

· 临床指南 ·

电针/经皮穴位电刺激技术在生殖医学中的应用专家共识

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(国家人口和计划生育委员会公益性科研专项课题组)

【摘要】 不孕不育症近年来呈上升趋势, 尽管现代医学解决了多种生殖障碍, 但是总体活产率徘徊在20%~30%, 仍有进一步提高的社会需求。针灸是中国传统医学的代表, 在妇科不孕症治疗中积累了很多临床经验。本文从针刺/电针(EA)/经皮穴位电刺激(TEAS)相关的原理与技术演变入手, 阐述其在生殖领域多种病症类型中的应用原则。从最佳刺激参数筛选, 穴位辨证, 疗程与治疗次数确定, 疗效情况, 基本原理等几方面详细论述EA/TEAS技术在诱导排卵、取卵镇痛、卵巢储备功能减退、改善子宫内膜容受性或胚胎种植及男性少弱精子症中的具体应用, 以期为广大临床医生正确使用该技术提供帮助。

关键词: 电针(EA); 经皮穴位电刺激(TEAS); 子宫内膜容受性; 卵巢储备功能减退; 少弱精子症

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• 临床指南 •

**Application of transcutaneous electrical acupoint stimulation
in reproductive medicine: a group consensus**

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【ABSTRACT】 There is an obvious tendency of rising incidence rate of infertility in recent years. With the rapid development of modern medicine and assisted reproductive technology (ART), part of reproductive disorders have been effectively resolved, but the live-birth rate after infertility treatment is still unsatisfactory stuck at 20% to 30%. Acupuncture is an important component of traditional Chinese medicine, known to be effective for certain clinical conditions in obstetrics and gynecology. This consensus illustrates the principle and technical evolution of acupuncture, and shows the effect of electroacupuncture (EA)/transcutaneous electrical acupoint stimulation (TEAS) in many aspects in reproductive medicine. It expounded the selection of optimal electrical parameters, correct acupoints, convenient time course and intervals of treatments, efficacy and certain mechanisms of EA/TEAS intervention in specific clinical conditions, including pain during oocyte retrieval, ovulation disorders, diminished ovarian reserve, low endometrial receptivity or embryo implantation, oligospermia and asthenospermia. It is attempted to serve as a guideline for using EA/TEAS in relevant clinical practice for the treatment of infertility.

Key words: electroacupuncture (EA); transcutaneous electrical acupoint stimulation (TEAS); endometrial receptivity; poor ovarian reserve; oligospermia and asthenospermia

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• 实验研究 •

子宫内膜异位症患者卵巢颗粒细胞 *SF-1*基因启动子甲基化状态的研究

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【摘要】目的: 探讨子宫内膜异位症(endometriosis, EMS)患者卵巢颗粒细胞中类固醇生成因子-1 (steroidogenic factor-1, SF-1)表达下降的可能机制。方法: 应用重亚硫酸盐测序法(bisulfite sequencing PCR, BSP)检测EMS患者和正常女性卵巢颗粒细胞SF-1基因启动子区5'CpG位点甲基化水平, 将测得的序列与原始序列比对, 统计甲基化位点、数量并分析EMS组和正常组甲基化程度。结果: BSP片段涵盖SF-1基因转录起始位点附近的13个CpG位点(从CpG-84到CpG+168), EMS组SF-1基因启动子区域的整体甲基化水平显著高于对照组($P<0.05$), 逐个位点的分析显示EMS组CpG+7、+18、+21、+42、+54、+60、+132以及+146位点相较于对照组呈现高甲基化水平($P<0.05$); 而EMS组CpG+77、+121和+141位点的高甲基化水平尤为显著($P<0.001$)。结论: EMS患者卵巢颗粒细胞SF-1基因启动子区5'CpG位点甲基化水平显著高于对照组, 可能是EMS患者卵巢颗粒细胞SF-1 mRNA表达降低的机制。

关键词: 子宫内膜异位症(EMS); 类固醇生成因子-1(SF-1); DNA甲基化; 启动子; CpG

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• 实验研究 •

Methylation of the 5'CpG sites of steroidogenic factor-1 in endometriotic granulosa cells

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【ABSTRACT】 Objective: To gain further insight into the mechanism for differential steroidogenic factor-1(SF-1) expression in normal and endometriotic granulosa cells. **Methods:** The methylation status of 5'CpG sites of SF-1 promoter in normal and endometriotic granulosa cells were evaluated using bisulfite sequencing PCR. **Results:** Methylation status of a total of 13 CpG sites across a 213-bp region in the approximately 252-bp CpG sites (-84/+186) at the SF-1 promoter was characterized by bisulfite genomic sequencing. Ten clones were checked for each involved subject. The 13 CpG sites of SF-1 were differentially methylated in normal group. However, increased methylation in endometriotic granulosa cells was observed when compared with normal granulosa cells ($P<0.05$). There found eleven significantly hypermethylated sites including CpG+7,+18,+21,+42, +54, +60, +77,+121,+132, +141 and +146 ($P<0.05$), in which CpG+77, +121 and +141 were highly hypermethylated ($P<0.001$). **Conclusion:** We demonstrated that hypermethylation status of 5'CpG site of SF-1 promoter in endometriotic granulosa cells, which may explain the mechanism for reduced SF-1 mRNA expression in granulosa cells of endometriosis.

