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复发性流产合并血栓前状态诊治中国专家共识

国家妇幼健康研究会生殖免疫学专业委员会专家共识编写组

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【摘要】　凝血功能异常，尤其是血液高凝状态——血栓前状态（prethrombotic state，PTS）是导致复发性流产（recurrent spontaneous abortion，RSA）等不良妊娠结局的常见原因。抗凝和/或抗血小板治疗在RSA合并PTS患者的防治方面疗效肯定，但由于缺乏相应的规范，过度检查、过度治疗和超适应证用药等现象普遍存在。为了进一步规范RSA合并PTS的诊治，国家妇幼健康研究会生殖免疫学专业委员会组织国内妇产科学、生殖免疫学、生殖医学、风湿免疫学、血液病学、检验医学以及循证医学专家，根据RSA合并PTS的诊治现状，结合国内外最新的研究证据和进展共同讨论，制定本共识，旨在为临床医师在临床实践中做出合理决策提供参考。

【关键词】　复发性流产；　凝血功能；　血栓前状态；　诊治；　共识
基金项目：国家自然科学基金面上项目（81671481、81871179）；广东省科技计划项目（2014A020212229）；广州市科技计划项目（201804010003）
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Chinese experts consensus on the diagnosis and treatment of recurrent spontaneous abortion with prethrombotic state

Experts Consensus Group on Reproductive Immunology, Maternal and Child Health Research Association
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【Abstract】　Abnormal blood coagulation, especially hypercoagulable state-prethrombotic state (PTS) is a common cause of adverse pregnancy outcomes

including recurrent spontaneous abortion (RSA). Anticoagulant and/or antiplatelet therapy is effective in the prevention and treatment of patients with RSA and PTS. However, over-examination, over-treatment, and over-indication medication are widespread due to the lack of related regulations. In order to standardize the diagnosis and treatment of RSA combined with PTS, expert group of Specialized Committee on Reproductive Immunology, Maternal and Child Health Research Association formulates this consensus after discussions among domestic experts in obstetrics and gynecology, reproductive immunology and reproductive medicine, rheumatology and immunology, hematology, laboratory medicine and evidence-based medicine, which is based on the current situation in diagnosis and treatment, and combined with the latest evidences and progress from domestic and overseas researches. This consensus aims to provide a reference for clinicians to make reasonable decisions in clinical practice.

【Key words】 Recurrent spontaneous abortion; Coagulation function; Prethrombotic state; Diagnosis and treatment; Consensus

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·综述·

智慧 IVF+梦计划：VR/AR 在人类辅助生殖手术中的应用前景分析

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【摘要】 本文列举智慧医疗中革新性的技术——虚拟现实（virual reality，VR）和增强现实（augmented reality，AR）技术在医学应用中较为成功的案例，对 VR 和 AR 技术在生殖中心的诊疗工作的应用前景进行了分析，提出将虚拟 3D 影像模型、虚拟的仿真模型、头戴式显示器、VR 眼镜、虚拟操纵杆、数据手套等设施以及 5G 网络应用于手术技能培训评估和考核、术前方案规划模拟和治疗方案的评估、手术辅助、远程手术、缓解疼痛等具体应用方案。同时，本文对未来 VR/AR 体系在人类辅助生殖技术（assisted reproductive technology，ART）领域的应用进行了勾画和展望，以搭建一个基于 VR/AR 技术的智慧生殖中心的架构模型。

【关键词】 虚拟现实； 增强现实； 智慧医疗； 生殖技术，辅助； 受精，体外； 胚胎移植

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Intelligent IVF+dream plan: analysis on the application prospect of VR/AR in human assisted reproductive technology

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【Abstract】 The successful application cases of virtual reality (VR) and augmented reality (AR) technology in medicine were demonstrated, and the prospect of VR/AR technology applied in the diagnosis and treatment in the reproductive medical center was analyzed. Virtual 3D image model, AR simulation model, head-mounted display (HMD), 3D VR glasses, virtual joysticks, data glove and 5G networks were suggested to be applied in the training of the operation skills, preoperative plan and simulation, operation assistance, remote operation and pain relief. The future of VR/AR system applied in human assisted reproductive technology is outlined and prospected, and an architecture system based on VR/AR technology in the reproductive medicine is built.

