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Abstracts

论文汇编

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Abstracts

P1-3

THE RESEARCHS ON THE ETIOPATHOGENESIS OF PREECLAMPSIA

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Pre-eclampsia is an important complication of pregnancy, which is characterized by an elevated blood pressure and proteinuria and probably accompanied with edema and impairment of many important organs. It maybe further develops into Eclampsia, which is a grave hazard to maternal and fetal health. However, the etiology of pre-eclampsia thus far remains unknown. Furthermore, the present measures for prevention and therapy are less effective. Hence, the clinical and basal research on pre-eclampsia is the important field of obstetrics all the time.

Since 1980s, preeclampsia research group in Ren Ji hospital have carried out a series of researchs on the etiopathogenesis of preeclampsia. The syndrome of preeclampsia has been ascribed to generalized maternal endothelial dysfunction, poor placentation and excessive maternal inflammatory response. Therefore, most of our researchs focused on the causes of endothelial dysfunction and poor placentation and abnormal maternal immune system.

1. Immunology and Preeclampsia

Since the end of 1980s, we have observed the changes of B lymphocyte and T lymphocyte subpopulations in blood from preeclampsia patients. We found the number of B lymphocyte significantly increased in patients. Furthermore, we found that the number of Ts decreased and the function of Ts was impaired significantly. The number of Ts cells decreased and Th/Ts ratio increased gradually along with the worsening of preeclampsia.

In 1992, we observed the immunopathology of uterine spiral arteries by immuno-histochemistry and found that the deposit on the arterial wall was only seen in preeclampsia and the IgG deposit on the arterial wall in preeclampsia patients was fewer than that in normal pregnant women.

The results above suggested that abnormal activation of innate and adaptive immune system was involved in the excessive maternal imflammatory response and placental ischemia.

2. Placental or trophoblastic ischemia and hypoxia

At present, the most accepted hypothesis is placental or trophoblastic ischemia and hypoxia. According to the hypothesis, the reduced invasion of trophoblast in preeclamptic placenta during the period of placentation leads to impediment of spiral artery remolding which causes placental or trophoblastic ischemia and hypoxia. In turn, it activates a cascade of responses, for example, oxidative stress. As a result, the subsequent dysfunction of endothelial cell gives rise to the manifestation of the disease.

In 2001, we assessed the expression of VEGF and PLGF in placentas from preeclampsia patients in order to clarify the relationship between angiogenesis and placental ischemia. We found that the expression of VEGF and PLGF decreased significantly in preeclamptic placentas. Furthermore, we assessed the expression of MMP-2, -9 and TIMP-1, 2and KiSS-1 in placentas from preeclampsia patients. We found that the expression of MMP-2、-9 decreased and the expression of TIMP-1、2and KiSS-1 increased significantly in placentas from the cases, which was involved in the poor placentation (reduced invasion of trophoblast) in preeclamptic placenta.

Recently, we found that the overly activated hypoxic response pathway of trophoblast in preeclamptic placenta, which is manifested as over-expression of HIF-2α, is the key point to hypoxic dysfunction of trophoblast. The decreased oxygen sensitivity (the reduced HPH-1 expression) of trophoblast in preeclamptic placenta was the most important intrinsic cause of trophoblastic hypoxia.

3. Oxidative stress and endothelial dysfunction

We measured the production of cytokines, TNF-α and TGF-β1, from cultured placenta villi under hypoxia and found that the production of TNF-α increased and that of TGF-β1 did not change. Furthermore, we found that the single-layer structure of vascular endothelial cell was damaged, cell shrinked, cell gap increased and microvilli reduced after adding the upper-layer fluid of hypoxia villi. These result suggested that excessive production of certain cytokines, such as TNF-α, under placental ischemia could lead to endothelial dysfunction.

In 2002, we reported the concentration of xanthine oxidase(XOD) and lipid peroxide(LPO) in serum from patients with preeclampsia were significantly higher than those in normal pregnant women respectively. We also found a significant direct correlation between the concentration of the XOD and that of LPO or mean arterial pressure(MAP). We concluded oxidative stress (peroxidation increasing) was also the key factor causing endothelial dysfunction in preeclampsia patients.

先兆子痫的病因病机研究

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先兆子痫是一种重要的妊娠并发症，表现为高血压和蛋白尿，可伴有水肿和重要器官脏器损伤。进一步发展为子痫，严重威胁着母婴健康。但是，先兆子痫的病因至今不明。而且，目前缺乏有效的预防和治疗措施。因此，先兆子痫的临床和基础研究一直是产科重要的研究领域。

从 20 世纪 80 年代起，仁济医院先兆子痫研究小组已经对先兆子痫进行了一系列的病因病机研究。目前认为，先兆子痫主要与全身血管内皮细胞功能异常、胎盘形成障碍和母体过度炎症反应有关。因此，我们的基础研究主要集中对导致内皮细胞功能异常、胎盘形成障碍、母体免疫系统异常原因的研究。

1. 先兆子痫与免疫

自从 20 世纪 80 年代末，我们观察了先兆子痫患者外周血 B 淋巴细胞和 T 淋巴细胞亚群的变化。我们发现患者的 B 淋巴细胞数量显著增加。进而，我们发现，Ts 淋巴细胞数量显著减少，且功能显著受损。Ts 淋巴细胞减少和 Th/Ts 比率增加与先兆子痫的病情轻重相关。

在 1992 年，我们采用免疫组化方法对子宫螺旋小动脉进行免疫病理检查发现，只有在先兆子痫患者的动脉壁上可见到免疫复合物沉着，而血管壁有 IgG 沉着的先兆子痫患者显著低于正常孕妇。

以上结果提示，母体先天和后天免疫系统异常激活与先兆子痫患者炎症反应过度和胎盘缺血有着密切关系。

2. 胎盘或滋养叶细胞缺血缺氧

目前公认的病因学说是胎盘或滋养叶细胞缺血缺氧学说。该学说认为，先兆子痫患者在胎盘形成阶段滋养叶细胞侵润能力下降导致了血管重铸障碍，从而导致胎盘或滋养叶细胞缺血缺氧。进而激发一系列后续反应，如氧化应激，导致内皮细胞损伤，最后引发先兆子痫的临床表现。

2001 年，我们检测了先兆子痫患者胎盘 VEGF 和 PLGF

的表达状况，试图明确先兆子痫胎盘血管形成状况与胎盘缺血的关系。我们发现，患者胎盘 VEGF 和 PLGF 的表达显著降低。另外，我们又对先兆子痫患者胎盘 MMP-2、-9 和 TIMP-1、2 和 KiSS-1 的表达进行检测发现，MMP-2、-9 表达显著降低，而 TIMP-1 和 KiSS-1 表达显著增高。结果提示，这些表达异常与胎盘形成障碍（滋养叶细胞侵润能力下降）有关。

最近我们研究发现，先兆子痫患者滋养叶细胞缺氧反应途径存在过度激活，表现为 HIF-2α 过度表达，是滋养叶细胞缺氧表现的关键。先兆子痫患者胎盘滋养叶细胞氧敏感性的降低（HPH-1 低表达）是滋养叶细胞缺氧的重要内在因素。