Key words: endometriosis (EMS); steroidogenic factor-1 (SF-1); DNA methylation; promoter; CpG site

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蛋白酪氨酸磷酸酶1B对子宫内膜癌细胞增殖和凋亡的影响

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【摘要】目的: 探讨蛋白质酪氨酸磷酸酶 1B (protein tyrosine phosphatase 1B, PTP1B) 对子宫内膜癌细胞增殖和凋亡的影响。方法: 体外培养人子宫内膜癌细胞株 (Ishikawa), 并将其分为 4 组, 即空白对照组 (A 组), 凋亡组 [B 组, 十二烷基硫酸钠 (SDS)], 空病毒载体凋亡组 (C 组, SDS+LacZ) 和过表达凋亡组 (D 组, SDS+PTP1B)。利用 Western blotting 检测 PTP1B 和 Bcl-2 表达; 四甲基偶氮唑蓝 (MTT) 检测细胞活力, 吖啶橙/溴化乙啶 (AO/EB) 双染色观察过表达 PTP1B 对 Ishikawa 形态学的影响。结果: Western blotting 显示 Ishikawa 无 PTP1B 表达, D 组 Ishikawa 高表达 PTP1B。A 组、B 组、C 组及 D 组的 Ishikawa 均有 Bcl-2 的表达, 且 D 组比 B 组高 37.04%。MTT 结果显示 D 组比 B 组的细胞存活率提高 30.66%。AO/EB 结果显示 D 组仅少量细胞有橙红色荧光, 细胞形态较规则。结论: 过表达 PTP1B 能在一定程度上促进子宫内膜癌 Ishikawa 细胞增殖并抑制其凋亡。

关键词: 子宫内膜癌; 蛋白酪氨酸磷酸酶 1B (PTP1B); 凋亡; 增殖

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Effect of PTP1B on the proliferation and apoptosis of endometrial carcinoma Ishikawa cell line

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【ABSTRACT】 Objective: To investigate the effect of protein tyrosine phosphatase 1B (PTP1B) on the proliferation and apoptosis of endometrial cancer Ishikawa cell line. **Methods:** Endometrial cancer cell line (Ishikawa) was divided into four groups after *in vitro* culture: group A (control group), group B (apoptosis group), group C (empty virus group) and group D (overexpressed PTP1B group). Then, the expressions of PTP1B and Bcl-2 were detected by Western blotting, the cell viability was tested by four methyl thiazolyl tetrazolium (MTT), and the morphology of endometrial cancer Ishikawa cell line was detected by acridine orange/ethidium bromide (AO/EB) staining, respectively. **Results:** Western blotting analysis showed that PTP1B was expressed in endometrial cancer cells with overexpress of PTP1B, without expression in the control endogenous endometrial cancer cells. Bcl-2 was visible for each group. And Bcl-2 protein content of group D increased by 37.04% compared with group B. MMT displayed that cell survival rate of group D raised by 30.66% than that of group B. Also, AO/EB analysis presented that only a few cells appeared orange-red fluorescence in group D, and the cell morphology was normal. **Conclusion:** PTP1B could improve the proliferation and inhibit the apoptosis of endometrial cancer cells to a certain extent.

Key words: endometrial cancer; protein tyrosine phosphatase 1B (PTP1B); apoptosis; proliferation

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尼古丁通过抑制可溶性血管内皮生长因子受体1 促进胎盘生长因子分泌并提高人滋养细胞 侵袭行为的分子机制

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【摘要】目的: 探讨尼古丁对人滋养细胞侵袭行为调控的分子机制。方法: 以低剂量尼古丁处理人绒毛膜癌细胞株 JEG-3, 以实时定量 RT-PCR 及 ELISA 方法分析可溶性血管内皮生长因子受体1(soluble fms-like tyrosine kinase 1, sFlt1)及胎盘生长因子(placental growth factor, PLGF)在 mRNA 及蛋白质水平的表达。以 PLGF 阻断性抗体及尼古丁共同处理人滋养细胞, Transwell 细胞侵袭实验分析滋养细胞的侵袭能力。结果: 低剂量的尼古丁通过抑制 sFlt1 表达促进 PLGF 分泌并改善滋养细胞的侵袭能力。结论: 尼古丁可能通过调控滋养细胞 PLGF 分泌改善滋养细胞的侵袭行为, 对妊娠高血压综合征(PIH)发挥保护作用。

关键词: 尼古丁; 滋养细胞; 可溶性血管内皮生长因子受体 1(sFlt1); 胎盘生长因子(PLGF); 细胞侵袭

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Nicotine promotes placental growth factor secretion by inhibiting soluble fms-like tyrosine kinase 1 and improves the invasiveness of human trophoblast cells

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【ABSTRACT】 Objective: To analyze the molecular mechanism of nicotine that regulates the cell invasion of human trophoblast cells. **Methods:** Human choriocarcinoma cells JEG-3 were treated with low-dose nicotine, mRNA and protein levels of soluble fms-like tyrosine kinase 1 (sFlt1) and placental growth factor (PLGF) were analyzed by realtime RT-PCR and ELISA assay. JEG-3 cells were then treated with nicotine and neutralizing PLGF antibody, cell invasion of human trophoblast cells was detected by Transwell cell invasion assay. **Results:** Low-dose nicotine promoted PLGF expression by inhibiting sFlt1 secretion and improved the invasion of human trophoblast cells. **Conclusion:** Nicotine may play a protective role in preeclampsia by promoting PLGF secretion and improving the invasiveness of human trophoblast cells.

