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## 围绝经期管理与绝经雌激素治疗

陶敏芳

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女性进入围绝经期后, 随着卵巢功能的下降, 雌激素分泌的减少, 会出现近期的症状, 包括潮热盗汗、心悸、乏力骨痛、抑郁焦虑、睡眠障碍等; 中期会出现阴道干涩、尿频尿急、性生活不适等症状; 晚期会出现骨质疏松及骨折、心脑血管疾病等。这些变化严重影响着中老年女性的生活质量, 同时还增加了社会和经济负担。

上个世纪六七十年代, 发达国家和地区的卫生工作者认识到了绝经后雌激素水平下降给患者所带来的危害后, 采用了雌激素治疗显著改善了患者绝经相关症状, 改善了绝经后骨质疏松并降低其骨折的风险, 使绝经后女性的生活质量显著提高。1960 年 Robert Wilson 的 *Women for Ever* 一书阐述了雌激素治疗给绝经后女性带来的福音。针对绝经后妇女心血管疾病增加的现象, 学者们试图探究雌激素治疗对绝经后心血管疾病的影响。然而雌激素治疗在对绝经症状和绝经后骨质疏松症取得良好疗效的同时, 也显现出一些不良反应, 如单纯使用雌激素可增加有子宫妇女的内膜癌发生率, 雌激素治疗可增加高龄妇女的心血管、卒中事件和乳腺癌的发生风险等。其中最著名的研究当属妇女健康促进 (WHI) 进行的一项激素替代治疗 (HRT) 研究<sup>[1-2]</sup>, 该研究为随机双盲研究, 启动于 1993 年, 共纳入了 161 808 例 50~79 岁的妇女。研究目的是聚焦绝经后妇女的心脏疾病、乳腺癌、骨质疏松骨折的发生情况, 并探索防治策略。不幸的是在研究 5.2 年后, 雌激素 + 孕激素组的中期评估显示, 心脏病事件发生风险增加了 29%, 中风发生风险增加了 41%, 浸润性乳腺癌发生风险增加了 26%, 结肠癌和髌骨骨折的发生风险分别减少 37% 和 34%。因此, 全世界暂停了绝经雌激素治疗。在随后的 10 年里, 相关专家对这项研究进行了重新分析和评估, 结果显示此研究存在诸多缺陷, 例如纳入人群年龄偏大 (平均 64 岁)、参加者肥胖比例过高 [ 雌激素 + 孕激素组平均体质质量指数 (BMI) 28.5 kg/m<sup>2</sup>, 雌激素组平均 BMI

30.1 kg/m<sup>2</sup> ]、研究对象丢失率过高 (38%~54%) 等。最终达成绝经雌激素治疗的共识: 绝经雌激素治疗是缓解女性绝经症状的最有效的方法, 在绝经 10 年内及年龄 <60 岁开始启动雌激素治疗利大于弊<sup>[3]</sup>。迄今为止该项研究已经发表了超过 1 400 篇文章, 其中 2017 年发表在 JAMA 的累积 18 年的随访结果<sup>[4]</sup>, 即激素治疗不影响全因、心血管和癌症死亡率为 WHI 研究划上圆满的句号。并对 WHI 的中期研究报告的出台进行了分析报道<sup>[5]</sup>。

除了 WHI 研究外, 围绕绝经雌激素治疗的国际著名研究还包括心脏与雌激素 - 孕激素替代疗法研究 (HERS)<sup>[6]</sup>, 也是一项随机双盲研究, 该研究目的是探究 HRT 对预防女性复发性冠心病的疗效和安全性, 以及之后随访过程中 HRT 对降低冠心病 (CHD) 风险的作用; 研究结论是 HERS 中 HRT 组的 CHD 事件在最后几年发生率较低, 在之后的随访期间并没有持续下降。在 6.8 年的研究期间, HRT 并没有减少 CHD 患者心血管事件的发生率。HRT 对预防患者冠心病的发生无显著有益作用。护士健康研究 (NHS) 其研究目的是探讨绝经后激素治疗的持续时间、剂量和类型以及心血管疾病的一级预防; 对 70 533 例 30~55 岁绝经后女性随访近 20 年得出结论: 正在使用激素治疗 (包括短期使用) 的患者, 冠状动脉事件发生率更低, 总体 RR 为 0.61, 即与不使用者相比, 风险降低 39%。此外针对雌激素治疗与乳腺癌的风险的研究有在法国进行的一项关于女性癌症的风险因素的前瞻性队列研究 (E3N)<sup>[7]</sup>, 该研究针对乳腺癌风险评估了不同 HRT 与乳腺癌发生风险的关系; 评估了 2 354 例绝经后乳腺癌患者; 显示与未使用 HRT 比, 单独使用雌激素的风险显著增加 1.29 倍 (95% CI=1.02~1.65); 雌孕激素联合与乳腺癌风险的关系与孕激素的类型有关: 雌激素 - 黄体酮的 RR 为 1.00 (95% CI=0.83~1.22), 雌激素 - 地屈孕酮 RR 为 1.16 (95% CI=0.94~1.43), 雌激素 - 其他孕激素 RR 为 1.69 (95% CI=1.50~1.91)。百万妇女研究 (MWS) 也针对特定类型 HRT 对



乳腺癌的影响展开研究, 研究显示, 正在使用 HRT 的比没有用过的发生乳腺癌风险更大 [调整后的  $RR=1.66$  (95%  $CI=1.58\sim 1.75$ )] 及死亡风险更大 [ $RR=1.22$  (95%  $CI=1.00\sim 1.48$ )]。过去使用过 HRT 的没有出现乳腺癌或致命疾病的风险增加 [ $RR=1.01$  (95%  $CI=0.94\sim 1.09$ ) 和  $RR=1.05$  (95%  $CI=0.82\sim 1.34$ )]。正在使用只含雌激素的 HRT [ $RR=1.30$  (95%  $CI=1.21\sim 1.40$ )]、雌孕激素 [ $RR=2.00$  (95%  $CI=1.88\sim 2.12$ )]、替勃龙 [ $RR=1.45$  (95%  $CI=1.25\sim 1.68$ )] 的风险均显著增加。雌孕激素的相关风险明显大于其他类型的 HRT。口服、经皮及皮下埋植的风险均显著增加 [ $RR=1.32$  (95%  $CI=1.21\sim 1.45$ );  $RR=1.24$  (95%  $CI=1.11\sim 1.39$ );  $RR=1.65$  (95%  $CI=1.26\sim 2.16$ )]。结论是正在使用各种类型的 HRT 患者中, 乳腺癌的风险随着持续使用时间的增加而增加。上述这些研究结果奠定了当今绝经期管理的基础, 也为全世界再次科学管理绝经相关健康问题提供了依据。中国作为人口大国, 随着人口老龄化社会的快速进展, 绝经人口日益增加, 伴随我国经济文化的不断发展, 人民对生活质量的追求也在不断提高, 因而寻求更年期保健的女性的数量也在不断增加。然而与发达国家相比, 我国绝经后妇女接受绝经雌激素治疗率仅为 3%~4%, 而发达国家超过 40%。超过 70% 的绝经后妇女存在各种症状, 因此绝大多数的妇女正在忍受绝经症状的折磨。之所以出现这种状况主要是我国更年期保健尚未纳入公共卫生管理有关, 临床缺少关注更年期健康的专业队伍。此外还与百姓对医学知识的缺乏, 尤其是对“激素”的恐惧, 以及“顺其自然”传统观念的影响有关。

为此中华医学会妇产科学分会在 2001 年成立了绝经学组, 至 2010 年围绝经期管理在全国已拥有 10 000 名医生。目前绝经相关问题受到越来越多的关注, 全国各地多个医院建立了更年期专病门诊; 更年期相关的科普知识讲座也积极开展; 针对专业人员的培训也在推行中。妇女保健人员在不同地区开展了围绕绝经相关症状的相关调查, 为推动更年期保健规范化、科学化提供依据。上海医学会妇产科分会绝经学组已开展了多形式的学术培训, 2015—2017 年上海市公共卫生三年行动计划——更年期重要健康问题综合防治——进一步推动了上海更年期保健的步伐。各区县妇幼保健单位先后设立了更年期保健门诊, 二、三级医院更年期专病门诊正在兴起。上海已率先开展了相关的临床研究, 包括系统阐述