3. 氧化应激和内皮细胞功能异常

我们检测了缺氧培养条件下的胎盘绒毛组织分泌细胞因子 TNF-α 和 TGF-β1 的状况。我们发现，TNF-α 分泌增加，TGF-β1 无改变。进而，我们研究发现，加入缺氧绒毛上清液后，血管内皮细胞单层结构破坏，细胞皱缩，细胞间隙增大，微绒毛减少。这些结果提示，缺氧条件下胎盘绒毛过度分泌某些细胞因子，如 TNF-α，可导致内皮细胞功能异常。

2002 年，我们报道先兆子痫患者血清黄嘌呤氧化酶（XOD）和过氧化脂质（LPO）的浓度显著高于正常妊娠。而且发现，患者血清 XOD 浓度分别与 LPO 浓度和平均动脉压呈正相关。因此，我们认为，氧化应激（过氧化反应增高）也是导致先兆子痫患者内皮细胞损伤的关键因素。

P2-3

MOLECULAR STUDY IN GYNAECOLOGICAL CANCERS

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Aims: Molecular study in gynaecological cancer is possible with the advance in technology and training in biomolecular science. Studies at molecular level allows for better understanding of carcinogenesis, a potential use of molecular tumour marker in diagnosis, monitoring and prognostication of cancer as well as therapy.

Materials and Methods: Proto-oncogenes, oncogenes, tumour suppressor genes and HPVwere studied in gynaecological cancers. Epigenetic event such as methylation was also studied.

Results: Using cervical cancer as example to illustrate the importance of molecular study in gynaecological cancers. HPV was found in more than 95% of cancer. HPV DNA was detected in 50% of patients with cervical cancer using q-PCR technique. Abnormal expression of p53, c-erbB2, c-myc, EGFR and ras showed controversial findings in association with prognosis though our studies showed no prognostic association with overexpression of these genes. However, our study showed that apoptosis and proliferative parameters had prognostic significance. Using macroarray technique in comparing gene expressions between radiosensitive and radioresistant cervical cancer samples, abnormal p73 expression was found to be associated with radiosensitivity and was regulated by methylation. Both p73 overexpression and hypomethylation were of prognostic significance. Hypermethylation of DAPK, p16, MGMT and E-cadherin were demonstrated in cervical cancers and cell lines and their significance need further study. In-vitro study showed the p53-adenovirus trasnfection can restore normal function of cancer cells and is a potential agent for gene therapy.

Conclusions: Molecular markers have the potential in clinical applications which need further study.

S1-1

PREGNANCY OUTCOME IN WOMEN WITH RECURRENT PREGNANCY LOSSES AND ANTIPHOSPHOLIPID ANTIBODIES

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The term "antiphospholipid syndrome" (APS) refers to the association between pregnancy loss and antiphospholipid antibodies (aPL) and/or thrombotic events. The identification of aPL as a new and treatable cause of recurrent pregnancy loss (RPL) represents the major advance in the subject over the past 20 years.

In women with RPL caused by APS, the prospective fetal loss rate may be as high as 85-90%. Among aPL, several studies indicate that positive tests for lupus anticoagulant and anticardiolipin antibodies can be found in up to 20% of women with RPL.

Several studies regarding treatment of APS in pregnancy found that heparin and low dose aspirin (LDA) are more effective in promoting live birth than aspirin alone. Most authorities agree that a low-dose thromboprophylactic regimen with a low molecular weight heparin (LMWH- e.g. enoxaparin 40-80 mg/day) or unfractionated heparin (UFH- twice daily injections at a dosage of 15000-20000 units per day) is sufficient in women with no history of thrombotic events and whose sole problem is RPL. Although most patients are started on LDA with a positive pregnancy test, there is no consensus on when to start heparin. Most experts prefer to add heparin after confirmation of fetal cardiac activity with transvaginal ultrasound exam at 6-7 weeks' gestation.

Data regarding the prevalence of antiphospholipid antibodies in women with recurrent pregnancy loss (RPL) being evaluated and followed in a RPL clinic will be presented. Pregnancy outcome including the live birth rate & obstetric complications will be compared in the subset of women with APS before & after treatment with LDA & LMWH. In addition, unsettled issues regarding the diagnosis of APS, as well as the obstetric care of women with RPL and aPLs will be discussed.

S2-1

MANAGEMENT OF GESTATIONAL TROPHOBLASTIC NEOPLASIA

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Aims: Gestational trophoblastic neoplasia (GTN) is an uncommon gynaecological malignancy that if treated appropriately has a high cure rate. However, in ultra-high risk GTN, it remains a therapeutic challenge. The management of GTN in our Department over the past 30 years was reviewed.

Materials and Methods: Records of patients with GTN managed in our Department were reviewed. From 1968 to present, changes were observed in the criteria for the diagnosis of GTN, the method of investigations, the staging

and risk scoring system and the chemotherapy protocols.

Results: Using 5 consecutive stationary hCG as diagnostic criteria for GTN, 11% of complete mole and 7% of partial mole required chemotherapy treatment. Since the FIGO 2000 recommendation of 4 consecutive readings, the numbers were too small to observe any change in incidence. Investigations for lung metastasis had been using chest X-ray and our study of CT lung did not show using information from CT lung for diagnosis of lung metastasis had any effect on treatment outcome. On the other hand, on reviewing patients diagnosed to have liver metastasis by hepatic arteriogram compared to ultrasound, we found that HAG is probably too sensitive as investigative tool. Comparison of treatment outcome by restaging patients with FIGO 1992 and WHO showed no major difference in treatment outcome. Similarly, FIGO 2000 also showed comparable outcome as WHO. For treatment of low risk GTN, we have changed from methotrexate (MTX) to etoposide and back to single dose MTX which all showed good response and survival. For the treatment of high risk GTN, we have been modifying the Bagshawe's CHAMOMA regimen to the current CHAMOC regimen and have good response and acceptable toxicity. For ultra-high risk GTN and relapse, we have good experience with methotrexate,bleomycin and etoposide (MBE).

Conclusions: GTN is an uncommon disease and its management had been very diversified. With the more common use of the FIGO 2000 recommendation, a more unified way of diagnosis, investigations, staging and treatment will enable better understanding and management in future.

S2-3

DIAGNOSIS AND MANAGEMENT OF GESTATIONAL TROPHOBLASTIC NEOPLASIA IN CHINA

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Gestational trophoblastic diseases (GTD) include hydatidiform mole, Invasive mole, Choriocarcinoma and placenta site trophoblasitic tumor (PSTT). Hydatidiform mole is more common in China than that in western countries. It has been estimated that about 5-20% may be received chemotherapy due to its malignant transformation (gestational trophoblastic neoplasia, GTN). GTN possesses high sensitivity to chemotherapy and becomes the first solid tumor that can be cured by chemotherapy even in the presence of widespread metastases. But some of them, especially high-risk diseases, become resistance or relapse. Correct diagnosis and pre-treatment evaluation are important precondition for correct management of GTN.

