多种因染色体失衡导致的疾病、微重复、微缺失等, 检测结果更加精确、敏感, 并能检测到≥ 10% 水平的嵌合体。基于其各种优点, 可见微阵列技术在胚胎PGS中具有重要的应用前景。

关键词: 植入前遗传学筛查(PGS); 植入前遗传学诊断(PGD); 比较基因组杂交阵列(aCGH); 单核苷酸多态性(SNP); 全基因组扩增(WGA)

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Applications of Microarray Technology in the Field of Preimplantation Genetic Screening

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【ABSTRACT】 Preimplantation genetic screening (PGS) is a low-risk preimplantation genetic diagnosis (PGD). A variety of techniques and methods are emerging and applied to clinical PGD, which greatly increases the accuracy of diagnosis, reducing the risk of misdiagnosis. And in recent years, research and clinic proved that microarray technologies such as microarray array comparative genomic hybridization (aCGH) and single nucleotide polymorphism (SNP) array applied to PGS in order to improve assisted reproductive technology implantation and pregnancy rates, lower abortion rates and birth defects provided an effective method. The technological breakthroughs of the past classic genetic testing techniques such as FISH and so many restrictions, can simultaneously detect a variety of diseases caused by chromosomal imbalances, microduplication, microdeletions in genome-wide, test results were more accurate, sensitive, and even can detect ⩾10% level of mosaic. Based on its various advantages, microarray technology will have an important application prospect in preimplantation screening.

Key words: preimplantation genetic screening (PGS); preimplantation genetic diagnosis (PGD); array comparative genomic hybridization (aCGH); single nucleotide polymorphism (SNP); whole genome amplification (WGA)

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血友病A遗传诊断和基因治疗的研究进展

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【摘要】 血友病A是伴X连锁隐性遗传病, 其病因是由于位于X染色体上的编码凝血因子FⅧ基因缺陷导致机体凝血机制紊乱而出血不止, 严重危害患者的身体健康和生命安全。血友病A可通过直接法和间接法检测进行诊断, 对血友病A携带者可于孕早期进行有创或无创的胎儿遗传学诊断, 行辅助生殖的携带者可于胚胎植入前遗传学诊断(PGD)。对血友病A的基因治疗目前尚处于动物研究阶段, 主要通过基因转移载体来实现提高机体FⅧ的分泌, 其最珍贵的靶细胞是造血干细胞, 有望不久的将来更好地服务于血友病患者及携带者。

关键词: 血友病A; 遗传风险; 基因诊断; 植入前遗传学诊断(PGD); 基因治疗

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Advancement of Hemophilia A in Genetic Diagnosis and Gene Therapy Research

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【**ABSTRACT**】Hemophilia A is associated with X-linked recessive genetic disease. It's caused by coagulation factor Ⅷ gene defects located on Xq28 which leads to blood coagulation disorder and bleeding, and seriously affects the health and life. Hemophilia A can be diagnosed by direct methods and indirect methods. Prenatal genetic diagnosis for hemophilia A carriers in first trimester pregnancy can be done by invasive and noninvasive methods, including preimplantation genetic diagnosis (PGD) for hemophilia A carrier after assisted reproductive technology. Gene therapy research has be made great progresses in animal models. The secretion of F Ⅷ can be enhanced in hematopoietic stem cell by gene transfer vectors, which is the most valuable target cell. It will bring more advantages for hemophilia A patients and carriers in the near future.

Key words: hemophilia A; inherited risk; genetic diagnosis; preimplantation genetic diagnosis (PGD); gene therapy

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精子中DNA甲基化修饰研究进展

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【摘要】DNA甲基化是表观遗传学的重要内容之一, 精子在发生过程中经历了甲基化和去甲基化过程, 精子DNA甲基化修饰的稳定性依赖于鱼精蛋白, 不育男性精液质量的降低与精子基因组甲基化水平改变有关, 但目前大家研究基因位点多而杂, 这些位点甲基化模式的改变是否有相互联系尚不清楚, 研究热点集中在某一些生精相关的印记基因的甲基化水平改变比较多, 但其机制仍然模糊, 精子DNA甲基化修饰改变是否影响辅助生殖结果目前也有争论, 各种理化环境因素对精子中DNA甲基化修饰影响已被越来越多的研究者发现, 但具体机制有待进一步研究。