Key words: nicotine; trophoblast cells; soluble fms-like tyrosine kinase 1 (sFlt1); placental growth factor (PLGF); cell invasion

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· 临床研究 ·

卵泡液中双酚A在多囊卵巢综合征发病中的作用及相关因素探讨

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【摘要】目的: 探讨卵泡液中双酚A(bisphenol A, BPA)在多囊卵巢综合征(PCOS)发病中的作用。方法: 于取卵日收集行体外受精/卵胞质内单精子显微注射(IVF/ICSI)的PCOS患者和非PCOS患者的卵泡液, 检测患者卵泡液BPA水平和卵泡液性激素水平, 并进一步与患者血清抗苗勒氏管激素(AMH)及临床结局等因素行相关性分析。结果: PCOS患者和非PCOS患者的卵泡液BPA水平(446.57 ± 63.57 ng/L vs 336.29 ± 59.02 ng/L, $P < 0.001$)、血清AMH水平(12.09 ± 4.78 μ g/L vs 5.69 ± 2.98 μ g/L, $P < 0.001$)、卵泡液FSH(5.58 ± 1.66 IU/L vs 3.95 ± 1.54 IU/L, $P = 0.008$)、LH(4.54 ± 2.97 IU/L vs 0.96 ± 1.10 IU/L, $P < 0.001$)和T(54.68 ± 34.34 nmol/L vs 32.48 ± 16.68 nmol/L, $P = 0.035$)组间比较有统计学差异。相关性分析显示, 卵泡液中BPA水平与血清AMH水平呈显著正相关($r = 0.577$, $P = 0.001$)。结论: 卵巢局部的BPA暴露可能参与了PCOS疾病的发生、发展。

关键词: 双酚A(BPA); 卵泡液; 抗苗勒氏管激素(AMH); 多囊卵巢综合征(PCOS)

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• 临床研究 •

Role of bisphenol A (BPA) in follicular fluid in the pathogenesis of polycystic ovary syndrome (PCOS)

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【ABSTRACT】 Objective: To explore the role of bisphenol A (BPA) in follicular fluid in the pathogenesis of polycystic ovary syndrome (PCOS). **Methods:** BPA concentration was measured in the follicular fluid (FF) collected from non-PCOS and PCOS patients who underwent *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI), and the correlation between BPA concentration in FF and serum anti-Müllerian hormone (AMH) level, sex hormone level in FF and clinical outcomes was analyzed. **Results:** BPA level in FF of PCOS patients was significantly higher than that in non-PCOS patients (446.57 ± 63.57 ng/L vs 336.29 ± 59.02 ng/L, $P < 0.001$). An increase of AMH level in serum was also discovered in PCOS group compared with non-PCOS group (12.09 ± 4.78 μ g/L vs 5.69 ± 2.98 μ g/L, $P < 0.001$). Concentrations of FSH (5.58 ± 1.66 IU/L vs 3.95 ± 1.54 IU/L, $P = 0.008$), LH (4.54 ± 2.97 IU/L vs 0.96 ± 1.10 IU/L, $P < 0.001$), T (54.68 ± 34.34 nmol/L vs 32.48 ± 16.68 nmol/L, $P = 0.035$) in FF of PCOS patients were also higher than those of non-PCOS patients. BPA concentration in FF and AMH level in serum showed a significantly positive correlation ($r = 0.577$, $P = 0.001$). **Conclusion:** BPA in FF may participate in the pathogenesis of PCOS.

Key words: bisphenol A (BPA); follicular fluid (FF); anti-Müllerian hormone (AMH); polycystic ovary syndrome (PCOS)

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抗苗勒管激素(AMH)在多囊卵巢综合征患者促性腺激素促排卵治疗中的预测意义

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【摘要】目的: 探讨多囊卵巢综合征(polycystic ovary syndrome, PCOS)患者高抗苗勒管激素(anti-Müllerian hormone, AMH)水平对人绝经期促性腺激素(hMG)促排卵结局的影响。方法: 采用前瞻性研究, 分析63例接受hMG促排卵的PCOS患者。比较对hMG有反应与无反应组间的AMH浓度。采用受试者工作特征(receiver operating characteristic, ROC)曲线评估AMH预测卵巢反应性价值。结果: 有反应组AMH水平明显低于无反应组($8.43 \pm 2.18 \mu\text{g/L}$ vs $11.05 \pm 2.85 \mu\text{g/L}$, $P < 0.001$)。多因素逐步回归分析提示AMH是预测卵巢反应性的唯一指标。ROC曲线分析显示AMH是一项潜在有效的预测卵巢反应性的指标。将血AMH界值 $10.12 \mu\text{g/L}$ 作为判断标准, 其预测卵巢对hMG反应的敏感性达91.7%, 特异性达66.7%。结论: 血清AMH可作为有效的预测PCOS患者对hMG反应性的指标。