基于中国男女更年期症状现患率、特征及影响因素, 阐述女性绝经相关的睡眠障碍、抑郁/焦虑的现患率以及国内外妇女对绝经雌激素治疗的认知度; 针对绝经后心血管疾病风险增加的情况, 开展了基于脉搏速率的血管硬化监测; 创新性地建立了规范的绝经雌激素治疗评价和随访系统, 并在全市以及周边省市推广。

目前我们依然缺乏大样本的基于中国人群的绝经相关健康问题的流行病学数据, 表现在各单中心的研究报道的绝经综合征现患率差异大, 低者在 45%, 高者达 90%; 绝经症状存在差异, 有报道认为乏力为第一症状, 也有报道称潮热盗汗为第一症状。此外我们还缺乏绝经雌激素治疗安全性的随机双盲研究; 我国从上个世纪九十年代引入绝经雌激素制剂, 由于受国际绝经雌激素治疗研究结果的影响以及国人对绝经健康管理意识的淡漠, 绝经雌激素治疗率仅在 3%~4%。绝经雌激素治疗的主要风险包括心脑血管疾病和乳腺癌风险。由于人种的差异, 我国妇女罹患心脑血管疾病和乳腺癌的风险也不一, 因此绝经激素治疗与心脑血管疾病和乳腺癌的风险也存在差异。然而我国并未开展多中心随机研究, 因而缺乏安全性的报告, 也无法建立基于中国人群循证依据的相关指南。因此开展多中心的临床研究是进一步提高围绝经期健康管理, 提高中老年妇女生活质量, 减少和延缓老年疾病的发生的重要工作。

#### 参 考 文 献

- [1] Beral V, Million Women Study Collaborators. Breast cancer and hormone-replacement therapy in the Million Women Study[J]. *Lancet*, 2003, 362(9382):419-427.
- [2] Nelson HD, Humphrey LL, Nygren P, et al. Postmenopausal hormone replacement therapy: scientific review[J]. *JAMA*, 2002, 288(7):872-881.
- [3] Baber RJ, Panay N, Fenton A, et al. 2016 IMS Recommendations on women's midlife health and menopause hormone therapy[J]. *Climacteric*, 2016, 19(2):109-150. DOI: 10.3109/13697137.2015.1129166.
- [4] Manson JE, Aragaki AK, Rossouw JE, et al. Menopausal hormone therapy and long-term all-cause and cause-specific mortality: the women's health initiative randomized trials[J]. *JAMA*, 2017, 318(10):927-938.
- [5] Langer RD. The evidence base for HRT: what can we believe?[J]. *Climacteric*, 2017, 20(2):91-96. DOI: 10.1080/13697137.2017.1280251.
- [6] Grady D, Applegate W, Bush T, et al. Heart and estrogen/progestin replacement study (HERS): design, methods, and baseline characteristics[J]. *Control Clin Trials*, 1998, 19(4):314-335.
- [7] Fournier A, Berrino F, Clavel-Chapelon F. Unequal risks for breast cancer associated with different hormone replacement therapies: results from the E3N cohort study[J]. *Breast Cancer Res Treat*, 2008, 107(1):103-111.

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# 更年期门诊妇女绝经综合征与抑郁症状相关性的初步研究

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**【摘要】** 目的 探讨更年期门诊妇女绝经综合征与抑郁症状的相关性。方法 将 2016 年 7 月—2017 年 2 月期间因围绝经期相关症状在中国福利会国际和平妇幼保健院更年期门诊首次就诊的妇女纳入本研究。调查研究对象的一般情况、健康状况, 应用 Kupperman 绝经指数量表(Kupperman menopausal index, KMI) 评估围绝经期相关症状, 采用患者健康问卷抑郁量表(patient health questionnaire, PHQ-9) 对抑郁症状进行量化评分。结果 共计调查 153 名门诊妇女, 平均年龄为  $(47.3 \pm 4.3)$  岁, 月经不规则者占 77.78%。73.86% 的调查对象患有绝经综合征(KMI>6), 疲乏(70.59%)、情绪波动(63.40%)、失眠(59.48%)、潮热出汗(56.21%) 和骨关节痛(52.29%) 是最常见的围绝经期症状; 35.95% 的门诊妇女存在抑郁症状(PHQ-9  $\geq 5$ )。绝经综合征的严重程度、相关症状的共患程度与门诊妇女是否患有抑郁症状显著相关。多因素分析显示, 抑郁症与潮热出汗、失眠、情绪波动、眩晕、疲乏、头痛、心悸、性生活等具体症状的严重程度均有统计学联系。结论 更年期门诊患者绝经综合征和抑郁症状间存在明显联系。未来应加强对围绝经期妇女心理健康问题的关注, 使更多的妇女平稳度过围绝经期。

**【关键词】** 围绝经期; 抑郁; 影响因素

**The relationship between menopause syndrome and depression among perimenopausal women in menopausal outpatient department** Jin Qin, Huang Cheng, Hua Qi, Jin Furui, Xie Jun, Ma Jing

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**【Abstract】 Objective** To explore the any correlations between menopause syndromes and depression among perimenopausal women attending a specialized “menopause outpatient clinic”. **Methods** Women aged 40–60 years were recruited face-to-face during their first visit for a survey conducted from July 2016 to February 2017. The questionnaire collected information on socio-demographics, physical health, menopause symptoms. Kupperman menopause index (KMI) and patient health questionnaire (PHQ-9) were chosen to measure menopause symptoms and major depressive disorders respectively. **Results** Of 153 participants, the average age was  $(47.3 \pm 4.3)$  years. A majority of them (77.78%) were considered to be at perimenopausal stage with 73.86% self-reported any menopause syndromes ( $KMI > 6$ ). The top five most common menopause-related symptoms were fatigue (70.59%), mood swings (63.40%), insomnia (59.48%), hot flashes/sweating (56.21%) and joint pain (52.29%). For depression, 35.95% of the participants were screened as having any major depression ( $PHQ-9 \geq 5$ ). Both the severity of menopause syndromes (higher KMI scores) and the co-occurrence of menopause-related symptoms were significantly associated with these women’s depression screening. Multivariable analysis further revealed that depression was closely associated with the following menopause-related symptoms: hot flashes/sweat, insomnia, mood swings, dizziness, fatigue, headaches, and palpitations (reaching statistical significance). **Conclusion** There is a clear link between menopause (severity and related symptoms) and depression in patients attending the specialized menopause outpatient clinic. More clinical care is needed to address the increased likelihood of co-occurring depression among perimenopausal female patients to improve their quality of life.

**【Key words】** Perimenopause; Depression; Influencing factors

# 绝经女性抑郁症状及其影响因素分析

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**【摘要】**目的 探讨绝经女性抑郁状况及其影响因素。方法 通过横断面研究, 采用问卷调查方式获取基本资料, 应用抑郁自评量表 (self-rating depression scale, SDS) 进行抑郁症状评估, 应用改良绝经症状量表 (modified Kupperman index scale, KMI) 进行绝经症状评估, 采用 SPSS20.0 软件进行数据分析。**结果** 共纳入 1 591 名女性, 年龄中位数为 52 岁。KMI、SDS 平均得分分别为  $13.9 \pm 8.8$ 、 $39.6 \pm 9.0$ , 绝经症状和抑郁症状发生率分别是 77.7%、15.3%, 围绝经期女性评分显著高于绝经后期女性评分, 差异有统计学意义 ( $P=0.027$ )。SDS 评分在不同年龄段女性的差异较小 ( $F=2.467$ ,  $P>0.05$ )。经二分类多因素 logistic 回归分析校正混杂因素后显示 KMI 评分  $>6$  分 ( $OR=1.148$ , 95%  $CI=1.127\sim 1.170$ )、生育 3 个以上子女 ( $OR=1.339$ , 95%  $CI=1.009\sim 1.776$ )、受教育程度  $<9$  年 ( $OR=1.768$ , 95%  $CI=1.167\sim 2.678$ )、癌症患病史 ( $OR=2.685$ , 95%  $CI=1.139\sim 6.334$ ) 的绝经女性更容易出现抑郁症状。而经济收入  $>5 000$  元 / 月的女性则不容易出现抑郁症状 ( $OR=0.597$ , 95%  $CI=0.417\sim 0.858$ )。**结论** 围绝经期和绝经后期女性抑郁症状发生率较高。临床上应该采取更多措施改善绝经女性生活质量。

**【关键词】** 绝经; 情绪障碍; 抑郁症状

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· 围绝经期专栏 ·

**Analysis of depression and its influencing factors in menopausal women** Zheng Yanwei, Zhu Rong,

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**【Abstract】 Objective** To study the depression and its influencing factors in menopausal women.