The diagnosis of GTN:

There is no consensus on criteria on the clinical diagnosis and diagnostic methods for GTN in the world till 2000. FIGO and IGCS guidelines recommend that HCG measurement is mainly, even only used for the diagnosis of GTN. However in China, HCG measurement should be combined with imaging (ultrasound, X-ray, CT & others) and symptoms and signs for the diagnosis of GTN. Ngan reported two different diagnostic criteria of GTN. In China, the differentiation between invasive mole and choriocarcinoma seems to be more emphasized, because choriocarcinoma is believed to have poorer prognosis and usually needed to obtain the more aggressive treatment. So, there are different clinical diagnostic criteria for invasive mole and choriocarcinoma.

Considering different diagnostic criteria in different regions in the world, FIGO conference established the uniform diagnostic criteria in 2000. The new FIGO criteria began to be used in China in 2002. ACOG recommended the FIGO criteria with some modifications in 2004.

Clinical staging of GTN

Different staging systems were used in the world, include: Song's clinical staging system (1962) in China, the FIGO staging system (1992), Hammond clinical classification system in USA and Others. Song's clinical staging was announced in 1962 and has been used in China since then. Considering that GTNs possess specific biologic behavior (blood metastases) and anatomical staging is not consistent with the progression and outcome of the disease, WHO recommended a prognostic scoring system in 1983. WHO scoring system, as a complement of clinical staging, is widespread used in the world, including in China. In 1982, FIGO accepted Song's clinical staging. In 1992, considering the significance of prognostic scoring, FIGO modified its staging system through adding two high risk factors into original staging. However, Song's staging combined with WHO scoring is widespread employed and FIGO staging is rarely used in China. Meanwhile, Hammond system is widespread used in USA. Different staging systems used in the different regions may produce problems. The FIGO Oncology Committee revised the staging system of GTN in 2000. The revised FIGO staging system includes FIGO anatomical staging and revised FIGO scoring system. In the new FIGO scoring system, Blood group is no longer used. The risk categories are simplify into low- risk(total score<7) and high-risk(total score $\geqslant$7). Imaging to be used for determining the number and size of metastases is standardized.

Chemotherapy on GTN

GTN is the first solid tumor that can be cured by chemotherapy. Considering its high sensitivity to chemotherapy and an ideal tumor marker HCG, it is reasonable to consider whether it is necessary to initial therapy immediately just after the diagnosis is made. ACOG recommends that the diagnosis of malignant sequelae as indicated by the need for chemotherapy. SOGC recommends chemotherapy indications including an abnormal hCG regression pattern, histologic diagnosis and the presence of metastases. In America and Canada, GTN is often immediately managed as soon as it is diagnosed. Thus, About 20% of registered molar patients may receive chemotherapy finally. However, the criteria of chemotherapy In European countries seem to be stricter. As a result, only 5% of registered molar patients may receive chemotherapy finally. In China, no criteria of chemotherapy on GTN are standardized by authorized organization at present. In most of the hospitals, chemotherapy is usually initiated promptly after diagnosis of GTN is made, just like in America. In Hong Kong, chemotherapy is initiated when β hCG plateau or rise occurs. To standardize a criterion of chemotherapy on GTN is very important. It should be a part of individual or strategy therapy on GTN.

The development and selection of chemotherapy regimens on GTN go through long history. In 1955, Li first reported the effectiveness of methotrexate (MTX) in treatment of patients with metastatic GTN in the world. In 1962, Song firstly reported the effectiveness of 6-mercapto-purine (6-MP) in treatment of patients with metastatic GTN in China. From 1958, several effective drugs were successfully used in China. Since late 60's of 20th century, the patients with GTN began to receive combination chemotherapy. Regimens include 5-Fu+KSM (Act-D) and AT1258+KSM(Act-D). Prof. Song

in Peking Union Hospital analyzed therapeutic experiences of 806 GTN patients in the periods of 1959 ~ 1975, compared the outcome of 64 GTN patients mainly treated with operation before 1959. The results showed that the patients treated with combination chemotherapy and combined special therapy for metastatic tumors had significant better prognosis than those treated with single drug chemotherapy. Wang reported the outcomes of the patient treated wit 5-Fu+AT1258 in 1979-1988. The results showed 100% of CR in low-risk, 97.7% in moderate-risk and 80% in high-risk (WHO scoring).

Initial treatment on low-risk GTN depends on patient's desire to preservation of childbearing. If the patient desires to retain her fertility, single-agent chemotherapy is the first choice. Of those, MTX is the most common used, while 5-Fu is more popularly used in China. Lu reported 37 GTN patients with low-risk (WHO scoring, 1983) primarily treated by single MTX. The results showed 91.9% of CR, and 0.9% needed salvage chemotherapy. Because middle risk group has been given up and all of score<7 are belong to low risk according FIGO Staging (2000), it should be considered if it is safe for all low risk patients to receive single drug chemotherapy. Matsui reported 272 low-risk GTN patients (new FIGO satging) treated with single MTX chemotherapy. They achieved 75.7% of CR, and found that scoring was significantly higher in failure of primary chemotherapy. Chen reported 61 GTN patients classified as low-risk according to new FIGO scoring (2000) and primary treated with single MTX. They achieved 68.6% of CR with 0.4mg/kg daily regimen for 5 days and 30% of CR with regimen of 1mg/kg on day 1, 3, 5, 7. Thus, CR of low risk patients appears to be lower after new FIGO staging is adopted, although all the patients can achieve CR after salvage chemotherapy. It may be worthful to investigate the value of further strategy therapy for the low risk GTN patients.

Combination chemotherapy regimens as Initial treatment on high-risk GTN are widespread accepted in China. EMA-CO and 5-Fu based combination regimens are most common used. 5-Fu based combination chemotherapy as the first line treatment for high-risk GTN can achieve 80% of CR. Ye reported 33 patients with high-risk and resistant GTN treated with EMA-CO regimen. The results showed 88.2% of CR in high-risk group and 73.3% in resistance group.