【Key words】 Virtual reality; Augmented reality; Intelligent medicine; Reproductive technology, assisted; Fertilization *in vitro*; Embryo transfer

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机器学习在体外受精-胚胎移植技术中的应用

于医萍　高一博　方兰兰　孙莹璞
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【摘要】 基于算法学习数据内部规律，进而对同类数据进行预测和判断的过程为机器学习。在体外受精-胚胎移植技术领域，基于机器学习算法建立的模型不仅可预测周期助孕结局，也可帮助胚胎学家挑选优质胚胎。本文共筛选出基于机器学习算法的周期结局预测模型和胚胎质量评估模型 30 个，其中基于传统机器学习算法模型 28 个，基于深度学习模型 2 个。采用受试者工作特征曲线的曲线下面积（area under curve， AUC）评价模型效果，基于传统机器学习算法的模型效果多不理想（0.60<AUC<0.86），深度学习算法准确率则较高（AUC>0.90）。完善的预测和评估模型有望提高助孕周期效率、标准化胚胎选择流程。

【关键词】 机器学习； 统计模型； 受精，体外； 周期结局； 胚胎质量

Application of machine learning in *in vitro* fertilization

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【Abstract】 Based on algorithm, machine learning could dig information from data and learn the rules between data, following by predicting and analyzing

new data. Machine learning can be used for the establishment of pregnancy outcome prediction model, as well as for the selection of embryos with the highest implantation potential. This review identified 30 models, among which 28 were based on traditional machine learning and 2 were based on deep learning. Area under the receiver operating characteristic curve (AUC) was adopted for the estimation of model performance. On the whole, models based on traditional algorithm were of low to medium performance (0.60<AUC<0.86), whereas deep learning models were of good performance (AUC>0.90). Prediction and estimation models may improve treatment efficiency and standardize embryo selection process.

【Key words】 Machine learning; Statistical models; Fertilization *in vitro*; Pregnancy outcomes; Embryo quality

·综述·

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慢性子宫内膜炎与生殖相关疾病的研究进展

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【摘要】 慢性子宫内膜炎（chronic endometritis，CE）的诊断标准是子宫内膜间质异常的浆细胞浸润。但因 CE 患者大部分无明显症状，部分有症状者又常常被混淆为盆腔炎性疾病、阴道炎等对症处理，所以 CE 在临床中常常被忽视。近几年来，随着人类微生物计划和人类辅助生殖技术的进展，越来越多的研究显示 CE 与生殖相关疾病（复发性流产、反复种植失败、子宫内膜异位症等）存在潜在联系。本文就 CE 与生殖相关疾病的研究进展进行综述。

【关键词】 慢性子宫内膜炎； 反复种植失败； 疾病

Research progress of chronic endometritis and reproduction-related diseases

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【**Abstract**】 The diagnostic criterion for chronic endometritis (CE) is abnormal plasma membrane infiltration of the endometrial stroma. However, because most of CE patients have no obvious symptoms, some symptomatic patients are often confused with symptomatic treatment of pelvic inflammatory disease and vaginitis, so CE are often ignored in the clinic. In recent years, with the progress of the human microbiology program and human assisted reproductive technology, more and more studies suggested that there was a potential relationship between CE and reproduction-related diseases such as repeated pregnancy loss, repeated implantation failure and endometriosis. This article reviewed the research progress of CE and reproduction-related diseases.