关键词: 表观遗传学; 精子甲基化; 男性不育; 精液质量

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Advances on Sperm DNA Methylation

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【**ABSTRACT**】DNA methylation is an important content of epigenetics, sperm DNA experienced methylation and demethylation in the process of spermatogenesis with its methylation modification depend on the stability of protamine, infertile men with lower quality of semen have sperm genome methylation level change, but now genetic loci we study are many and miscellaneous, whether there is a correlation with these locus of these methylation patterns change is not clear, the mechanism which researchers focused on some locus related to sperm production is still vague, whether these sperm DNA methylation modification changes have an influence on the outcome of assisted reproduction is controversial. More and more researchers have found that physical and chemical environmental factors have effects on the sperm DNA methylation modification, but the specific mechanism needs further research.

Key words: epigenetics; sperm methylation; male infertility; semen parameters

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卵子成熟障碍综合征的特征及分子机制

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【摘要】 卵子成熟障碍发生于体外受精技术的促排卵过程中, 如果反复发生且不能通过卵子体外成熟培养来解决时, 即称为卵子成熟障碍综合症。根据卵子减数分裂阻滞在不同的时期将卵子成熟障碍综合症分为 GV 期阻滞、M_I 期阻滞、M_{II} 期阻滞和混合型阻滞。目前认为, 卵子体内成熟过程中的不同时期的主要信号传导通路障碍, 将导致不同类型的卵子成熟障碍的发生。

关键词: 卵子成熟; 卵子阻滞; 减数分裂阻滞; 不孕症

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Feature and Molecular Mechanism of Oocyte Maturation Failure Syndrome

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【**ABSTRACT**】Oocyte maturation failure occurs during the progress of controlled ovarian hyperstimulation in *in vitro* fertilization cycle. If it occurs repeatedly and the arrested oocytes could not complete maturate *in vitro*, it is called oocyte maturation failure. According to the oocyte meiotc arrest at different periods, oocyte maturation syndrome can be divided into GV stage blockage, M_I stage blockage, M_{II} stage blockage and mixed stage blockage. Presently, the main signal transduction disorder in different periods of oocyte maturation leads to the occurrence of different stages of oocyte maturation failure syndrome.

Key words: oocyte maturation; oocyte arrest; meiosis arrest; infertility

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乙肝病毒在辅助生殖实验室中可能的传播途径及阻断方式探讨

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【摘要】 病毒性乙型肝炎(乙肝)是一种危害极大的传染病。乙肝病毒(HBV)感染者在进行辅助生殖技术(ART)助孕人群中的比例正不断增加, 在ART实验室中HBV可经精子和卵母细胞由亲代遗传性传播给子代, 也可以因水平传播导致其他正常的配子和胚胎感染。高度警惕HBV的传染途径, 对健康亲代进行免疫预防, 对有传染性的标本进行洗涤, 加强实验室安全管理, 施行亚甲蓝光化学法灭活病毒等相应阻断措施, 是安全进行ART的必要保证。

关键词: 乙型肝炎病毒; 传播; 辅助生殖技术(ART); 实验室; 阻断

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Possible Transmission Routes of Hepatitis B Virus and Ways to Block Them in Assisted Reproductive Technology Laboratory

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【**ABSTRACT**】 Viral hepatitis B (HBV) is a serious infectious disease. The quantity of HBV infected persons in cases of performing assisted reproductive technology (ART) population is increasing. In ART laboratory HBV can be tranmitted from parents to offsprings by sperms and eggs. The virus can also infect other normal gametes and embryos through horizontal transmission. Paying attention to routes of HBV transmission and taking appropriate blocking measures are necessary to ensure the safety of ART. Blocking measures include health parents taking the hepatitis B vaccine, washing infectious specimens, strengthening the laboratory safety management and inactivating virus by methylene blue-light treatment of infected things.

Key words: hepatitis B virus (HBV); transmission; assisted reproductive technology (ART); laboratory; blocking