我国妊娠滋养细胞肿瘤的诊治现状

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妊娠滋养细胞疾病（Gestational trophoblastic diseases，GTD）包括葡萄胎、侵蚀性葡萄胎、绒毛膜癌和胎盘部位滋养细胞肿瘤。我国葡萄胎的发生率明显高于西方国家，估计其中 5%-20%由于向恶性转化成妊娠滋养细胞肿瘤（Gestational trophoblastic neoplasia，GTN）而需接受化疗。妊娠滋养细胞肿瘤对化疗高度敏感，是最先能用化疗治愈的实体肿瘤，即使有广泛转移也能通过化疗治愈，但一些高危病例仍对化疗耐药或复发。准确的诊断和治疗前的评估是正确治疗 GTN 的先决条件。

GTN 的诊断

直到 2000 年，国际上才对 GTN 的诊断标准达成共识。在 FIGO 和 IGCS 指南中推荐 hCG 是其主要甚至是唯一的诊断手段。但在我国，诊断 GTN 需结合 hCG、症状体征和超声、X 线、CT 及其他一些影像学检查。Ngan 报道了两种不同的 GTN 诊断标准。我国似乎更强调侵蚀性葡萄胎和绒毛膜癌的区别，认为绒毛膜癌预后较差而需更强烈的化疗。因此，对侵蚀性葡萄胎和绒毛膜癌也有不同的诊断标准。

考虑到国际上不同地区对 GTN 有不同的诊断标准，2000 年 FIGO 提出了统一的诊断标准，我国 2002 年才开始用此标准，ACOG 在 2004 年对 FIGO 诊断标准又做了一些修改。

GTN 的临床分期

国际上有不同的分期法：1962 年的宋氏临床分期，1992 年的 FIGO 分期法，美国的 Hammond 临床分类法等。宋氏临床分期在 1962 年提出并已在国内广泛应用。鉴于 GTN 具有极易血行转移的生物学特性并且解剖学分期并不能与预后一致，WHO 在 1983 年提出了预后评分系统。作为临床分期的补充，WHO 预后评分已在我国普遍应用。1982 年 FIGO 采纳了宋氏临床分期。考虑到预后评分的重要性，1992 年 FIGO 修改了原来的分期系统，将两个高危因素加入到分期系统中。然而，由于宋氏临床分期结合 WHO 预后评分已在我国广泛应用，国内很少应用 FIGO 分期法。同时，Hammond 分期法仍在美国广泛应用。不同国家和地区采取不同的分期法带来了一些问题。FIGO 肿瘤组在 2000 年又修订了 GTN 的分期系统。修订后的 FIGO 分期系统包括了 FIGO 的解剖学分期和新的 FIGO 预后评分。在新的 FIGO 预后评分中不包括血型，并分成低危（总分<7 分）和高危（总分≥7 分）两类。同时对影像学判断转移灶数目和大小的标准作了规定。

GTN 的化疗

GTN 是最先能用化疗治愈的实体肿瘤。由于其对化疗的高度敏感和有理想肿瘤标志物—hCG，有理由考虑是否一旦诊断就必须开始化疗？ACOG 推荐 GTN 一经诊断就开始化疗。SOGC 推荐的化疗指征包括异常的 hCG 回归、组织学证据或存在转移灶。在美国和加拿大一旦诊断即开始化疗，结果约有 20%登记的葡萄胎患者最终接受化疗。然而欧洲一些国家的化疗指征相对比较严格。结果仅 5%登记的葡萄胎患者接受化疗。我国目前尚无权威性机构制定的 GTN 开始化疗的标准。多数医院同美国一样一旦诊断即予化疗。在香港当 hCG 出现平台或上升即予化疗。明确开始化疗标准是 GTN 治疗个体化的重要部分。

化疗方案的选择经历了很长时间的演变。1955 年 Li 首次报道了 MTX 治疗有转移 GTN 的有效性。在我国，1962 年宋报道了用 6-MP 治疗有转移 GTN 的疗效。从 1958 年开始，相继有多种药物在我国成功应用。从上一世纪 60 年代末开始，GTN 患者接受联合化疗方案主要有 5-FU+KSM 和 AT1258+KSM。北京协和医院宋教授分析了 1959 年~1975 年接受化疗的 806 例 GTN 患者的疗效，并与 1959 年前以手术为主要手段的 64 例患者比较。结果发现有转移 GTN，接受联合化疗和结合一些特殊治疗手段的预后较接受单一化疗的好。Wang 报道了 1979 年~1988 年 258 例接受 5-FU+AT1258 患者的疗效，结果按 WHO 预后评分标准低危组、中危组、高危组的完全缓解率分别为 100%、97.7%和 80%。

低危 GTN 的初次治疗选择根据患者对保留生育功能的要求。如果患者要求保留生育功能则单药化疗是首选的初次治疗。尽管我国 5-FU 的应用较广泛，但国际上 MTX 更常用。吕等报道了 37 例 GTN 患者治疗结果，按照 1983 年 WHO 评分，低危组采用单药 MTX 完全缓解率 91.1%，0.9%需补救化疗。由于依据 2000 年 FIGO 分期系统取消了中危组，将<7 分的均归低危组，对低危组采用单药治疗是否安全值得探讨。Matsui 报道了 MTX 单药治疗，根据新 FIGO 分期的低危患者 272 例，结果完全缓解率为 75.7%，失败组的预后评分明显高于完全缓解组。陈报道

了 61 例低危（新 FIGO 分期）患者，采用 MTX 0.4mg/kg .d 连续 5 天单药治疗，结果完全缓解率 68.6%，而采用 MTX+CF 组完全缓解率仅 30%。采用新 FIGO 分期后，MTX 单药治疗低危 GTN 的完全缓解率有所下降。虽然 MTX 单药治疗失败者改用补救化疗后，100%能达到完全缓解，但对采用新分期法的危低患者最佳的初次化疗方案的选择仍值得进一步探讨。

我国高危 GTN 患者普遍采用联合化疗。联合化疗方案主要有 EMA-CO 或以 5-FU 为主的联合化疗。高危患者初次治疗采用 5-FU 为主联合化疗的完全缓解率为 80%。叶报道 33 例高危和耐药的 GTN 患者给予 EMA-CO 方案化疗。结果，高危组完全缓解率 88.2%，耐药组 73.3%。

S3-3

MENOPAUSE-RELATING SURVEY OF THE MIDLIFE WOMEN IN SOUTHERN CHINA

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Objective: To describe the prevalence of menopausal symptoms experienced by women aged 40-65 who lived in Guangdong province, China, and to elucidate some factors associated with these symptoms, as well as the average age of menopause; and to investigate the proportion of women searching for medical care or receiving hormone replacement therapy.

Method: This cross-sectional study included 9939 women aged 40-65 who were selected by multistage cluster sampling and a face-to-face interview with given questionnaire.

Result: The onset of natural menopause age is 48.99 years old. The prevalence of menopausal symptoms is significantly different among the pre-, peri- and postmenopausal women, and the prevalence is higher in the latter two groups. For the women in Guangdong, the most prevalent symptom reported was insomnia (36.4%) while that of hot flushes which was seems as one of the classical menopausal symptoms was only 17.5%. The factors relating to the menopausal symptoms include the profession, education, the manner of menopause, physical and emotional problems. 0.8% participation had ever used HRT while the current use account for 1.3%. Only 28.9% has searching for the health care due to the menopausal symptoms.

Conclusion: Comparing to the north of Chinese women and the white women, the menopausal symptom in southern Chinese women is different, and the principle symptoms are psychiatric ones in Guangdong menopausal women. The proportion of women who used HRT is very small and so do that of women searched for the medical care because of the menopausal symptoms, which would be a challenge to our healthcare work.