关键词: 多囊卵巢综合征(PCOS); 抗苗勒管激素(AMH); 人绝经期促性腺激素(hMG); 促排卵

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Circulating anti-Müllerian hormone (AMH) as a predictor of ovarian response to gonadotrophins in women with polycystic ovary syndrome

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【ABSTRACT】 Objective: To investigate the impact of high circulating anti-Müllerian hormone (AMH) level on the outcome of ovulation induction using human menopausal gonadotropin (hMG) in women with polycystic ovary syndrome (PCOS). **Methods:** This prospective study included 63 anovulatory women with PCOS who underwent hMG ovarian stimulation. Serum AMH concentrations were compared between responders and non-responders. The receiver-operating characteristic (ROC) curve was used to evaluate the prognostic value of circulating AMH. **Results:** hMG responders had a significantly lower serum AMH concentration compared with non-responders ($8.43 \pm 2.18 \mu\text{g/L}$ vs $11.05 \pm 2.85 \mu\text{g/L}$, $P < 0.001$). In multivariate Logistic regression analysis, AMH was an independent predictor of ovulation induction by hMG in PCOS patients. ROC curve analysis showed AMH should be a useful predictor of ovulation induction by hMG in PCOS patients, having 91.7% specificity and 66.7% sensitivity when the threshold AMH concentration was $10.12 \mu\text{g/L}$. **Conclusion:** Serum AMH can be used as an effective parameter to predict ovarian response to hMG treatment in PCOS patients.

Key words: polycystic ovary syndrome (PCOS); anti-Müllerian hormone (AMH); human menopausal gonadotropin (hMG); ovulation induction 中图分类号: R173 文献标识码: A

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自然周期 IVF 取卵时机的掌控

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【摘要】目的: 寻找自然周期体外受精-胚胎移植(IVF-ET)技术取卵时机的敏感指标。方法: 对206例不孕妇女实施自然周期IVF-ET治疗, 分析不同获卵结局与血清激素及尿黄体生成素(LH)变化的关系。结果: 206例患者, 获卵率为75.2%、提前排卵率为15%、未获卵率为9.7%。雌二醇(E₂)和LH水平在取卵前、后变化最明显, LH峰值日血清E₂和LH水平在获卵组、提前排卵组和未获卵组间无统计学差异($P>0.05$), 而决定取卵时获卵组E₂为 $119.4 \pm 21.7 \mu\text{g/L}$, LH为 $13.3 \pm 9.4 \text{ IU/L}$; 孕酮(P)为 $1.19 \pm 0.57 \mu\text{g/L}$, 与提前排卵组(E₂: $77.6 \pm 22.5 \mu\text{g/L}$, LH: $3.0 \pm 1.6 \text{ IU/L}$; P: $3.35 \pm 1.64 \mu\text{g/L}$)和未获卵组(E₂: $167.8 \pm 53.5 \mu\text{g/L}$, LH: $30.8 \pm 11.3 \text{ IU/L}$; P: $0.84 \pm 0.45 \mu\text{g/L}$)比较有统计学差异($P<0.05$)。应用半定量尿LH试纸变化确定取卵时机显示, 自尿LH峰下降到10~25 IU/L和5~10 IU/L时获卵率最高, 分别为80.6%和84.8%。结论: E₂和LH水平在排卵前、后变化最明显, 是预测自然周期取卵时机的敏感指标。当出现LH峰时, 尿LH自峰值降至5~25 IU/L, 血清E₂水平降至100 $\mu\text{g/L}$ 左右, 血清LH水平在10~20 IU/L是最适宜的取卵时机。

关键词: 自然周期; 体外受精-胚胎移植(IVF-ET); 取卵时机

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Timing of oocyte pick-up in natural cycle IVF

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【ABSTRACT】 Objective: To find indicators for determining appropriate oocyte pick-up time to improve oocyte retrieval rate in natural cycle *in vitro* fertilization (IVF). **Methods:** The relationship between different oocyte retrieval outcome and the changes of serum hormone and urinary luteinizing hormone (LH) level of 206 natural cycle IVF cases was analyzed. **Results:** The oocyte retrieval rate of 206 natural cycle IVF cases was 75.2%, the premature ovulation rate was 15.0% and the oocyte retrieval failure rate was 9.7%. Among oocyte retrieved group, premature ovulation group and oocytes retrieved failure group, there were no differences of serum E₂ and LH levels at LH peak day. At the time of oocyte pick-up, E₂ level was 119.4 ± 21.7 ng/L; LH level was 13.3 ± 9.4 IU/L and P level was 1.19 ± 0.57 μg/L of oocyte retrieved group, which had statistical differences with other two groups. Semi-quantitative urinary LH test paper was used to determine oocyte pick-up time. When the urinary LH decreased to 10–25 IU/L and 5–10 IU/L from the peak, oocytes retrieval rate was 80.6% and 84.8%, which were higher than those decreased to 25–45 IU/L and 0–5 IU/L. **Conclusion:** E₂ and LH are sensitive indicators for determining oocyte pick-up time in natural cycle. The most appropriate oocyte pick-up time is serum E₂ level fell to about 100 ng/L, serum LH level fell to 10–20 IU/L or the urinary LH level fell to 5–25 IU/L from the corresponding peak value.