【**Key words**】 Chronic endometritis; Repeated implantion failure; Disease

·综述·

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慢性子宫内膜炎在胚胎植入中的研究进展

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【摘要】 慢性子宫内膜炎是一种临床症状不明显的慢性持续性子宫内膜炎症，以子宫内膜间质区浆细胞浸润为主要特征，主要通过 CD138 免疫组织化学法、宫腔镜检查等进行诊断。研究显示慢性子宫内膜炎影响子宫内膜蜕膜化、免疫细胞及细胞因子的表达等，不利于胚胎植入，与复发性流产、反复种植失败有关。慢性子宫内膜炎的主要治疗方法是应用抗生素，近年来子宫内膜机械性刺激、宫腔灌注也成为治疗慢性子宫内膜炎的新手段。本文围绕慢性子宫内膜炎的病因、诊断、影响胚胎植入的可能机制和治疗展开综述。

【关键词】 子宫内膜炎； 不孕症； 反复种植失败； 复发性流产； 宫腔镜检查

基金项目：国家自然科学基金（81971386）

Research progress of chronic endometritis in embryo implantation

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【Abstract】 Chronic endometritis (CE) is a chronic persistent endometrial inflammation with no obvious clinical symptoms. It is mainly characterized by plasma cell infiltration in endometrial stroma and is mainly diagnosed by CD138 immunohistochemistry and hysteroscopy. Studies have found that CE affects the decidualization of endometrium and the expression of immune cells and cytokines, which is not conducive to embryo implantation, and is related to recurrent spontaneous miscarriage and repeated implantation failure. The main treatment of CE is antibiotic treatment. In recent years, endometrial mechanical stimulation and intrauterine perfusion have also become new methods for the treatment of CE.

【Key words】 Endometritis; Infertility; Recurrent implantation failure; Recurrent spontaneous abortion; Hysteroscopy

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·综述·

不孕症女性促排卵后发生卵巢切除病因及预防的研究进展

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【摘要】 不孕症女性接受促排卵治疗是导致卵巢扭转的重要原因之一。由于卵巢扭转的临床表现为非特异性，且目前缺乏特效诊断方法，容易造成诊断及治疗延误，导致卵巢切除。卵巢能否保留对于有生育期望的女性尤为重要，任何接受促排卵治疗的不孕症女性，临床怀疑出现卵巢扭转时均应高度重视，及时诊断并治疗，避免发生卵巢切除。本文对不孕症女性接受促排卵治疗后发生卵巢切除的病因及临床预防措施方面作一综述，以期对临床诊断及治疗决策有所帮助。

【关键词】 促排卵治疗； 卵巢切除； 卵巢扭转； 不孕症； 生殖技术，辅助

Research progress on the etiology and prevention of ovariectomy in female infertility after ovulation induction treatments

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【Abstract】 Infertility females receiving ovulation induction therapies is one of the important reasons of ovarian torsion. As the lack of specific diagnoses and the non-specific clinical manifestations, ovarian torsion is prone to delay in diagnosis and treatment which leading to ovariectomy. Ovarian function is particularly important for fertile women. Doctors should pay attention to ovarian torsion when clinically suspected for the patients after ovulation induction treatments, and make diagnosis and treatment in time to avoid ovariectomy. This paper mainly reviewed the etiology and clinical preventive measures of ovariectomy in female infertility after ovulation induction treatments, in order to contribute to clinical diagnosis and treatment.

【Key words】 Ovulation induction; Ovariectomy; Ovarian torsion; Infertility; Reproductive technology, assisted

·综述·

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肠道菌群在肥胖导致的女性生育障碍中的作用研究进展

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【摘要】 肥胖通过多种复杂的机制影响着女性生育能力，如肥胖引起的慢性低度炎症和胰岛素抵抗（insulin resistence，IR），以及随之而来的高雄激素血症可影响排卵、子宫内膜容受性，从而导致不孕。近年来研究表明，肠道菌群作为一个新的影响因素在肥胖的发生、发展中发挥重要作用，通过改善肠道菌群来减轻体质量可改善女性生育能力，但其在肥胖导致的女性生育障碍中的作用具体机制仍需进一步研究。本文围绕肠道菌群在肥胖导致的女性生育障碍中的作用展开综述。

【关键词】 肥胖； 不孕症； 肠道菌群

Research progress on the role of gut microbiota in female fertility disorders caused by obesity

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【Abstract】 Obesity has an effect on fertility in women through multiple and complex mechanisms. Briefly, chronic low-grade inflammation and insulin resistance caused by obesity, as well as subsequent hyperandrogenemia, can affect ovulation and endometrial receptivity, and ultimately infertility. Recent studies have shown that the gut microbiota plays an important role in the occurrence and development of obesity. Weight loss by improving gut microbiota can also improve fertility in women. Further studies are needed to investigate the role and mechanism of gut microbiota in the development and progression of female fertility disorder caused by obesity.