**Methods** A multicenter cross-sectional study was conducted to obtain basic data, self-rating depression scale (SDS) was used to evaluate depression and modified Kupperman index scale (KMI) was used to evaluate menopausal symptom. SPSS20.0 software was used for data analysis. **Results** A total of 1 591 women were enrolled, with a median age of 52 years old. The average scores of KMI and SDS were  $13.9 \pm 8.8$  and  $39.6 \pm 9.0$ , respectively. The prevalences were 77.7% and 15.3%, respectively. The scores of perimenopausal women were significantly higher than those of postmenopausal women ( $P=0.027$ ). There was no significant difference about SDS score among women of different ages (40–60 years old) ( $F=2.467$ ,  $P>0.05$ ). After adjusting for confounding factors by logistic stepwise regression with binary classification, we found that having children more than three ( $OR=1.198$ , 95%  $CI=1.098-1.425$ ), KMI score  $>6$  ( $OR=1.153$ , 95%  $CI=1.131-1.175$ ), a history of cancer ( $OR=3.092$ , 95%  $CI=1.221-7.828$ ) were risk factors for depressive symptoms. Women with economic income  $> 5\ 000$  yuan/month were less prone to depressive symptoms ( $OR=0.344$ , 95%  $CI=0.172-0.689$ ).

**Conclusion** The incidence of depression in perimenopausal and postmenopausal women is higher. More clinical measures should be taken to improve the quality of life of postmenopausal women.

**【Key words】** Menopause; Mood disorders; Depression symptoms

**Fund program:** Science and Technology Commission Shanghai Municipalit (15211950202); Shanghai Municipal Commission of Health and Family Planning (GWIV-15; 15GWZK0401)



# 上海市围绝经期门诊就诊妇女治疗效果的随访研究

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**【摘要】** 目的 分析影响围绝经期综合征妇女选择治疗方法的相关因素。方法 将连续 2 个月内因围绝经期症状在上海市城乡二三级医院绝经专病 / 妇科门诊就诊且接受治疗的妇女纳入本研究, 并开展 1 年随访, 通过问卷调查收集妇女的社会人口学信息, 围绝经期综合征程度采用改良 Kupperman 评分(modified Kupperman index, KMI)判断。结果 就诊的 349 例妇女中共有 161 例接受治疗并进入队列, 其中 108 例(67.1%)选择激素替代疗法(menopausal hormone therapy, MHT)。治疗后 KMI 评分正常的女性比例(37.9%)显著高于治疗前(13.0%,  $P=0.000$ ), 治疗后 KMI 总分( $17.3 \pm 10.0$ )显著低于治疗前( $10.6 \pm 8.2$ ,  $P=0.000$ ), 治疗后 13 个症状单项得分均显著降低于治疗前( $P<0.005$ )。多因素 logistic 回归分析提示, 同时患有 1 种[调整  $OR(aOR)=0.277$ ]和 2 种及以上( $aOR=0.249$ )慢性疾病的妇女接受 MHT 治疗的可能性显著低于无慢性病共患妇女。月经不规则( $aOR=5.317$ )和已停经( $aOR=11.070$ )妇女更可能接受 MHT 治疗。结论 上海市围绝经期综合征妇女治疗效果较好, 其是否接受 MHT 受自身健康状况和当前月经状态的影响。

**【关键词】** 围绝经期综合征; 治疗效果; 激素替代治疗(MHT)

**基金项目:** 上海市妇幼中心上海市加强公共卫生体系建设三年行动计划更年期项目(GWIV-15); 上海市妇幼中心上海市第四轮公共卫生三年行动计划妇幼卫生重点学科建设(15GWZK0401)

· 围绝经期专栏 ·

**Treatment effect of outpatient women in perimenopausal clinics—a follow-up study in Shanghai** Yang Lin,

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**【Abstract】 Objective** To analyze the treatment effectiveness of perimenopausal syndrome and factors influencing the therapy selection. **Methods** A cohort study with a 1-year-follow-up was conducted for outpatients who developed perimenopausal symptoms and received treatment in postmenopausal/gynecological clinics at secondary and tertiary hospitals in urban and suburban areas in Shanghai for 2 consecutive months. The social demographic data were collected through questionnaires and perimenopausal symptoms were evaluated by modified Kupperman index (KMI). **Results** A total of 161 among 349 women in clinics received treatment and were included in the cohort, among which 108 women (67.1%) received menopausal hormone therapy (MHT). After treatment, the proportion of normal KMI (13.0%) and total KMI score ( $17.3 \pm 10.0$ ) was significantly decreased compared with before treatment (37.9%,  $P=0.000$ ;  $10.6 \pm 8.2$ ,  $P=0.000$ ), and scores of 13 symptoms were all significantly decreased ( $P<0.005$ ). Multivariate logistic regression analysis showed that women with 1 or  $\geq 2$  non-communicable diseases (NCDs) were less likely to receive MHT compared with those not developing NCDs [adjusted OR (aOR)=0.277; aOR=0.249], while irregular menstruation women (aOR=5.317) and menstruated women (aOR=11.070) were more likely to receive MHT. **Conclusion** The effectiveness of MHT was satisfactory among perimenopausal women in Shanghai and the acceptance of MHT was influenced by women's health and menstrual status.

**【Key words】** Perimenopausal syndrome; Treatment effectiveness; Menopausal hormone therapy (MHT)

**Fund program:** The Fourth Round of the Three-Year Public Health Action Plan of Shanghai, China (GWIV-15); the Fourth Round of the Shanghai Three-year Action Plan on Public Health Discipline and Talent Program: Women and Children's Health (15GWZK0401)

# 甘肃省围绝经期女性的中医体质流行病学调查

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**【摘要】**目的 探讨围绝经期女性的中医体质与围绝经期综合征及相关症状发生的相关性。方法 按照多阶段整群随机抽样的方法, 通过一般情况调查问卷、改良 Kupperman 评分量表、中医体质分类与判定表, 对甘肃省 40~55 岁女性进行一次横断面调查。结果 调查人群中, 平和质占 32.91%, 偏颇质占 67.09%。偏颇质女性的年龄、患冠心病率、糖尿病率、曾进行子宫或卵巢切除术占比、妊娠次数、Kupperman 评分、围绝经期综合征发生率、相关症状发生率均显著高于平和质者, 初潮年龄、停经年龄、活产数、骨质疏松发生率差异均无统计学意义。结论 偏颇质女性更易发生围绝经期综合征及绝经相关症状。

**【关键词】**绝经; 中医体质; 围绝经期综合征; 骨质疏松

· 围绝经期专栏 ·

**Epidemiological investigation of Chinese Medicine constitutional types in perimenopausal women of Gansu Province** Wang Liyan, Zhang Rui, Jin Panpan, Sun Xiaoyan, Zhang Xuehong

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**【Abstract】 Objective** To explore the correlation between perimenopausal women's Chinese Medicine constitutional types and perimenopausal syndrome. **Methods** Stratified multistage cluster sampling method was used to investigate women aged 40–55 years in Gansu Province by general situation questionnaire, modified Kupperman score, Classification and Determination of Traditional Chinese Medicine (TCM) Constitutions. **Results** In the survey normal constitution accounted for 32.91%, and abnormal constitution accounted for 67.09%. In abnormal constitution, age, rate of coronary heart disease, rate of diabetes mellitus, hysterectomy or oophorectomy, number of pregnancy, Kupperman score, the incidence of perimenopause syndrome and related symptoms were significantly increased than normal constitution. Menarche age, menopause age, number of live birth and osteoporosis were not significantly different. **Conclusion** The women with abnormal constitution were more likely to occur perimenopause syndrome and related symptoms.