Key words: natural cycle; *in vitro* fertilization-embryo transfer (IVF-ET); oocyte pick-up time

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• 流行病学研究 •

柳州市壮族与汉族女性 5, 10- 亚甲基四氢叶酸还原酶、甲硫氨酸合成酶还原酶基因型和等位基因频率的分布

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【摘要】目的: 调查柳州市壮族与汉族女性中 5, 10- 亚甲基四氢叶酸还原酶(*MTHFR*)及甲硫氨酸合成酶还原酶(*MTRR*)基因的单核苷酸多态性分布特征。方法: 通过横断面调查研究方法, 以广西省柳州市 372 位壮族和 478 位汉族女性为研究对象, 检测其 *MTHFR* C677T、A1298C 和 *MTRR* A66G 基因位点多态性, 统计分析该地区基因多态性的分布特征, 并与已报道的其他地区少数民族女性数据进行比较。结果: 该地区壮族和汉族女性比较, *MTHFR* C677T 的基因型频率差异在两者间有统计学意义($P < 0.05$), 而 *MTHFR* A1298C 和 *MTRR* A66G 两者间无统计学差异($P > 0.05$); *MTHFR* C677T 和 A1298C 的等位基因频率在两民族间的差异有统计学意义($P < 0.05$), 而 *MTRR* A66G 则无统计学差异($P > 0.05$)。该地区壮族女性 *MTHFR* C677T 的基因型频率和等位基因分布与延边朝鲜族、新疆维吾尔族、银川回族、思南苗族、思南土家族、柳州苗族、三亚黎族间差异均有统计学意义($P < 0.05$); 而该地区壮族女性 *MTHFR* A1298C 的基因型频率和等位基因分布与延边朝鲜族、银川回族、思南苗族、思南土家族间亦有统计学差异($P < 0.05$); *MTRR* A66G 的分布上则与新疆维吾尔族、思南苗族、思南土家族、南宁壮族、三亚黎族有统计学差异($P < 0.05$)。结论: 广西省柳州市壮族女性的 *MTHFR* 和 *MTRR* 基因多态性分布特征与该地区汉族女性不同, 与其他地区少数民族也不相同。

关键词: 壮族女性; 5, 10- 亚甲基四氢叶酸还原酶(*MTHFR*); 甲硫氨酸合成酶还原酶(*MTRR*); 基因型频率; 民族比较

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• 流行病学研究 •

**Distribution of the genotype and allele frequency of *MTHFR* and *MTRR* in
Zhuang and Han women from Liuzhou City**

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【ABSTRACT】 Objective: To investigate the methylenetetrahydrofolate reductase (*MTHFR*) C677T, A1298C and methionine synthase (*MTRR*) A66G gene polymorphisms among Chinese Zhuang and Han women in Liuzhou City of Guangxi Province. **Methods:** A total of 372 Zhuang minority samples and 478 Han nationality samples were recruited from Liuzhou City, and *MTHFR* and *MTRR* gene polymorphisms were detected. The distribution of gene polymorphisms of this study was analyzed and compared with the samples reported in other minorities. **Results:** Compared between the Zhuang and Han women from Liuzhou city, the genotype frequency of *MTHFR* C677T was different significantly, whereas *MTHFR* A1298C and *MTRR* A66G genotypes were not statistically significant. *MTHFR* C677T and A1298C alleles' distribution were significantly different between Zhuang and Han women while *MTRR* A66G was not statistically significant. There was a statistically significant difference about the genotype and allele frequency of *MTHFR* C677T of Zhuang women from Liuzhou City, compared with Korean women from Yanbian City, Uyghur women from Xinjiang Province, Hui women from Yinchuan City, Miao women from Sinan City, Tujia women from Sinan City, Miao women from Liuzhou City and Li women from Sanya City ($P<0.05$), with the same result about the genotype and allele frequency of *MTHFR* A1298C between Zhuang women from Liuzhou City and Korean women, Hui women, Miao women from Sinan City, Tujia women ($P<0.05$). The genotype and allele frequency of *MTRR* of Zhuang women was different from Uyghur women, Miao women from Sinan City, Tujia women, Zhuang women and Li women ($P<0.05$). **Conclusion:** The distribution of *MTHFR* and *MTRR* polymorphism among Zhuang women is different from Han women locally, as well as it compared with other minority women.