【Key words】 Obesity; Infertility; Gut microbiome

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·综述·

外泌体在子宫内膜异位症中的研究进展

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【摘要】 子宫内膜异位症（endometriosis，EMS）是妇科的一种常见病、多发病，具有侵袭性强、病灶广泛、易反复的特点，然而其发病机制尚不清楚。外泌体是广泛存在于多种体液及细胞的微小囊泡体，具有分泌、摄取及运载等功能。本文通过对外泌体及其携带的非编码 RNA 等在 EMS 的相关研究进行总结，综述其在 EMS 发生发展中子宫内膜增殖与凋亡、在位子宫内膜迁移、异位病灶血管生成和纤维化等方面的作用，未来可能成为非侵入性诊断 EMS 特异性强、灵敏度好、精准度高的候选物，并为未来 EMS 临床靶向治疗提供思路。

【关键词】 子宫内膜异位症； 外泌体； 诊断标志； 治疗

Research progress of exocrine in endometriosis

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【Abstract】 Endometriosis (EMS) is a common and frequently-occurring disease in gynecology, which has the characteristics of strong invasiveness, wide range of lesions and easy recurrence. However, its pathogenesis is not clear. Exocrine bodies are microvesicles that widely exist in a variety of body fluids and cells, and have the functions of secretion, uptake and transport. This paper summarized the related studies of exosomes and their non-coding RNA in EMS, and their roles in cell proliferation and apoptosis, intimal migration, angiogenesis and fibrosis in the occurrence and development of EMS. Exosomes may become a non-invasive diagnostic markers of EMS with high specificity, sensitivity and accuracy, which provide ideas for clinical targeted therapy of EMS in the future.

【Key words】 Endometriosis; Exosome; Diagnostic markers; Treatment

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·综述·

Sirtuins 1 在生理和病理妊娠中的调节机制及其激动剂对妊娠相关疾病治疗作用的研究进展

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【摘要】 在妊娠相关疾病如子痫前期、胎儿生长受限、早产、妊娠期糖尿病的发生发展过程中，氧化应激引起的细胞损伤与凋亡起着重要的作用。近年来的研究表明，沉默信息调节因子 1（Sirtuins 1）在女性生殖过程中扮演重要角色，其可通过调节滋养细胞分化、血管生成活性以及维持免疫耐受进而影响胚胎及胎盘的发育；还可发挥抗氧化应激、调控自噬等作用，进而参与生理和病理妊娠的发展过程。本文就 Sirtuins 1 在生理和病理妊娠中的调节机制及通过激活 Sirtuins 1 治疗妊娠相关疾病的研究进展做一综述，以期为妊娠相关疾病的病理机制及临床治疗的进一步研究提供参考。

【关键词】 沉默信息调节因子 1； 妊娠； 子痫前期； 胎儿生长受限

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Research progress on the regulatory mechanism of Sirtuins 1 in physiological and pathological pregnancy and the therapeutic effect of its agonists on pregnancy-related diseases

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【Abstract】 Cell damage and apoptosis caused by oxidative stress play an important role in the development and progression of pregnancy-related diseases such as preeclampsia, fetal growth restriction, premature delivery, and gestational diabetes mellitus. Recent studies have shown that Sirtuins 1 plays an important role in the process of female reproduction. It can affect the development of embryo and placenta by regulating trophoblast differentiation, angiogenesis activity and maintaining immune tolerance. It can also play the role of antioxidant stress and regulation of autophagy, thus participating in the development process of physiological and pathological pregnancy. In this paper, the regulation mechanism of Sirtuins 1 in physiological and pathological pregnancy and the research progress in the treatment of pregnancy-related diseases by activating Sirtuins 1 were reviewed in order to provide reference for further research on the pathological mechanism and clinical treatment of pregnancy related diseases.