**【Key words】** Menopause; Chinese Medicine constitutional types; Perimenopausal syndrome; Osteoporosis



# 萎缩性阴道炎患者的阴道菌群结构分析

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**【摘要】** 目的 揭示萎缩性阴道炎患者阴道群落特征, 并探讨阴道菌群结构与萎缩性阴道炎发病之间的潜在关联。方法 共纳入 30 名萎缩性阴道炎患者参与本研究(萎缩性阴道炎组), 另有 30 名进行体检的绝经后健康妇女作为对照组。以 16S rRNA 基因为研究靶点, 采用 Illumina 第二代高通量测序技术结合生物信息学分析, 得阴道菌群结构数据。采用正则变量的逐步判别分析, 对两组间群落组成的关联和差异进行比较。采用 Spearman 等级回归分析, 探讨单个物种数量与疾病严重程度间的关系。结果 在所有 60 例中, 总共测得 288 个属的细菌。萎缩性阴道炎组和对照组间阴道菌群总体结构差异有统计学意义 ( $P < 0.05$ )。其中 12 个属的主要细菌相对丰度差异显著。在绝经后正常妇女的阴道内, 乳酸杆菌占据整个阴道微生物群落主导地位。萎缩性阴道炎组阴道加德纳菌相对丰度 (41.7%) 显著高于对照组 (16.7%,  $P < 0.000 1$ ), 并取代乳酸杆菌成为阴道群落中生物优势最大的种群。萎缩性阴道炎组的乳酸杆菌失去了其生物优势地位, 相对丰度 (11.2%) 显著低于对照组 (53.2%,  $P < 0.000 1$ )。相关性分析显示, 萎缩性阴道炎组患者生殖道症状的严重程度与乳酸杆菌的相对丰度呈显著负相关 ( $r = -0.301$ ,  $P < 0.001$ ), 而与加德纳菌 ( $r = 0.278$ ,  $P < 0.001$ ) 及奇异菌属 ( $r = 0.166$ ,  $P < 0.05$ ) 的数量呈显著正相关。结论 阴道微生物群落失衡与萎缩性阴道炎发病存在关联。对于绝经后女性而言, 处于生物优势地位的乳酸杆菌在维持阴道健康方面起到更为重要的作用。而阴道加德纳菌属和奇异菌属与绝经后妇女生殖道萎缩症状的严重程度有关, 且这 2 种微生物的过度生长可能增加了罹患萎缩性阴道炎的风险。

**【关键词】** 阴道菌群; 萎缩性阴道炎; 乳酸杆菌; 奇异菌; 加德纳菌

**The profiles of vaginal microbiota in postmenopausal women with atrophic vaginitis** Ge Tan, Shen Jian,

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**【Abstract】 Objective** To identify the profiles of vaginal microbiota in postmenopausal women with or without atrophic vaginitis (AV), and investigate the potential correlations between vaginal bacterial composition and AV pathogenesis. **Methods** Thirty eligible patients, who were suffering with AV, were designated as AV group. In addition, a group of post-menopausal women remaining genital symptoms free were enrolled and designated as control group. The structure of bacteria communities present in the samples were identified by classifying 16S rRNA gene sequences in each sample using next-generation deep sequencing and bioinformatic analysis. To investigate differences of community composition between the two groups, a stepwise discriminant analysis was performed using the log-ratio-transformed proportions and canonical transformation for the species. In order to determine if a statistical relationship existed between species relative abundance and genital symptom score, the Spearman's correlation coefficient analysis were used. **Results** A total of 60 vaginal samples were sequenced and the retrieved sequences were from 288 genera. The canonical variable transformed from total species proportions differed significantly between AV group and control group ( $P<0.05$ ), while the relative abundance of 12 key vaginal genera were also significantly different between groups. *Lactobacilli* universally existed in most healthy post-menopausal women's vaginal communities with a predominant abundance. The relative abundance of *Gardnerella* (41.7%) in AV women significantly increased compared with control group (16.7%) and played a dominant role in vaginal communities in place of *Lactobacilli* (53.2%,  $P<0.0001$ ). Meanwhile, the relative abundance of *Lactobacilli* in AV group significantly decreased from 53.2% to 11.2% ( $P<0.0001$ ), and lost its biological superiority. The results also indicated that among the most 5 key taxa present in all communities, *Lactobacillus* was negative correlated ( $r=-0.301$ ,  $P<0.001$ ) with symptom score, whereas *Gardnerella* ( $r=0.278$ ,  $P<0.001$ ) and *Atopobium* ( $r=0.166$ ,  $P<0.05$ ) was positively correlations with genital symptom. **Conclusion** The pathogenesis of atrophic vaginitis were closely related to disruption of vaginal commensal microbiota in postmenopausal women. After menopause, *Lactobacillus* in dominant proportion drove the main protective functions and maintaining the health of vagina. Along with *Lactobacillus*, we noted that two genera, *Gardnerella* and *Atopobium*, were detected to have association with genital symptom score. The overgrowth of these two genera might increase the risk of AV.

**【Key words】** Perimenopausal syndrome; Treatment effectiveness; Menopausal hormone therapy

## G 蛋白耦联雌激素受体介导雌激素治疗机制研究进展

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**【摘要】** 女性绝经后会出现一系列与雌激素缺乏有关的症状和疾病, 补充雌激素是目前主要的治疗方法。雌激素除了通过与传统的核受体 ER $\alpha$ 、 $\beta$  结合产生基因组效应外, 雌激素膜受体 -G 蛋白耦联雌激素受体 (G protein-coupled estrogen receptor, GPER) 介导的雌激素对靶器官的快速效应也得到了证实。近些年, 关于 GPER 介导雌激素在不同靶细胞的特异生理功能及其作用机制的研究层出不穷, 本文从生殖系统、神经系统、心血管系统、内分泌代谢及骨代谢方面, 综述这些年来研究发现的 GPER 介导的雌激素作用的相关机制。

**【关键词】** 绝经; 雌激素; G 蛋白耦联雌激素受体 (GPER); G 蛋白耦联受体 30(GPR30); 激素补充治疗

· 围绝经期专栏 ·

**Advances in the mechanism of G protein coupled estrogen receptor mediated estrogen therapy** *Hu Jiangshan, Tao Minfang*

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**【Abstract】** There will be a series of symptoms and diseases associated with estrogen deficiency after menopause, and the main treatment is menopause hormone therapy. In addition to the genomic effects of estrogen binding to the traditional nuclear receptors ER $\alpha$  and  $\beta$ , a recently discovered G protein-coupled estrogen receptor (GPER) has also confirmed the rapid effects of estrogen on target organs. In recent years, studies on GPER-mediated estrogen specific physiological functions in different target cells and its mechanism of action are emerging. This review summarizes the possible mechanisms of GPER mediated estrogen therapy in the treatment of menopausal symptoms and diseases from the aspects of reproductive system, nervous system, cardiovascular system, endocrine metabolism and bone metabolism.

**【Key words】** Menopause; Estrogen; G protein-coupled estrogen receptor (GPER); G protein-coupled receptor 30 (GPR30); Hormone replacement therapy



# 安宫黄体酮方案治疗低反应患者的体外受精疗效评估

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**【摘要】** 目的 探讨人绝经期促性腺激素 (human menopausal gonadotropin, hMG) 联合安宫黄体酮 (medroxyprogesteron acetate, MPA) 方案治疗卵巢低反应 (poor ovarian response, POR) 患者的疗效。方法 回顾性分析助孕后仅有 1 个卵泡的 517 个体外受精 (*in vitro* fertilization, IVF) 周期, 分为 hMG 联合 MPA 组 ( $n=316$ ) 和自然周期组 ( $n=201$ ), 比较两组患者临床结局指标。结果 hMG 联合 MPA 组的获卵周期率 (82.9%) 和卵子双原核 (2PN) 周期率 (55.4%) 均显著高于自然周期组 (74.6%,  $P=0.02$ ; 41.3%,  $P=0.00$ ); 获 M<sub>II</sub> 卵子周期率 (73.7%) 和优质胚胎周期率 (39.9%) 均略高于自然周期组 (68.2%,  $P=0.17$ ; 33.8%,  $P=0.17$ )。所获胚胎的种植率、流产率和宫外孕率与自然周期组均相似 ( $P>0.05$ )。结论 hMG 联合 MPA 方案治疗 POR 患者的效果优于自然周期, 是安全有效的促排卵方案。

**【关键词】** 卵巢低反应 (POR); 体外受精 (IVF); 胚胎质量; 种植率

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**Therapeutic evaluation of medroxyprogesterone acetate protocol in *in vitro* fertilization treatment of patients with poor ovarian response** Si Jiqiang, Zhu Xiuxian, Kuang Yanping, Lyu Qifeng

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**【Abstract】 Objective** To analyze the clinical outcomes of the human menopausal gonadotropin (hMG) and medroxyprogesterone acetate (MPA) protocol in patients with poor ovarian response (POR). **Methods** The data of 517 IVF cycles were collected retrospectively. Patients were divided into two groups: the hMG and MPA protocol group ( $n=316$ ) and natural cycle group ( $n=201$ ). **Results** The rate of cycle with oocyte retrieved (82.9%) and rate of cycle with two pronucleus (2PN) zygote (55.4%) were significantly higher in hMG and MPA protocol group than in natural cycle group (74.6%,  $P=0.02$ ; 41.3%,  $P=0.00$ ), while rate of cycle with M<sub>II</sub> oocyte (73.7%) and rate of cycle with top-quality embryo (39.9%) were slightly higher in hMG and MPA protocol group than those in natural cycle group (68.2%,  $P=0.17$ ; 33.8%,  $P=0.17$ ). The implantation rate, the miscarriage rate and the ectopic rate in hMG and MPA protocol group were comparable to those in natural cycle group ( $P>0.05$ ). **Conclusion** Clinical outcomes of hMG and MPA protocol on poor ovarian responders were more effective than natural cycles, it was a safe and effective protocol.