KEY WORDS: menopause menopausal symptoms epidemiology

广东省 40-65 岁妇女绝经症状的流行病学调查

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目的： 了解广东省 40-65 岁妇女绝经症状的特点和发展变化的规律。

方法： 采用分层整群抽样的方法，在广东省 20 多个调查点对 9939 名 40-65 岁的妇女进行问卷调查。

结果： 平均绝经年龄为 48.99 岁。绝经症状的发生率在绝经前、围绝经和绝经后组妇女中有很大差异，以后两组的发生率较高。广东省妇女绝经症状发生率最高的是失眠（36.4%），而被认为是典型的绝经症状的潮热在广东妇女的发生率仅为 17.5%。与绝经症状发生相关的因素有职业、教育程度、对绝经的态度、身体和情感问题。曾用过激素疗法（HRT）的仅为 0.8%，正在使用者占 1.3%。仅有 28.9%因为绝经症状求医。

结论： 与西方国家和中国北方的报道比较，广东妇女的绝经症状发生有其特点。最常见症状是精神神经症状。广东妇女的绝经症状发生率较低，程度较轻。广东妇女 HRT 使用者少，为绝经症状求医的人数也较少。

S4-2

STUDY ON REGULATION MECHANISM OF MATERNAL-FETAL ENDOCRINE-IMMUNITY NET DURING EARLY SPONTANEOUS ABORTION OF KIDNEY DEFICIENCY WITH KIDNEY & QI REPLENISHING HERBS

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Objectives: Over 80% pathogenesis of early recurrent spontaneous abortion (RSA) may be caused by regulation disorder of maternal-fetal endocrine and immune system, which the traditional Chinese medical pattern differentiation diagnosis is the deficiency of kidney. Research discovered that using replenish the Kidney and the qi formula in prevention the cause of abortion can have 88% pregnant successful rate ,with the levels of BE(Block Effect), P(progesterone ,P) PRL (prolactin ,PRL) and β -hCG (human chorionic gonadotropin- β) increasing gradually. This article further investigates the pathogenesis mechanism of maternal-fetal endocrine -immunity system on kidney deficiency with RSA and effect of using kidney replenishing herb treatment

Materials and Methods: A series study of in reproductive endocrinology, immunology was measured by radioimmunoassay, morphology immunohistochemistry, cell and molecular biology, serum-pharmacology and FCM and so on. It includes:

1. **Experiments in vivo:** Set up SD rat model of bromocriptine induced early abortion (BAR), which pregnant rats were injected 3mg/kg.d of bromocripitine, subcutaneously during 6 to 8days of gestation ,then which were randomized into BAR group ,herb group (feeding kidney-replenishing herbs of BAR, herb group) and control group (normal pregnant rats), All rats were sacrificed at the 12 day to observe the outcome of pregnancy and drawed materials for experiments of measuring and observing the following in comparing between: **(1)** Abortive rate, success rate, number of embryo and the rat placenta morphology. **(2)** Measure the composition of synthesis. secretion and biologic efficiency of hormone: levels of P, PRL in serum, expression of PR(Progesterone, receptor, PR)、PRLRmRNA (Prolactin Receptor, PRLR) of decidua respectively. Besides, measure

on progesterone synthesis enzymes in placenta , incuding of the expression of P450scc (P-450 side chain cleavage enzyme, P450scc) , 3β-HSD (3β-hydroxysteroid dehydrogenase, 3β-HSD), LDLR(Low density lipoprotein receptor, LDLR) IGFs mRNA(insulin-like growth or factors ,IGFS),and PR . (3) Determine change on balance of immunized Th1 cytokines / Th2 cytokines and biologic activity on NK cell of decidua (4) change between proliferate and apoptosis on both trophoblast and decidua. The expression of HB-EGF, PCNA, Fas / FasL both deciduas and trophoblast: the expression of Caspase-8, Caspase-3 mRNA and activity of Caspase-3. in decidua. 2. Experiment invitro: Set up in cultured human trophoblastic cells from early placenta villi for experimental research on the growth of decidua and trophoblast, the effect of using serum containing herbs of kidney replenishing in. Testing subject includes: (1) Change on microstructure of trophoblast apoptosis, distribution among the trophoblast proliferation cycle and effect of the invasion ability in extravillous trophoblast by TNF-α (Tumor necrosis factor-beta, TNF-α), IFN-(Interferon gamma, IFN-γ) treated in the cultured human trophoblastic cells (2) Effect on the trophoblast growth , P450scc,3β—HSD,:LDLR and P levels by treated IGFs-1 or / and serum containing Chinese herbs in the cultured human trophoblastic cells.

Results: Effects on morphology, maternal-fetal immunity, endocrine for SD rat model of bromocriptine induced early abortion (BAR) with Kidney & qi Replenishing herbs

(1) Pregnant outcomes and morphologic changes in three groups : The abortive rae of BAR group was always about 70%~90% and total number of embryo were significantly decrease , the pregnant rate of herb group up to 70%-90%, the amount of embryo increase rapidly. On the electron microscope: Placenta tissue of BRA group: The basement membrane of the trophoblastic epithelium was thickened and tortuous. There were lots of dense microspherical particles within the basement membrane. Mitochondrial showed coagulating and vacant. The cisternae of the rough endoplasmic reticulum (rER) were dilated and contained flocculus material. A degranulation of ribosomes on the rER was frequently found. The capillary endothelium was thicked with microvilli-like projections In herb group : the weight 、diameter of placenta in herb group was more increaser. Villi blood sinusoid enlarged, vascular became abundant and more regular in formation than BAR group. Smooth endoplasmic reticulum (sER) increased and dilated, and there were plenty of mitochondria and some lipid droplet in cytoplasm. organella were normal mainly. So these changes have supplied a normal morphology base on exchanging of substance between maternal and fetal, and satisfied with the fetal development require. (2) Adjust secrete mechanism of PRL.P with herbs :In BAR group: levels of P、PRL in serum, expression of PR, PRLmRNA in decidua and expression of IGF-I, IGF-II, IGF-IIR, P450scc, 3β-HSDmRNA in placenta of BAR group were all decreased significantly compared with those of herb group. In herb group we discover that the level of PRL, P in serum increased gradually, the expression of PR.,PRLRmRNA in decidua all increased with Kidney & qi Replenishing herbs, It down-regulated IGF-ⅠR, IGFBP3gene expression, up-regulated the expression of IGF-Ⅰ, IGF-Ⅱ, IGF-ⅡR, P450SCC, 3beta-HSD, LDLRmRNA and PR protein in decidua , and strength increased gradually companied with the process of pregnancy and time of treating, here was obvious relativity with progesterone secretion in serum. (3) Stregthening the maternal fetal immune tolerance : In BAR group: we found the cytotoxities of both decidual lymphatic NK cells were activated, the expression of Th1 cytokines (TNF-α and IFN-γ mRNA were significantly higher , whereas the Th2 cytokines(IL-4 and IL-10mRNA), the ratio of IL-10/ IFN-γ were significantly lower and a tendency toward the model of Th1 cytokines than those in control group. Significant low levels of expression in $CD56^+$ NK, decidual , decidual $CD56^+$ NK and CD94 of BAR group, whereas higher ratio of expression in CD69/CD94 of BRA group., which than control group。 In herb group: Adjust the balance of maternal-fetal immunity in ratio of Th1 /Th2 and lean to Th2 with herbs; Add the amount of CD56+NK in decidua and restrain the activity of CD56+NK, adjust the balance of CD69 / CD94 on the surface of CD56+NK in decidua and lean to restraining receptor, thereby restrain the toxicity that NK produced to embryo.(4) The proliferation and apoptosis of dicidua , trophoblast cell intend to normal with herbs: Expression of PCNA and HB-EGF increased in the trophoblast and decidua; expression of TNF-a. Fas FasL in the trophoblast and decidua , Caspase-8, Bax in decidua all decreased, but expression of Bcl-2 increased, so the ratio of Bax and Bcl-2 was reduced (5) endocrine result in abnormity of immunity system: We discover on the above the pearson correlation analysis studies; a positive relation between PR and PCNA、HB-EGF, whereas an indirect relation between PR and TNFα, and an indirect relation between TNF-α and Fas FasL apoptosis. (6) chinese herbs can promote prolifiration differentiation. Syncretize.invade of trophoblast cell in normal early pregnancy, and can keep the normal structure and function of placenta .We built the cultured system of human villous trophoblast cells in vitro: Experiments showed: we cultivated the human early pregnant trophoblast with the serum which contain kidney-replenishing formula: and find herbs can promoted the trophoblast cell differentiation. Scan electron microscope results showed: tiny villus became more abundance, cell syncretize; and promoted hCG-β synthesize. secretion; light microscope showed: Invadeing activity of trophoblast out of villous increased; DNA doubleness body presented cycle distributing with FCM method, cell period of S increased obviously, cell in the period of G2-MDecreased,the results showed: cell located in the period of DNA synthesize and mitosis, chinese herbs can promoted trophoblast cell proliferation, depressed the rate of cell apoptosis; research also found that along with the activity of trophoblast increasing,they can resisted the toxicity of embryo by TNF-α and IFN-γ induced, inhanced the capability of thophoblast grew in the condition of Th1 citokine, which can restrained cell apoptosis, restrained activity of caspase-3 enzyme