Key words: Zhuang women; methylenetetrahydrofolate reductase (*MTHFR*); methionine synthase reductase (*MTRR*); genotype frequency; comparative nationalities

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• 综述 •

DNA甲基化和组蛋白修饰对 反复自然流产的影响

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【摘要】近年来,越来越多的研究表明表观遗传学(epigenetics)与多种疾病密切相关。而胚胎发育的不健全是导致自然流产的重要原因。本文中,我们通过探讨表观遗传学中DNA甲基化和组蛋白修饰与胚胎发育的关系,阐明表观遗传学对反复自然流产(recurrent spontaneous abortion, RSA)的影响,并概述最近几年在动物和人类研究中的进展。

关键词: 反复自然流产(RSA); 表观遗传学; DNA甲基化; 组蛋白修饰;

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• 综述 •

Role of DNA methylation and histone modification in recurrent spontaneous abortion

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【ABSTRACT】 In recent years, a growing number of researches reveal that epigenetics is closely related to many diseases. And the faulty embryogenesis is an important reason of spontaneous abortion. In the present review, we discuss the relationship between recurrent spontaneous abortion (RSA) and embryo development on the basis of DNA methylation and histone modification, present the role of epigenetics in RSA and outline the progress in both animal and human research in recent years.

Key words: recurrent spontaneous abortion (RSA); epigenetics; DNA methylation; histone modification

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家族性复发性葡萄胎及相关致病基因的研究进展

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【摘要】家族性复发性葡萄胎(FRHM)是葡萄胎的一种特殊形式,常有家族聚集倾向,绝大多数患者不能获得正常胎儿,临床尚无有效干预措施。已有研究表明该疾病与 *NLRP7* 和 *KHDC3L* 基因突变有关,而且这2种基因在进化来源、细胞定位等方面具有一定的相似性。基因突变类型不同,对葡萄胎表型、后续妊娠结局的影响不同。本文对家族性复发性葡萄胎的发现过程、致病基因的研究现状、基因突变在葡萄胎发生中的作用及存在的问题等进行综述。

关键词: 家族性复发性葡萄胎(FRHM); *NLRP7*; *KHDC3L*

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Advances in familial recurrent hydatidiform mole and its pathogenic genes

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【ABSTRACT】 Familial recurrent hydatidiform mole (FRHM) is a special kind of molar pregnancy with a familial aggregation tendency, largely patients suffering FRHM cannot have a healthy baby. What doctors could do is limited. Two disease-causing genes have been identified to be related to FRHM, which are *NLRP7* and *KHDC3L*. Both of them have some similarities in genetic evolution and cellular localization. Molar types and subsequent pregnancy outcomes are influenced by these two genes. Here we reviewed the discovery of FRHM, the current understanding of these genes and the influence of gene mutation on molar pregnancies.

Key words: familial recurrent hydatidiform mole (FRHM); *NLRP7*; *KHDC3L*

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女性免疫避孕的研究进展

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【摘要】 免疫避孕疫苗的发展在计划生育及控制人口方面具有重要意义。本文对国内外女性免疫避孕疫苗的研究情况, 包括抗 GnRH 疫苗、抗人绒毛膜促性腺激素疫苗及抗卵透明带疫苗的研究现状以及近年来取得的研究进展, 进行了综述, 重点阐述了抗卵透明带疫苗的发展历程。

关键词: 女性免疫避孕; 促性腺激素释放激素(GnRH); 人绒毛膜促性腺激素(hCG); 卵透明带(ZP)

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Advances of female contraceptive vaccine

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【ABSTRACT】 The development of immunocontraceptive vaccines is important to birth control. In this article, we reviewed current progress in the research on the domestic and foreign female immunocontraceptive vaccines, including anti-gonadotropin-releasing hormone (GnRH) vaccine, anti-human chorionic gonadotrophin (hCG) vaccine and anti-zona pellucida (ZP) vaccine, especially focusing on the anti-ZP vaccine development.

Key words: immune-contraception; gonadotropin-releasing hormone (GnRH); human chorionic gonadotrophin (hCG); zona pellucida (ZP)

关键词: 女性免疫避孕; 促性腺激素释放激素(GnRH); 人绒毛膜促性腺激素(hCG); 卵透明带(ZP)

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我国常见生殖系统疾病流行概析

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【摘要】梅毒、淋病和前列腺癌、宫颈癌等是我国常见生殖系统疾病。生殖系统传染性疾病多病种流行特征各异, 表现为梅毒疫情严峻, 存在胎传梅毒流行风险; 淋病流行减缓显著; 艾滋病感染途径转为以性传播为主。生殖系统恶性肿瘤发病和死亡整体呈上升趋势, 存在显著城乡差异, 表现为前列腺癌在城市地区明显高发, 中老年男性为高危人群; 宫颈癌发病死亡上升趋势较缓, 农村负担重于城市, 贫困地区女性为易感人群。除社会文化观念改变和人口流动频繁外, 母婴传播阻断困难、艾滋病难以治愈等多种原因导致性传播疾病流行; 多种肿瘤危险因素多重累积暴露可能是肿瘤发病趋势增加的重要原因。我国正面临常见生殖系统传染性疾病和慢性非传染性恶性肿瘤流行的双重负担。需倡导个体安全性行为, 减少肿瘤危险因素暴露, 完善生殖健康教育、服务及监测体系, 遏制生殖系统疾病负担进一步加重。