**【Key words】** Poor ovarian response (POR); *In vitro* fertilization (IVF); Embryo quality; Implantation rate

**Fund program:** National Natural Science Foundation of China (81571486); Training Program for Young University Teachers of Shanghai (ZZjdyx12107)

# 冷刀与电刀实施宫腔粘连手术对子宫内膜影响的对比研究

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**【摘要】** 目的 探讨宫腔镜手术方式的选择。方法 选取 2016 年 1 月—2017 年 8 月经宫腔镜检查确诊为中重度宫腔粘连 (IUA) 患者共 128 例, 随机分为冷刀组和电刀组。冷刀组使用微型手术剪分离 IUA 带。电刀组使用针状电极分离粘连, 环形电极切除瘢痕组织。比较 2 种手术方式患者术中情况、术后宫腔镜 2 次探查宫腔情况及术后三维经阴道超声检查子宫内膜的情况。结果 冷刀组平均手术时间  $(15.7 \pm 4.1)$  min, 电刀组平均手术时间  $(22.8 \pm 5.6)$  min, 冷刀组显著短于电刀组 ( $P=0.000$ ); 冷刀组治愈率  $[28.12\% (18/64)]$  高于电刀组  $[9.38\% (6/64)]$  ( $P=0.007$ ); 冷刀组患者的子宫内膜容积  $[(1.55 \pm 0.19) \text{ cm}^3]$ 、血管指数  $(2.60\% \pm 0.77\%)$ 、血流指数  $(7.65 \pm 1.96)$ 、血管血流综合指数  $(0.96 \pm 0.25)$  的增加值均高于电刀组  $[(0.59 \pm 0.11) \text{ cm}^3, 0.64\% \pm 0.16\%, 3.69 \pm 0.89, 0.25 \pm 0.04, P$  均  $=0.000]$ 。结论 冷刀手术分离中重度 IUA 与电刀组相比手术效率更高, 术后改善子宫内膜容积、子宫内膜及内膜下肌层的血液供应更佳。

**【关键词】** 宫腔粘连 (IUA); 宫腔镜; 冷刀手术; 子宫内膜

· 临床研究 ·

**Comparative study on the effect of intrauterine adhesion cold knife surgery and electric cauterly on endometrium** Qin Xiaomei, Li Liuming, Qin Guirong, Jiang Xiaoli

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**【Abstract】 Objective** To discuss the choice of hysteroscopic operation. **Methods** A total of 128 patients with moderate or severe intrauterine adhesions diagnosed by hysteroscopy were randomly divided into cold knife group and electric knife group. The cold knife group used miniature surgical scissors to separate the intrauterine adhesives and bands. The electric group used needle electrode to separate the adhesion, and the ring electrode was used to excision scar tissue. Two groups of patients were compared in the intraoperative condition, postoperative hysteroscopy, two times of uterine cavity exploration and postoperative three-dimensional transvaginal ultrasound examination of endometrium. **Results** The average operation time of the cold knife group was  $(15.7 \pm 4.1)$  min, the average operation time of the electric knife group was  $(22.8 \pm 5.6)$  min. The operation time of the cold knife group was shorter than that of the electric knife group ( $P=0.000$ ). The cure rate of the cold knife group [28.12% (18/64)] was higher than that of the electric knife group [9.38% (6/64)] ( $P=0.007$ ), and the endometrium volume of the cold knife group was  $(1.55 \pm 0.19)$  cm<sup>3</sup>, the value of the vascular index  $(2.60\% \pm 0.77\%)$ , the blood flow index  $(7.65 \pm 1.96)$  and the blood flow comprehensive index  $(0.96 \pm 0.25)$  were higher than these of the electric knife group [ $(0.59 \pm 0.11)$  cm<sup>3</sup>,  $0.64\% \pm 0.16\%$ ,  $3.69 \pm 0.89$ ,  $0.25 \pm 7.65$ ,  $P=0.000$ ]. **Conclusion** The operation efficiency of the treatment of severe uterine adhesion by cold knife surgery is higher than that of the electric knife group. The blood supply of endometrium, endometrium and intima of the endometrium is better after the operation.

**【Key words】** Intrauterine adhesions (IUA); Hysteroscopy; Cold knife surgery; Endometrium



# 核因子 $\kappa$ B 和肿瘤坏死因子 $\alpha$ 与多囊卵巢综合征患者糖脂代谢指标相关性研究

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**【摘要】** 目的 探讨血清中核因子  $\kappa$ B(NF- $\kappa$ B) 和肿瘤坏死因子  $\alpha$ (TNF- $\alpha$ ) 与多囊卵巢综合征 (PCOS) 患者糖脂代谢指标的相关性。方法 选择 80 例 PCOS 患者为研究组, 同期来院就诊的 80 例非 PCOS 不孕症患者为对照组。根据体质量指数 (BMI) 是否  $\geq 25 \text{ kg/m}^2$ , 将研究组分为 PCOS 肥胖亚组 (A 组, 40 例)、PCOS 非肥胖亚组 (B 组, 40 例); 对照组分为非 PCOS 肥胖亚组 (C 组, 40 例) 和非 PCOS 非肥胖亚组 (D 组, 40 例)。检测静脉血 NF- $\kappa$ B、TNF- $\alpha$  及血糖血脂相关指标, 并对各因素间关系采用 Spearman 相进行相关性分析。结果 A 组稳态胰岛素评价指数 (HOMA-IR)、空腹胰岛素 (FIN)、甘油三酯 (TG) 和低密度脂蛋白胆固醇 (LDL-C) 水平指标明显高于 B 组 ( $P$  值分别为 0.022、0.036、0.044、0.023)、C 组 ( $P$  值分别为 0.014、0.029、0.021、0.018) 及 D 组 ( $P$  值分别为 0.007、0.021、0.014、0.003), B 组 HOMA-IR 及 FIN 指标高于 C 组 ( $P$  值分别为 0.041、0.033) 及 D 组 ( $P$  值分别为 0.030、0.017); A 组血清中总胆固醇 (TC) 水平高于 D 组 ( $P=0.023$ ); B 组血清中 TG 和 LDL-C 水平高于 D 组 ( $P$  值分别为 0.032、0.026); A 组血清中高密度脂蛋白胆固醇 (HDL-C) 水平低于 D 组 ( $P=0.001$ ); A 组血清中 NF- $\kappa$ B 水平 [(655.59 $\pm$ 273.41) IU/L] 高于 B 组 [(502.84 $\pm$ 165.48) IU/L] ( $P=0.034$ )、C 组 [(352.10 $\pm$ 132.45) IU/L] ( $P=0.019$ ) 及 D 组 [(319.62 $\pm$ 112.57) IU/L] ( $P=0.005$ ), B 组血清中 NF- $\kappa$ B 水平高于 C 组 ( $P=0.039$ ) 及 D 组 ( $P=0.031$ ); A 组血清中 TNF- $\alpha$  水平 [(86.18 $\pm$ 18.32) ng/L] 高于 B 组 [(66.86 $\pm$ 22.71) ng/L] ( $P=0.042$ )、C 组 [(58.40 $\pm$ 17.90) ng/L] ( $P=0.029$ ) 及 D 组 [(54.67 $\pm$ 22.34) ng/L] ( $P=0.013$ ), B 组血清中 TNF- $\alpha$  水平高于 D 组 ( $P=0.038$ ); 在相关性分析中显示, PCOS 患者中 NF- $\kappa$ B 及 TNF- $\alpha$  均与 BMI、FIN、HOMA-IR、TG、LDL-C 等指标有相关性 ( $P<0.05$ ), 且 NF- $\kappa$ B 与 TNF- $\alpha$  也有相关性 ( $P<0.05$ )。结论 TNF- $\alpha$  可能与 NF- $\kappa$ B 相互作用共同参与 PCOS 的糖脂代谢紊乱的发生及发展, 为临床治疗 PCOS 提供了新的思路。