Conclusions: (1) according to traditional Chinese medical theory on " Kidney control reproduction" and mordern reproductive medical theory, using the research idea and method of integrated traditional Chinese and western medicine, We adapt model of bromocriptine-induced abortion (BAR), focus on the influence of between endocrine to maternal-fetal immunity , carry out pathogenesis of Deficiency of the Kidneys research. Bring forward abnormal mechanism of PRL secretion affect secretion of progesterone and activity of PR, mediated balance malajustment of TH1 and Th2 cytokines in the decidua, so that bring a series of disorder from decidua. trophoblast to apoptosis control, primary show the relationship of between pathogenesis of Deficiency of the Kidneys abortion and disorder of

maternal-fetal endocrine and immunity net. (2) Kidney-replenishing formular can adjust the disorder condition of maternal-fetal endocrine and immunity net, increase the tolerance of maternal-fetal immunity from many different target. we pointed out that progesterone play an important and key role in balancing the Th1/Th2 cytokines, regulating the cytotoxicity of natural killer cells and apoptosis and proliferation of trophoblasts, strengthening the maternal fetal immune tolerance, however kidney-replenishing formular can greatly progeaterone secretion ,so get to balance of materal-fetal endocrine and immunity and prevent abortion. (3) we established the SD rats model of bromocriptine-induced abortion (BAR) at first in nation , the abortive rate of the model group was always about 70-90%, and the total of embryo are significantly lowered, the characteristics were similar between BAR and patients with abortion, when these model rats were taken by kidney replenishing herb, the pregnant successful rates amounted to 75-90%, so we can explore the mechanism of the herbs, pathogenesis of this type of abortion and the development of new drugs in this repetitive and steady animal model

补肾方治疗肾虚型流产对母胎内分泌-免疫网络调控机理研究

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研究目的：反复自然流产 80%以上病因是母胎免疫和内分泌调节异常引起 ,中医辩证为肾虚胎元不固，采用补肾益气方治疗，妊娠成功率为 88%，血封闭抗体、P(progesterone,P) PRL(Prolactine,PRL) ，β-hCG（human chorinonic gonadotropin-β）水平升高。本研究进一步探讨肾虚型流产母胎内分泌--免疫网络失调发病机制及补肾益气方疗效作用机理。

研究方法：运用形态学、免疫组化学、分子生物学、血清药理学及细胞定量分析等方法，进行系列研究：(1). 在体实验：SD 孕鼠 6d~8d 每日皮下注射溴隐停 0.3mg/kg。建立改良溴隐停致流产鼠模型：设模型组(bromocripitin abortion rat , BAR group) ，灌服中药组(herb group)及正常孕鼠组(controal group)，均于孕 12d 处死取材作以下的观察和测检：① 流产率、妊娠成功率,胎仔数,胎盘形态学的比较；②内分泌激素生成、分泌、效应水平测定：血清 P、PRL 及蜕膜 PR(Progestorone receptor,PR)、PRLR（Prolactine Receptor,PRLR）表达水平;胎盘孕酮生成酶系 P450scc(P-450 side chain cleavage enzyme P450scc,),3β-HSD(3β-hydroxysteroid dehydrogenase , 3β-HSD), LDLR(Low density lipoprotein receptor,LDLR)表达水平与 IGFsmRNA (insulin-like growth Factors ,IGFS)表达对孕酮生成的影响；③母胎免疫 Th1 细胞因子（TNF-α,IFN-γ），Th2 细胞因子（IL4、L10）平衡及蜕膜 NK 细胞生物学活性的变化。④蜕膜、滋养细胞增殖和凋亡的比较：检测蜕膜，滋养细胞增殖及凋亡 HB-EGF、PCNA；Fas / FasL 的表达水平 ； 蜕膜 Caspase-8 、Caspase-3mRNA 表达水平 , Caspase-3 活性的变化。(2) 体外实验：建立早孕人绒毛滋养层细胞培养，察补肾益气方含药血清干预的影响：①对 TNF-α (Tumor necrosis factor-beta,TNF-α)IFN-(Interferon gamma,IFN-γ) 诱导滋养细胞凋亡超微结构变化,细胞增殖 ,分化、融合、侵袭力的影响;②IGFs 调节滋养细胞增殖，P450scc、3β—HSD,:LDLR 表达对孕酮分泌的影响。