【Key words】 Sirtuins 1; Pregnancy; Preeclampsia; Fetal growth restriction

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·综述·

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卵巢组织移植后缺血再灌注损伤的干预策略

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【摘要】 2015 年中国新发恶性肿瘤数据统计表明，30 岁以下女性患者为 3.88 万，这些恶性肿瘤患者急需得到医生关于生育力保护和保存的建议，而卵巢组织冷冻方法是保存内分泌功能和生育能力的最佳方法。目前影响卵巢组织存活的关键是解决卵巢组织移植后的缺血再灌注损伤问题，本文将从卵巢组织移植后缺血再灌注的机制，以及抗氧化剂、促血管生成和远处缺血预处理等干预方法进行系统地文献梳理，有助于结合生物技术与医疗技术开发更有效、安全和可操作的解决方案，以改善卵巢移植后缺血状态，解决日益增长的女性生育力保护需求。

【关键词】 卵巢组织移植； 缺血再灌注； 血管再生； 女性生育力保护

Intervention strategies of ischemia and reperfusion injury after ovarian tissue transplantation

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【Abstract】 According to the statistics of new malignant tumors in China in 2015, there were 38 800 female patients under 30 years old, who urgently needed doctors' advices and suggestions on fertility protection and preservation. Ovarian tissue freezing method is the best way to preserve female endocrine function and fertility. At present, the key to the survival of ovarian tissue is to solve the problem of ischemia and reperfusion after ovarian transplantation. In this paper, we will

systematically review the mechanism of ischemia and reperfusion after ovarian transplantation, as well as some intervention methods including antioxidants, angiogenesis and remote ischemic preconditioning. This will promote the combination of the latest biotechnology and medical technology, develop more effective, safer and operable solutions to improve the ischemic state after ovarian transplantation, and strive for early clinical use to address the increasing need for female fertility preservation.

【Key words】 Ovarian tissue transplantation; Ischemia and reperfusion; Angiogenesis; Female fertility preservation

·综述·

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人类子宫移植的研究进展及伦理困惑

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【摘要】 世界首例子宫移植术后婴儿的出生给广大子宫因素不孕患者带来了新的希望，但由于该手术存在难度高、风险大、成功率低、伦理争议等问题，仍面临着许多挑战，并引起广泛的关注。本文就子宫移植技术的进展和伦理焦点作一综述。

【关键词】 子宫性不孕；　子宫移植；　器官移植

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Research progress and ethical confusion of human uterine transplantation

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【Abstract】 The firstly successful birth in the world following the uterus transplantation brings new hope to the majority of infertility women with uterine factors, but due to the difficulty of the operation, the high risk, the low success rate,

and ethical issues, it still faces many challenges, which has caused widespread concern. The research progress and ethical issues of uterine transplantation were reviewed in this paper.

【 **Key words** 】 Uterine infertility; Uterine transplantation; Organ transplantation

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血-睾屏障损伤的影响因素及其相关机制

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【摘要】 血-睾屏障由相邻支持细胞间多种蛋白质复合体组成，它通过在生精上皮参与构建生精微环境、提供免疫屏障并赋予细胞极性来维持正常精子发生。血-睾屏障的结构与功能易受外界不良环境因素影响，但血-睾屏障损伤的影响因素及其相关机制尚未系统阐明。本综述概括血-睾屏障的结构、功能及生理调控机制，总结损伤血-睾屏障的化学、物理、生物因素，并归纳不良环境因素通过影响表观遗传修饰、信号通路表达、细胞因子与内分泌激素含量损伤血-睾屏障结构与功能的相关机制，这对于保障精子质量、避免睾丸损伤具有重要的指导意义，也为预防男性不育提供理论依据。