**【关键词】** 核因子  $\kappa$ B(NF- $\kappa$ B); 肿瘤坏死因子  $\alpha$ (TNF- $\alpha$ ); 多囊卵巢综合征 (PCOS); 低度慢性炎症  
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· 临床研究 ·

**Correlation between tumor necrosis factor- $\alpha$  and nuclear factor- $\kappa$ B and related indicators on glucose metabolism and lipid metabolism in women with polycystic ovary syndrome** Zhang Yan, Yang Yuqing,

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**【Abstract】 Objective** To explore the correlation between the serum inflammatory markers of nuclear factor- $\kappa$ B (NF- $\kappa$ B), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and related indicators on glucose metabolism and lipid metabolism in women with polycystic ovary syndrome (PCOS). **Methods** Eighty patients with PCOS were selected in the observe group, and 80 infertile patients without PCOS were collected in control group. The patients were subdivided to 4 groups according to body mass index (BMI) levels, including the obese (BMI  $\geq 25$  kg/m<sup>2</sup>) patients with PCOS (group A,  $n=40$ ), the non-obese (BMI $<25$  kg/m<sup>2</sup>) patients with PCOS (group B,  $n=40$ ), the obese (BMI  $\geq 25$  kg/m<sup>2</sup>) patients without PCOS (group C,  $n=40$ ), and the non-obese (BMI $<25$  kg/m<sup>2</sup>) patients without PCOS (group D,  $n=40$ ). The serum samples were collected from all the patients for detecting TNF- $\alpha$ , NF- $\kappa$ B and related indicators on glucose metabolism and lipid metabolism. The parameters were analyzed and compared among the four groups by using two independent samples  $t$ -test and Spearman correlation analysis.

**Results** The indexes of homeostasis model assessment-insulin resistance (HOMA-IR) and fasting insulin (FIN) in group A were significantly higher than those in group B ( $P$  were 0.022 and 0.036, respectively), group C ( $P$  were 0.014 and 0.029, respectively) and group D ( $P$  were 0.007 and 0.021, respectively), while they were significantly higher in group B than those in group C ( $P$  were 0.041 and 0.033, respectively), and group D ( $P$  were 0.030 and 0.017, respectively). Serum total cholesterol level (TC) in group A was higher than that in group D ( $P=0.023$ ). The indexes of triglyceride (TG) and low-density lipoprotein cholesterol (LDL-C) in group A were higher than those in group B ( $P$  were 0.044 and 0.023, respectively), group C ( $P$  were 0.021 and 0.018, respectively) and group D ( $P$  were 0.014 and 0.003, respectively), while they were higher in group B than those in group D ( $P$  were 0.032 and 0.026, respectively). Serum high-density lipoprotein cholesterol (HDL-C) level in group A was lower than that in group D ( $P=0.001$ ). Serum NF- $\kappa$ B level [(655.59 $\pm$ 273.41) IU/L] in group A was higher than that in group B [(502.84 $\pm$ 165.48) IU/L] ( $P=0.034$ ), group C [(352.10 $\pm$ 132.45) IU/L] ( $P=0.019$ ) and group D [(319.62 $\pm$ 112.57) IU/L] ( $P=0.005$ ), while it was higher in group B than in group C ( $P=0.039$ ) and group D ( $P=0.031$ ). Serum TNF- $\alpha$  level [(86.18 $\pm$ 18.32) ng/L] in group A was higher than that in group B [(66.86 $\pm$ 22.71) ng/L] ( $P=0.042$ ), group C [(58.40 $\pm$ 17.90) ng/L] ( $P=0.029$ ) and group D [(54.67 $\pm$ 22.34) ng/L] ( $P=0.013$ ), while it was higher in group B than in group D ( $P=0.038$ ). The indexes of NF- $\kappa$ B and TNF- $\alpha$  were related to BMI, FIN, HOMA-IR, TG, LDL-C in patients with PCOS ( $P<0.05$ ), NF- $\kappa$ B was also associated with TNF- $\alpha$ .

**Conclusion** TNF- $\alpha$  may interact with NF- $\kappa$ B to participate in the occurrence and development of glucose and lipid metabolism disorder of PCOS. It may provide a new clinical thinking for the clinical treatment of PCOS.

**【Key words】** Nuclear factor- $\kappa$ B (NF- $\kappa$ B); Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ); Polycystic ovary syndrome (PCOS); Chronic inflammation

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# ERBB3 表达下调对宫颈癌细胞增殖迁移和侵袭的影响

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**【摘要】** 目的 探讨 erb-b2 受体酪氨酸激酶 3(ERBB3) 在调节癌细胞的迁移和侵袭及其在宫颈癌的发生和进展过程中的作用。方法 收集 2014 年 4 月—2016 年 12 月期间在本院接受治疗的 25 例宫颈鳞状细胞癌患者和 25 例宫颈腺癌患者。通过荧光定量 PCR (qRT-PCR) 检测了宫颈鳞状细胞癌和宫颈腺癌患者体内肿瘤组织和癌旁组织中 *ERBB3* mRNA 的表达水平。用 siRNA 转染宫颈鳞状细胞癌细胞沉默 ERBB3 的表达后, 应用 Transwell 细胞迁移实验检测细胞迁移和侵袭能力, 利用 CCK-8 检测细胞增殖, 应用 Western blotting 检测 MTK-1 蛋白的表达变化。结果 宫颈鳞状细胞癌和宫颈腺癌患者癌组织中 *ERBB3* mRNA 水平均低于其正常组织 ( $P=0.00$ ,  $P=0.00$ )。HPV 感染对 ERBB3 蛋白在宫颈鳞状细胞癌细胞系的表达水平为  $10.30 \pm 0.07$ (HPV 阳性)、 $7.99 \pm 0.75$ (HPV 阴性) 和正常宫颈细胞系中的表达水平为  $3.02 \pm 0.47$ (HPV 阳性)、 $3.16 \pm 0.22$ (HPV 阴性), 差异均无统计学意义 ( $P$  均  $>0.05$ )。ERBB3 siRNA 沉默后宫颈鳞状细胞癌细胞 SiHa 和 C33A 的增殖 ( $0.20 \pm 0.10$ ,  $0.16 \pm 0.08$ )、迁移 ( $64.87 \pm 0.26$ ,  $55.02 \pm 0.06$ ) 和侵袭 ( $49.99 \pm 0.06$ ,  $62.80 \pm 0.19$ ) 能力显著低于正常宫颈细胞系中 SiHa 和 C33A 的增殖 ( $0.86 \pm 0.49$ ,  $0.60 \pm 0.34$ )、迁移 ( $99.99 \pm 0.31$ ,  $100.07 \pm 0.23$ ) 和侵袭 ( $99.89 \pm 0.35$ ,  $99.89 \pm 0.14$ ) 能力, 差异具有统计学意义 ( $P < 0.05$ )。ERBB3 通过 siRNA 沉默后 MTK-1 蛋白的表达水平也显著降低。结论 ERBB3 的下调很可能通过抑制 MTK-1 的表达来抑制宫颈癌细胞的增殖、迁移和侵袭, 从而抑制肿瘤的发展。

**【关键词】** 宫颈癌; erb-b2 受体酪氨酸激酶 3(ERBB3); 丝裂原活化蛋白激酶激酶 4(MTK-1)

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· 实验研究 ·

**Down-regulation of ERBB3 decreases the proliferation, migration and invasion of cervical cancer cells**

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**【Abstract】 Objective** To explore the role of erb-b2 receptor tyrosine kinase 3 (ERBB3) in regulating the migration and invasion of cancer cells, and its role in the occurrence and progression of cervical cancer.