关键词: 生殖系统疾病; 生殖流行病学; 中国

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General analysis of common reproductive system diseases in China

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【ABSTRACT】 Syphilis, gonorrhea, prostate cancer and cervical cancer, etc., are common reproductive system diseases in China. Different infectious diseases varied in epidemiological characteristics: congenital syphilis became a new threat; the incidence of gonorrhea decreased significantly; sexual transmission became the predominant infection route of HIV/AIDS. Morbidity and mortality of malignant reproductive tumors was increasing with significant urban-rural disparities. A high incidence of prostate cancer existed in urban areas, especially among the middle-aged and elderly men, however, diseases burden of cervical cancer were much heavier in counties than in cities. The epidemics of STDs were caused by significant changes on cultural value, frequent population flow, difficulty on blocking maternal-neonatal transmission and hard-to-treat feature. China is facing a double burden on infectious and chronic non-communicable reproductive diseases. To effectively curb the rising burden, more attention should be paid to advocate individual safety behavior, avoid exposure to risk factors, promote the propaganda and education on reproductive health, and improve the health service and monitoring system.

Key words: reproductive system diseases; reproductive epidemiology; China

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· 临床报道 ·

β2 糖蛋白 I(β2GPI)在卵泡液中的表达水平及其与卵泡发育的关系

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【摘要】目的: 探讨β2糖蛋白 I(β2GPI)与卵泡发育的关系。方法: 选取体外受精/卵胞质内单精子注射(IVF/ICSI)助孕治疗的卵巢功能正常者 100 例(NC 组)、多囊卵巢综合征(PCOS)患者 85 例(PCOS 组), 卵巢储备功能低下(DOR)患者 62 例(DOR 组), 长方案促排卵, 收集人绒毛膜促性腺激素(hCG)注射日血清及取卵日优势卵泡的卵泡液, 应用酶联免疫吸附试验法(ELISA)测定各组卵泡液中β2GPI的水平; 电化学发光法测定 hCG 注射日血清 E₂ 水平, 并对 IVF/ICSI 周期卵泡液中β2GPI 水平与 hCG 注射日血清 E₂ 水平、获卵数以及卵成熟率进行相关性分析。结果: 各组卵泡液中β2GPI 浓度相比均无统计学差异($P>0.05$); NC 组 IVF/ICSI 周期中卵泡液中β2GPI 的水平与 hCG 注射日血清 E₂ 水平、获卵数及卵成熟率均呈负相关($r=-0.279, P<0.05$; $r=-0.243, P<0.05$; $r=-0.711, P<0.01$)。结论: 卵泡液中β2GPI 的水平与卵巢功能无显著相关性, 卵泡液中β2GPI 的表达水平与 IVF/ICSI 周期中卵泡的发育存在负相关。

关键词: β2 糖蛋白 I(β2GPI); 卵泡发育; 颗粒细胞; 增殖; 凋亡

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• 临床报道 •

Expression level of β 2-glycoproteinI in follicular fluid and the relationship between β 2GPI and follicular development

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【ABSTRACT】 Objective: To investigate the relationship between β 2-glycoprotein I (β 2GPI) concentration and follicular development. **Methods:** One hundred female patients with normal ovarian function (NC group), 85 polycystic ovary syndrome (PCOS) patients (PCOS group) and 62 diminished ovarian reserve (DOR) patients (DOR group) for *in vitro* fertilisation/intracytoplasmic sperm injection (IVF/ICSI) were selected. Conventional long protocol was performed for ovulation induction, the serum on hCG injection day and the follicular fluid of dominant follicles on oocyte retrieval day were collected. Enzyme-linked immunosorbent assay (ELISA) was used to determine the concentration of β 2GPI in follicular fluid, and electrochemiluminescence immunoassay was used to detect the E_2 levels in serum. The correlations between β 2GPI concentration and serum E_2 levels on hCG injection day, the number of oocytes and oocyte maturation rate in IVF/ICSI cycle were analyzed. **Results:** The level of β 2GPI between PCOS group and NC group was not statistically different ($P>0.05$), which was also not statistically different between DOR group and NC group ($P>0.05$). The level of β 2GPI in follicular fluid with normal ovarian function was negatively correlated with the serum E_2 level on hCG injection day, the number of oocytes and oocyte maturation rate ($r=-0.279$, $P<0.05$; $r=-0.243$, $P<0.05$; $r=-0.711$, $P<0.01$). **Conclusion:** There was no significant correlation between β 2GPI concentration and ovarian function; the expression level of β 2GPI in follicular fluid was related to follicle development in IVF/ICSI cycles.