【关键词】 血-睾屏障； 表观遗传； 信号通路； 细胞因子； 内分泌激素

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Influencing factors of blood-testis barrier injury and their related mechanisms

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【 Abstract 】 The blood-testis barrier is composed of multiple protein complexes between adjacent Sertoli cells. It maintains normal spermatogenesis in the spermatogenic epithelium by participating in the construction of the spermatogenic environment, providing an immune barrier and giving cells polarity. It is known that the structure and function of the blood-testis barrier are susceptible to damage from external adverse environmental factors, but influencing factors of blood-testis barrier injury and their related mechanisms have not been systematically elucidated. This review outlines the structure, function, and physiological regulation mechanism of the blood-testis barrier, summarizes the chemical, physical, and biological factors that impair the blood-testis barrier, and generalizes the related mechanisms of adverse environmental factors that damage the structure and function of the blood testis barrier by affecting epigenetic modifications, signaling pathway expressions, cytokine and endocrine hormone levels, which has an important guiding significance for ensuring sperm quality and avoiding testicular damage, and also provides a theoretical basis for preventing male infertility.

【 Key words 】 Blood-testis barrier; Epigenetics; Signaling pathways; Cytokines; Endocrine hormones

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·综述·

克氏综合征早期筛查诊断与不育症治疗策略

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【摘要】 克氏综合征是男性不育中最常见的染色体异常疾病，还可引起发育障碍、认知障碍、雄激素缺乏和代谢综合征等疾病。目前其早期筛查和诊断率较低。克氏综合征引起的男性不育主要通过睾丸显微取精术/辅助生殖技术助孕。本文旨在对克氏综合征的早期筛查诊断和不育症诊疗策略进行综述，重点探讨克氏综合征患者早期筛查诊断和生育相关治疗等相关问题。

【关键词】 克氏综合征； 男性不育； 无精子症； 睾丸取精术

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Analysis of the screening and diagnosis of Klinefelter's syndrome and management strategy to the related male infertility

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【Abstract】 Klinefelter's syndrome (KS) is the most common chromosomal abnormality in male infertility, which could also lead to developmental disorders, cognitive disorders, androgen deficiency, metabolic syndrome and other diseases. However, the early screening and diagnosis rate of KS is still low. KS related male infertility is mainly treated by microdissection testicular sperm extraction (MD-TESE)/assisted reproductive technology (ART). We aimed to review the diagnosis and treatment strategies of KS and mainly focused on screening and the treatment to male infertility of patients with KS.

【 Key words 】 Klinefelter's syndrome; Male infertility; Azoospermia; Testicular sperm extraction

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·综述·

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多囊卵巢综合征的啮齿类动物模型

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【摘要】 多囊卵巢综合征（polycystic ovary syndrome，PCOS）是育龄女性常见的生殖内分泌疾病，其病因复杂，临床异质性高。代谢异常是 PCOS 的重要特征，在 PCOS 发病中有重要作用。本文主要综述 PCOS 啮齿类动物模型的造模方法及其生殖内分泌和代谢特征，讨论了各种模型所适用的研究类型，为 PCOS 病因学研究及防治策略探索所需啮齿类动物模型的选择提供参考。

【关键词】 多囊卵巢综合征；　啮齿类动物模型；　代谢异常；　生殖内分泌紊乱；　造模方法

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Rodent models of polycystic ovary syndrome

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【**Abstract**】 Polycystic ovary syndrome (PCOS) is a common reproductive endocrine disease in women of reproductive age. Its etiology is complex and its clinical heterogeneity is high. Metabolic abnormality is an important characteristic of PCOS and plays a crucial role in the pathogenesis of PCOS. This paper mainly reviews the reproductive endocrine disorders and metabolic abnormalities of rodent models induced by various modeling methods, discusses the applicable research of various models and provides a reference for the selection of PCOS rodent models, which matter in the etiology research and therapy exploration of PCOS.

【**Key words**】 Polycystic ovary syndrome; Rodent model; Metabolic abnormality; Reproductive endocrine disorder; Model methods

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