**Methods** Totally 25 patients with cervical squamous cell carcinoma and 25 patients with cervical adenocarcinoma were enrolled who were treated in our center from April 2014 to December 2016. Expression level of ERBB3 in patients with cervical squamous cell carcinoma and cervical adenocarcinoma was detected by qRT-PCR. After ERBB3 siRNA silencing on cervical squamous cell, Transwell experiment was used to analyze the capability of migration and invasion, and CCK-8 kits was used to analyze the capability of proliferation, and Western blotting was used to detect S-methyl-5-thioribose kinase 1 (MTK-1) protein level. **Results** qRT-PCR results showed that the expression levels of ERBB3 decreased in cervical squamous cell carcinoma and cervical adenocarcinoma were lower than those in the normal cervical cell lines ( $P=0.00$ ,  $P=0.00$ ). The expression level of HPV infection to ERBB3 protein in cervical squamous cell carcinoma cell lines was  $10.30 \pm 0.07$  (HPV positive),  $7.99 \pm 0.75$  (HPV negative) and normal cervical cell lines were  $3.02 \pm 0.47$  (HPV positive) and  $3.16 \pm 0.22$  (HPV negative), with no statistical significance ( $P>0.05$ ). After ERBB3 siRNA silencing, the capabilities of SiHa and C33A in cervical squamous cell carcinoma in proliferation ( $0.20 \pm 0.10$ ,  $0.16 \pm 0.08$ ), migration ( $64.87 \pm 0.26$ ,  $55.02 \pm 0.06$ ), and invasion ( $49.99 \pm 0.06$ ,  $62.80 \pm 0.19$ ) were significantly lower than those in normal cervical cell lines ( $P<0.05$ ). In addition, the expression level of MTK-1 protein was also significantly reduced after MTK-1 siRNA silencing. **Conclusion** Down-regulation of ERBB3 can decrease the proliferation, migration and invasion of cervical cancer cells by inhibiting the expression of MTK-1.

**【Key words】** Cervical cancer; Erb-b2 receptor tyrosine kinase 3 (ERBB3); S-methyl-5-thioribose kinase 1 (MTK-1)

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# 雌激素调节阴道常驻菌诱导的阴道上皮细胞免疫应答实验研究

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**【摘要】**目的 探讨雌激素调节阴道上皮细胞对 2 种阴道常驻菌的天然免疫状态的影响, 揭示萎缩性阴道炎潜在的发病机制。**方法** 以阴道上皮细胞株 VK2/E6E7 为模型, 在不同雌激素环境下, 分别给予不同浓度阴道奇异菌和弯曲乳酸杆菌进行体外刺激, 酶联免疫吸附法 (ELISA) 测定培养上清液中炎症细胞因子 [白介素 (IL)-1 $\alpha$ 、IL-1 $\beta$ 、IL-6、肿瘤坏死因子 (TNF) $\alpha$ ] 和趋化因子 IL-8 的分泌水平。**结果** 阴道奇异菌诱发阴道上皮出现显著天然免疫反应, 且 IL-6 和 IL-8 分泌呈现出一定程度的剂量依赖特性, 菌液浓度为  $4 \times 10^6$  CFU/mL, 刺激 12 h 时 IL-6 为  $(176.562 \pm 11.991)$  ng/L, IL-8 为  $(1\ 049.883 \pm 121.348)$  ng/L; 而阴道弯曲乳酸杆菌并未诱发阴道上皮细胞产生明显的天然免疫反应。在雌激素环境下, 阴道上皮细胞对阴道奇异菌刺激所产生免疫反应的强度显著变弱; 但 IL-8 的分泌时间显著延迟到刺激后 4 h, 且 IL-6 和 IL-8 的最大上升幅度显著下降 (IL-6,  $P=0.001\ 9$ ; IL-8,  $P=0.008\ 7$ )。**结论** 奇异菌能够诱导阴道上皮以剂量依赖的方式分泌炎症细胞因子; 同时, 雌激素能调节 IL-6 和 IL-8 的分泌, 从而调节后续的保护机制, 拮抗病原微生物的入侵和过度生长, 维持阴道的健康。

**【关键词】** 萎缩性阴道炎; 阴道上皮; 天然免疫; 雌激素

**Estrogen regulates the natural immunity of vaginal epithelial cells to the resident bacteria of vagina**

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**【Abstract】 Objective** To explore the effects of estrogen regulating vaginal epithelial cells on the natural immune status of two kinds of vaginal resident bacteria, and to reveal the pathogenesis of atrophic vaginitis potential. **Methods** Vaginal epithelial cell lines VK2 / E6E7 were treated as model. Under the different environmental estrogen, different concentrations of *Atopobium* and *Lactobacillus curvatus* were given to *in vitro* stimulate vaginal epithelial cell lines. Enzyme-linked immunosorbent assay (ELISA) method was used to determine the secretion of inflammatory cytokine and chemokine. **Results** Vaginal epithelium induced a significant natural immune response, and the secretion of interleukin-6 (IL-6) and IL-8 presented a certain amount of dose-dependent characteristics. However, *Lactobacillus crispatus* did not induce innate immune response in vaginal epithelial cell lines. In the estrogen environment, the strength of the immune response of vaginal epithelial cells in the stimulation of *Atopobium vaginae* was significantly changed. IL-8 secreted time delayed, the maximum increase of IL-6 and IL-8 decreased significantly (IL-6,  $P=0.001\ 9$ ; IL-8,  $P=0.008\ 7$ ). **Conclusion** *Atopobium vaginae* can induce the secretion of inflammatory cytokines in the vaginal epithelium by dose-dependent manner. At the same time, estrogen regulates the secretion of IL-6 and IL-8 synthesis, at relatively low and manageable level, adjust the subsequent protection mechanism of disease-resistant original microbial growth, invasion and maintaining the health of the vagina.

**【Key words】** Atrophic vaginitis; Vaginal epithelium; Natural immunity; Estrogen

## 外周血 CD16<sup>++</sup> 单核细胞对多囊卵巢综合征主要临床特征及短期疗效的评估

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**【摘要】** 目的 探讨外周血 CD16<sup>++</sup> 单核细胞 (CD16<sup>++</sup> Mo) 在多囊卵巢综合征 (PCOS) 主要临床特征及短期疗效的分布特征。方法 收集复旦大学附属妇产科医院内分泌门诊的 PCOS 患者 70 例, 非 PCOS 对照组 60 例, 通过流式细胞仪检测患者外周血 CD16<sup>++</sup> Mo 在总单核细胞中的比例。结果 治疗前的 CD16<sup>++</sup> Mo 比例在 PCOS 组中显著高于非 PCOS 组, 尤其是伴有高雄激素血症 (HA)、肥胖、胰岛素抵抗 (IR) 的 PCOS 患者中。进一步分析表明 CD16<sup>++</sup> Mo 比例对 HA 有一定的诊断价值。治疗后的 PCOS 患者 CD16<sup>++</sup> Mo 比例显著下降。结论 治疗前的 CD16<sup>++</sup> Mo 比例对 PCOS 患者的 HA 有一定的诊断价值, 而治疗后 CD16<sup>++</sup> Mo 比例的显著下降与 PCOS 患者的临床表现、内分泌及脂质代谢紊乱的改善相关。

**【关键词】** 多囊卵巢综合征 (PCOS); CD16<sup>++</sup> 单核细胞 (CD16<sup>++</sup> Mo); 高雄激素血症; 达英-35; 二甲双胍

**Evaluation of CD16<sup>++</sup> monocyte in peripheral blood towards main clinical features and short-time therapeutic effects of polycystic ovary syndrome** Tang Lingli, Liu Yukai, Shi Yingli, Zhu Xiaoyong

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**【Abstract】 Objective** To evaluate the relationship of CD16<sup>++</sup> monocyte (CD16<sup>++</sup> Mo) in peripheral blood under the main clinical features and short-time medical therapeutic effects of polycystic ovary syndrome (PCOS). **Methods** Totally 92 PCOS patients (PCOS group) and 60 non-PCOS women (control group) enrolled in the study from the Obstetrics and Gynecological Hospital Affiliated to Fudan University. At last 70 PCOS patients finished the re-examination. The proportion of CD16<sup>++</sup> Mo was detected by flow cytometry. **Results** The proportion of CD16<sup>++</sup> Mo significantly expressed higher in PCOS patients than in non-PCOS controls especially in the subgroup of hyperandrogenism and obesity. Further analysis found that the proportion of CD16<sup>++</sup> Mo showed a moderate accuracy of diagnosing hyperandrogenism. The CD16<sup>++</sup> Mo significantly decreased in primary clinical features and medical treatment after three months. **Conclusion** The proportion of CD16<sup>++</sup> Mo most significantly correlated with hyperandrogenism before treatment. The distinct decrease of CD16<sup>++</sup> Mo after treatment represented some accordance with the apparent improvement of clinical manifestation and biochemical parameters, indicating that the CD16<sup>++</sup> Mo probably may be used as both the pathogenesis and prognostic indicators of PCOS.