结果：补肾方对肾虚型流产疗效，母胎免疫，内分泌的影响①妊娠结局及形态学变化：BAR 组流产率达 70%～90%，胎仔数明显减少。胎盘血管面积、绒毛面密度和毛细血管密度明显低于正常孕鼠对照组，胎盘子宫蜕膜螺旋动脉内皮细胞肿胀，管腔狭窄等病理改变。模型流产鼠灌服中药后(herb group)妊娠率达 70%~90%，胎仔数明显增加，胎盘的光、电镜超微结构显示：胎盘重量较流产鼠明显增加；绒毛血窦表面积增大，血管含量丰富，管腔形态规则，着床部位蜕膜腺体丰富；血管合体细胞膜明显增多；滑面内质网增加，线粒体丰富，胞质内有大量脂滴，显示胎盘超微结构已正常，为母儿间气血、物质交换、胎儿生长发育母胎界面功能提供了形态学基础 。②调整 PRL,P 的内分泌机制：BAR 组具有低血 P、PRL 的分泌特点；蜕膜蛋白 PR、PRLmRNA 表达；胎盘 IGF-Ⅰ、IGF-Ⅱ、IGF-ⅡR、P450scc、3β-HSDmRNA 表达水平均明显低于 Control 组，影响 P 合成、分泌和生物效应。Herb 组血 PRL 、P 水平明显递增；蜕膜 PR、PRLRmRNA 的表达均增加 ;降调胎盘 IGF-ⅠR、IGFBP-3mRNA 表达，升调胎盘 IGF-Ⅰ、IGF-Ⅱ、IGF-ⅡR、LDLR、P450scc、3β-HSDmRNA 和蜕膜 PR 蛋白表达强度 与血 P 水平升高显著相关，明显高于 BRA 组， 提高孕酮的合成、分泌和生物学效应 。③纠整母胎免疫 Th1/Th2 平衡和 NK 细胞的杀伤活性：BRA 组蜕膜 Th1 型细胞因子（TNF-α↑,IFN-γ↑）明显高于control组；而Th2型细胞因子（IL4↓、L10↓）；(IL-10 / IFN-γmRNA)比值明显低于 control 组 ，显示 Th1/Th2 平衡异常--偏向 Th1 型；蜕膜淋巴细胞中 $CD56^+$ NK 的比例及 $CD56^+$ NK 细胞 CD94 表达（抑制性受体）下降，CD69/CD94 比值异常升高，其综合作用诱导蜕膜 $CD56^+$ NK 细胞杀伤活性增加。Herb 组 ：调整母胎免疫 Th1/Th2 平衡 ，而偏向 Th2 型；增加蜕膜 CD56+NK 细胞的数量， 蜕膜 $CD56^+$ NK 细胞表面的 CD69/CD94 平衡偏向抑制性受体，从而抑制 CD56+NK 活性对胚胎的毒性。④促使蜕膜、滋养细胞增殖，凋亡趋于正常 ：在 BAR 组：蜕膜 HB-EGF 表达及蜕膜、滋养细胞 PCNA 表达下降；TNF-α、Fas / FasL 表达的增加；蜕膜 Caspase-8 、Bax 表达的增加，Bcl-2 表达降低，Bax/Bcl-2 比值升高，综合表现滋养细胞、蜕膜细胞凋亡过度。Herb 组：滋养细胞、蜕膜的 PCNA 表达及滋养细胞 HB-EGFmRNA 表达上升；蜕膜、滋养细胞 TNF-α、Fas FasL 及蜕膜 Caspase-8 、Bax 的表达下降，Bcl-2 表达增加，降低 Bax/Bcl-2 比值，滋养细胞增殖/凋亡趋于正常，提高母胎免疫耐受。 ⑤内分泌对免疫异常的影响：经统计学 pearson 偏相关分析发现：P 与 IL-10/IFN-γ比值呈明显的正相关 ；PR 与 PCNA、HB-EGF 呈正相关,与 TNFα、Fas 均呈负相;TNF-α与 Fas FasL 均呈正相关。⑥ 补肾益气方具有促进正常早孕滋养层细胞增殖、分化、融合、侵袭能力，以维持胎盘结构和功能的作用；含中药血清培养人早孕滋养层细胞后， 滋养层细胞微绒毛更加丰富，促进细胞融合，绒毛外滋养层细胞的侵袭活性增强；DNA 二倍体细胞周期分布：S 期细胞明显增多，G_2-M 细胞减少，提示细胞处于 DNA 合成期及有丝分裂期，促进细胞增殖，降低细胞凋亡的发生率；研究还发现滋养层细胞活力提高，促进早孕期人滋养层细胞生长，拮抗 TNF-α和 IFN-γ诱导的胚胎毒活性，提高在 Th1 型细胞因子环境下滋养层细胞生长能力。

结论：(1) .以中医“肾主生殖”理论和现代生殖医学理论为指导，运用中西医结合研究的思路和方法，利于建立改良溴隐亭致流产鼠模型，从内分泌对母胎免疫的影响为切入点，贯穿母胎内分泌--免疫网络为主线，开展肾虚型流产发病机理研究。 提出 PRL 分泌机制异常影响孕酮、

合成、分泌及其受体的生物学活性，介导蜕膜 Th1/Th2 的平衡失调，连锁引起蜕膜、滋养细胞增殖 / 凋亡调控异常，使蜕膜发育及滋养细胞增殖不良，影响受孕的微环境，诱导母胎免疫耐受下降，其相互影响构成一个独特内分泌--母胎免疫网络调节的异常，对胚胎损伤增强，在流产的发病机理中起着主导作用，初步揭示肾虚型流产的发生、发展与母胎内分泌--免疫网络异常有内在本质的联系。(2) 补肾益气方从整体－器官－组织－细胞－分子水平的多层次、多途径、多靶点的作用，调整母胎内分泌—免疫网络失调，并着重提出中药促进孕酮合成、分泌生物学效应是调控蜕膜 Th1 /Th2 的平衡、滋养细胞增殖 / 凋亡正常化、增强母胎免疫耐受、维持妊娠的关键性激素。(3) 在国内首先建立改良溴隐亭致大鼠流产模型，发现其具有相似于临床内分泌-免疫网络失调的特点，流产率达 75-80%，具稳定性、重复性和可逆性，灌服中药后妊娠率高达 75-90% 故可作为此类型流产深入研究及新药开发的动物模型。

S5-1

PRENATAL DIAGNOSIS, THE PROBLEMS WE ARE FACING IN CHINA

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1. The needs for genetic service has greatly increased in China, In year 2000,the infant death rate is 32.7‰,birth defect is one of the leading cause. There are no well organized training courses in medical school and no certificating agencies, and not enough genetic laboratories.
2. Primary prevention of birth defect: Compulsory premarital exam was cancelled for two years→birth defect ↑. Folate supplementation works better in Northern China, but not necessarily in Southern China.
3. Secondary prevention of birth defect:
1) Maternal biochemical screening for Down Syndrome and NTD, First trimester (7-14 weeks): < 5% coverage, Second trimester (15-18 weeks): 20% coverage, mostly with two markers for cost –effect reason. There are more than 3-4 kinds of methods for testing biochemical markers, but with no good QC/QA, especially external QC/QA. Different laboratories use different Cut-off values, the choice is too arbitrary. The false positive rate is not well controlled, resulting in a higher rate of amniocentesis. More attention has been paid to biochemical screening, but amniocentesis and chromosome karotyping are overlooked, we don't have enough qualified genetic laboratories and clinical geneticists
2) Lack of well trained Ultrasonographer for birth defect: level I>level II >level III, the ultrasonographer is now facing an enormous pressure of malpractice:ranks No.1 in Ob/Gyn malpractice lawsuit
4. Newborn screening: PKU, T3, T4, well organized, compulsory screening with a coverage rate of more than 95%, government takes care of the affected children.