Key words: β 2-glycoproteinI (β 2GPI); follicular development; granulosa cell; proliferation; apoptosis

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氧化低密度脂蛋白(ox-LDL)、白细胞介素(IL)-22 在子痫前期患者血清及胎盘中的表达

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【摘要】目的: 探讨血清及胎盘中氧化低密度脂蛋白(ox-LDL)、白细胞介素(IL)-22 的表达与子痫前期(PE)发生的关系。方法: 收集 PE 患者 30 例, 其中轻度 PE 15 例(轻度组), 重度 PE 15 例(重度组)。另选同期正常妊娠孕妇 30 例(正常组), 分别采用 ELISA、免疫组织化学方法检测血清、胎盘组织中 ox-LDL、IL-22 的表达水平。结果: ① PE 轻度组和重度组患者血清及胎盘中 ox-LDL 水平均明显高于正常组($P < 0.05$), 且重度组明显高于轻度组($P < 0.05$); ② PE 轻度组患者血清及胎盘中 IL-22 水平较正常组有升高趋势, 但差异无统计学意义($P > 0.05$), 而重度组患者血清及胎盘中 IL-22 水平明显高于正常组及轻度组($P < 0.05$); ③ PE 患者血清中 ox-LDL 与 IL-22 水平呈明显的正相关($r = 0.941, P < 0.05$); PE 患者胎盘中 ox-LDL 与 IL-22 水平呈明显的正相关($r = 0.754, P < 0.05$)。结论: 血清及胎盘中 ox-LDL 高表达可能与 PE 发生、发展有关, 而 IL-22 在此过程中可能起到代偿性保护作用。

关键词: 子痫前期(PE); 白细胞介素(IL)-22; 氧化低密度脂蛋白(ox-LDL); 内皮细胞损伤

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Expression of ox-LDL and IL-22 in serum and placenta of patients with preeclampsia

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【ABSTRACT】 Objective: To compared the expression of oxidized low-density lipoprotein (ox-LDL) and interleukin (IL)-22 in serum and placenta between the patients with preeclampsia (PE) and normal pregnant women. **Methods:** Thirty women with PE were recruited in the study, including 15 women with mild PE (mild group) and 15 women with severe PE (severe group), and 30 healthy pregnant women were taken as normal group. Enzyme-linked immunosorbent assay (ELISA) was used to measure the serum concentrations of ox-LDL and IL-22 in these women. Immunohistochemical method was used to detect the expression levels of ox-LDL and IL-22 in placenta. **Results:** 1) The serum concentrations of ox-LDL in mild group and severe group were significantly higher compared with normal group ($P<0.05$); and the concentration of ox-LDL in severe group was significantly higher than that of mild group ($P<0.05$); the same pattern was seen in placenta. 2) The serum concentration of IL-22 in mild group had a trend of increase compared with normal group, but the difference was not statistically significant ($P>0.05$); the serum concentration of IL-22 in severe group was significantly higher than that in normal group and mild group ($P<0.05$); the same pattern was seen in placenta. 3) The serum concentrations of ox-LDL and IL-22 in PE were significantly positively correlated ($r=0.941, P<0.05$). The expressions of ox-LDL and IL-22 in placenta of PE were significantly positively correlated ($r=0.754, P<0.05$). **Conclusion:** High expression of ox-LDL in serum and placenta of patients may be related to PE, but IL-22 may be a compensatory protective effect of the body in PE.

Key words: preeclampsia (PE); interleukin (IL)-22; oxidized low-density lipoprotein (ox-LDL); endothelial cell injury

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• 讲座 •

中医药防治米非司酮配伍米索前列醇 抗早孕药物流产副反应的研究概况

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【摘要】米非司酮配伍米索前列醇抗早孕在临床上已得到广泛应用,但是药物流产后的近期副反应及其可能带来的严重并发症是我们不能忽视的。中医药在防治药物流产后副反应方面的疗效已得到认可。目前针对中医药防治药物流产后副反应的研究主要集中于临床研究,包括病因病机、临床研究方法等方面;其中,临床研究方法主要可分为中药、针灸和针药并用3种。但是对于其机制研究及中药疗效机理等方面的研究却相对缺乏。今后需进一步深入研究,使中医药在防治药物流产后副反应发挥更大的作用。

关键词: 药物流产; 副反应; 中医药

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• 讲座 •

Research on the side effects of traditional Chinese medicine in preventing and treating early pregnancy induced abortion by mifepristone combined with misoprostol

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【ABSTRACT】 Mifepristone combined with misoprostol against early pregnancy has been widely used in clinical applications. But the recent side effects of drug abortion and the possible serious complications can't be ignored. Traditional Chinese medicine in the prevention and treatment of adverse reactions after drug abortion has been recognized. At present, the research on the side effects of traditional Chinese medicine in the prevention and treatment of drug abortion is mainly focused on clinical research, such as on the etiology and pathogenesis, clinical research methods. The clinical research methods can be divided into Chinese medicine, acupuncture and combination of acupuncture with Chinese medicine. But there is a lack of research on the mechanism of various research methods and the efficacy mechanism of traditional Chinese medicine. We need to further study about the mechanisms of various research methods in the future, so that traditional Chinese medicine may play a greater role in the prevention and treatment of side effects after drug induced abortion.

Key words: drug abortion; side effects; traditional Chinese medicine

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