**【Key words】** Polycystic ovary syndrome (PCOS); CD16<sup>++</sup> monocyte (CD16<sup>++</sup> Mo); Hyperandrogenism; Diane-35; Metformin

## 超促排卵后卵巢过度刺激综合征并发迟发性颅内静脉窦血栓 1 例并文献复习

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**【摘要】** 目的 报道 1 例超促排卵后卵巢过度刺激综合征 (ovarian hyperstimulation syndrome, OHSS) 并发迟发性颅内静脉窦血栓, 并对 OHSS 并发血栓进行文献复习。方法 经典长方案超促排卵, 取卵后发生重度 OHSS, 给予补液、抗凝、纠正低白蛋白血症等对症治疗, 症状好转 2 个月后出现颅内静脉窦血栓, 经抗凝、抗血小板聚集、脱水减轻脑水肿、营养神经、改善脑循环等对症治疗。随后检测到蛋白 C 活性显示为 45%, 提示有血栓形成倾向, 其为血栓高危人群。结果 随访至今, 患者出院后于当地医院继续降颅压及营养神经治疗, 仍留有神经后遗症。结论 OHSS 伴血栓形成是辅助生殖技术的罕见却极其严重的并发症, 临床医生应高度警惕。此外, 预防 OHSS 的发生是预防其并发血栓的关键因素。

**【关键词】** 体外受精 - 胚胎移植 (IVF-ET); 卵巢过度刺激综合征 (OHSS); 迟发性颅内静脉窦血栓

· 个案报道 ·

**Late-onset cerebral venous and sinus thrombosis after ovarian hyperstimulation syndrome in *in vitro* fertilization: a case report and literature review** Ma Yalan, Zhang Xin, Xu Xin, Zhang Di, Xu Ying

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**【Abstract】 Objective** To report one case of late-onset cerebral venous and sinus thrombosis after ovarian hyperstimulation syndrome (OHSS) in *in vitro* fertilization and review the associated literatures. **Methods** After (classical) long protocol ovulation induction and oocyte retrieval, the patient was diagnosed with severe OHSS. So we corrected hypoalbuminemia, anti-inflammatory and the patient was almost recovery. However, the patient was diagnosed with late-onset cerebral venous after 2 months. Though we made thrombosis anticoagulation, antiplatelet aggregation, dehydration, improvement of cerebral circulation. The patient was not cured. After testing, the patient was observed in thrombosis high-risk (protein C activity was 45%), suggesting the tendency of thrombosis. **Results** After discharge, the patient was followed up, and continued to reduce intracranial pressure and nutritional nerve treatment at the district hospital. **Conclusion** OHSS with thrombosis is a rare but serious complication, and we should pay more attention to it. In addition, prevention of OHSS is one of the key factors to prevent thrombosis.

**【Key words】** *In vitro* fertilization-embryo transfer (IVF-ET); Ovarian hyperstimulation syndrome (OHSS); Delayed intracranial venous sinus thrombosis



## 多囊卵巢综合征子宫内膜胰岛素抵抗的分子机制及生物学效应

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**【摘要】** 多囊卵巢综合征 (PCOS) 作为一种生殖障碍与代谢紊乱并存的内分泌疾病, 是育龄期妇女不孕的最常见原因。PCOS 患者以无排卵性不孕为主, 但通过促排卵药物纠正后, PCOS 患者仍存在低种植率、高流产率的现象, 其重要原因之一是 PCOS 患者内分泌及代谢紊乱影响其子宫内膜功能。胰岛素抵抗 (IR) 作为 PCOS 的代谢特征之一, 已有证据显示子宫内膜 IR 影响子宫内膜生理功能, 可能降低子宫内膜容受性, 并增加子宫内膜疾病的发病风险。进一步了解子宫内膜 IR 的分子机制及生物学效应, 将有助于为 PCOS 患者提供更好的治疗策略。

**【关键词】** 多囊卵巢综合征 (PCOS); 子宫内膜; 子宫内膜容受性 (ER); 子宫内膜癌; 胰岛素抵抗 (IR)

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**Molecular mechanism and biological effects of endometrial insulin resistance in polycystic ovary syndrome**

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**【Abstract】** Polycystic ovary syndrome (PCOS) is the most common infertile reason in reproductive-age women. Anovulation is the main cause for PCOS infertility. However, even with the ovulation induction, the implantation rate is still low and abortion rate is high in PCOS. One of the important reasons is that the endometrial function is affected by the endocrine and metabolic disorder. Insulin resistance, as a characteristic metabolic feature in PCOS, affects the physiological function in uterine endometrium including the impairment of endometrial receptivity and the increased incidence of endometrial disease. To further understand the molecular mechanism and biological effects of endometrial insulin resistance may help to provide better treatment strategy for PCOS patients.

**【Key words】** Polycystic ovary syndrome (PCOS); Uterine endometrium; Endometrial receptivity (ER); Endometrial cancer; Insulin resistance (IR)

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## 胚胎反复种植失败的免疫学预测指标

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**【摘要】** 随着辅助生殖技术 (ART) 的发展, 体外受精 / 卵胞质内单精子显微注射 (IVF/ICSI) 妊娠率不断提高, 但是仍有部分患者经历多次胚胎移植失败。关于胚胎反复种植失败 (RIF) 的免疫学病因存在争议, 本文就预测 RIF 的免疫学指标方面做一综述, 同时进行深入探讨和归纳总结, 以期为未来的基础研究和临床治疗提供参考。

**【关键词】** 反复种植失败 (RIF); 免疫学; 体外受精 - 胚胎移植 (IVF-ET)

**Immunological biomarkers of recurrent implantation failure**     *Liu Xitong, Lu Na, Li Pei, Shi Juanzi, Li Na*  
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**【Abstract】** With the rapid development of assisted reproductive technology, the pregnancy rates of *in vitro* fertilization/intracytoplasmic sperm injection (IVF/ICSI) have continued rising. However, there are still some patients suffering from recurrent implantation failure (RIF). There are controversies about the immunological etiology of RIF. Therefore, in this article we presented an overview of RIF and provided an in-depth discussion and summary of the immunological mechanism of RIF, with a view to providing reference for future basic research and clinical management.

**【Key words】** Recurrent implantation failure (RIF); Immunology; *In vitro* fertilization-embryo transfer (IVF-ET)

## 孕期外源物暴露致 DNA 甲基化异常与发育源性疾病的关系研究

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**【摘要】** “健康与疾病的发育起源”(DOHaD)学说在近年来逐渐兴起,发育源性疾病的发生机制也受到关注。多项动物实验及流行病学调查研究显示,孕期外源物暴露致 DNA 甲基化异常在发育源性疾病发生机制中发挥着重要的作用。孕期根据时间顺序可分为三期,分别为孕早期、孕中期、孕晚期,不同时期的外源物暴露致 DNA 甲基化变化与发育源性疾病的关系也不尽相同。现就孕期外源物暴露致 DNA 甲基化变化与发育源性疾病的关系研究进行综述,为发育源性疾病的预防和治疗提供理论基础。

**【关键词】** 发育源性疾病; DNA 甲基化; DOHaD 学说; 孕期暴露; 外源物

**Relation of abnormal DNA methylation induced by prenatal xenobiotics exposure and the development origins of disease** Jin Ling, Zhang Yuanzhen

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**【Abstract】** Recently, “Developmental Origins of Health and Disease (DOHaD)” theory has come into sight gradually. The mechanism of development origins of disease has also been concerned. A number of animal experiments and epidemiological studies indicated that DNA methylation aberrance induced by prenatal xenobiotics exposure plays a vital of importance role in development origins of disease. Gestation can be divided into three semesters, which are the first trimester, the second trimester, the third trimester. The relation of DNA methylation induced by different trimesters xenobiotics exposure and the development origins of disease are different. This review summarizes the relation of abnormal DNA methylation induced by prenatal xenobiotics exposure and the development origins of disease in order to provide theory base and new direction for the prevention and new treatment method of development origins of disease.

**【Key words】** Development origins of disease; DNA methylation; DOHaD theory; Prenatal exposure; Xenobiotics