产前诊断，中国面临的问题与困惑

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1.中国对于产前诊断的需求明显增加，2000 年中国的婴幼儿死亡率为 32.7‰，其中出生缺陷占第一位，但是在中国没有正规的机构培养临床遗传学方面的医生，而且只有少数的临床遗传实验室。
2.出生缺陷的一级预防：强制婚前医学检查已经被取消 2 年，出生缺陷有明显上升的趋势，补充叶酸在北方地区有比较好的减少神经管缺陷的作用，但是在南方地区效果不明显。
3. 出生缺陷的二级预防：
1)母亲血清筛查唐氏综合征和 NTD，早孕筛查（7-14 周）：只覆盖不到＜5% 人群，孕中期筛查（15-18 周）只覆盖不到 20% 的人群。出于卫生经济学的考虑，目前多数用两项指标，检出率比较低。在筛查方面，目前有 3-4 种实验室方法，缺乏比较好的 QC/QA。不同实验室采用不同的切割值，导致筛查阳性率不一致。不少地区重视筛查，忽视确诊，除了经济原因外，缺乏合格的临床遗传学家和临床遗传实验室也是一个重要因素。
2) 缺乏合格的超声产前诊断方面的医生，而且医生也面临着巨大的医疗事故诉讼压力。在上海，产前诊断，特别是超声产前诊断已经成为妇产科医疗纠纷的第一位。
4. 出生缺陷的三级预防：有组织良好的新生儿 PKU,T3,T4 等先天代谢病的筛查计划，在上海覆盖率超过 95%，政府帮助负担 PKU 孩子的抚养。

S5-2

CORRELATION BETWEEN AMNIO-POLYMERASE CHAIN REACTION (PCR) AND CONVENTIONAL CYTOGENETIC STUDY IN WOMEN AT HIGH RISK FOR FETAL ANEUPLOIDY

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Objective: To test the accuracy of PCR using fetal DNA from amniotic fluid for the rapid prenatal diagnosis of the common trisomies in women at high risk for fetal aneuploidy.
Methods: Over an 18-month study period, amnio-PCR was performed, at the discretion of the obstetrician, on uncultured amniocytes using short tandem repeat markers for chromosomes 13, 18 and 21, in women with advanced maternal age (≥ 35 year-old), positive serum biochemical screen, and/or abnormal ultrasound findings. All samples were subsequently analyzed by conventional karyotyping methods.
Results: 369 amnio-PCR samples were analyzed. Mean gestational age at diagnosis was 17.8 +/- 2.4 weeks. Amnio-PCR detected all autosomal trisomies without a false-positive or false-negative result. Eighteen (4%) samples showed abnormal results (16 Trisomy 21 and 2 Trisomy 18), and all of them were confirmed by traditional karyotype on cultured amniocytes. Amnio-PCR results were available within 6 to 24 hours.
Conclusions: 1) Rapid prenatal diagnosis of common trisomies using amnio-PCR is an accurate technique that helps in decision-making regarding further perinatal care. 2) Amnio-PCR normal results alleviated parental anxiety in 96% of the cases, during the 2 to 3-week waiting time for the conventional cytogenetic study report.

S6-1

TREATMENT OF OVARIAN CANCER

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Current systemic treatment for ovarian cancer consists of chemotherapy with the two-drug combination of carboplatin and paclitaxel (CARBO/PAC). Using this regimen following cytoreductive surgery, approximately 75% of the patients will be in a clinical complete remission. Unfortunately, most patients will recur with a median time to disease progression of 18-20 months. Numerous strategies have been tested in an effort to prevent or delay recurrences, including intraperitoneal (I.P.) chemotherapy and radioisotopes, immunotherapy, whole abdominal radiation therapy, and high-dose chemotherapy with peripheral stem cell support. None of these strategies has been shown to improve survival. A Gynecologic Oncology Group (GOG) trial compared 3 months versus 12 months of paclitaxel maintenance therapy, and while there was a longer time to disease progression for patients treated with 12 months of therapy, there was no improvement in overall survival. The GOG will be performing another randomized trial of observation versus paclitaxel versus pegylated paclitaxel in patients who enter a clinical complete remission following induction therapy. Three large trials have also evaluated the role of I.P. chemotherapy in patients with small-volume (no tumor nodule >1 cm after initial surgery), stage III disease. In the most recent GOG trial, there was an improvement in time to progression and overall survival for patients treated with the I.P. regimen. However, the substantial toxicity of I.P. therapy has led to additional trials of I.P. regimens to determine whether toxicity can be decreased without compromising the efficacy. For patients with recurrent ovarian cancer, it has recently been shown in two large trials that combination chemotherapy with CARBO/PAC or gemcitabine plus CARBO is superior to treatment with single-agent platinum in patients with platinum-sensitive disease. Treatment options for patients with platinum-resistant recurrent ovarian cancer include encapsulated doxorubicin, gemcitabine, and topotecan.

S6-3

ADVANCES AND RESEARCHES IN THE DIAGNOSIS AND TREATMENT OF OVARIAN MALIGNANCIES

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Cancer of the ovary has become increasingly important in the last few decades and ranks as the leading cause of death among gynecological malignancies. While clinicians are devoting themselves to the study of the behavior of ovarian cancer, as well as to the search for more effective therapeutic modalities, little progress has been made in fight against ovarian cancer except of malignant germ cell tumors.This phenomenon was based on the three factors: 1. more than 70% of cases diagnosed ovarian cancer had advanced diseases; 2. more than 70% of cases developed recurrence or progressive disease after initial therapy.3. Most patients with relapse or progressive diseases had chemoresistence.

Studies of epidemiology have shown that: use of oral contraceptive pills; shorter duration of reproductive years; conditions of chronic anovulation; history of breastfeeding and multiparity are prevention & protective factors for epithelial ovarian cancer. Family history is the strongest risk factor for ovarian cancer. Risk rate is 20%-50% in the member of HOCS. BRCA1 & BRCA2 gene associated with HOCS. For early diagnosis RMI was more accurate than any individual criterion in diagnosing cancer. Using a RMI cut-off level of 200 to indicate ovarian malignancies, the sensitivity is 87.3%, specificity 84.4%, and positive predictive value 82.1%. Surgery is very important treatment in ovarian cancer. And the role of surgery depended on the patient,s diseases. Lymph nodes metastasis is a very important parthway of spread and retroperitonal lymphadenectomy should be performed in epithelial ovarian cance. Chemotherapy is standard adjuvant treatment. CGOG conducted a multicenter randomized clinical trial of weekly paclitaxel and carboplatin vs three weeks paclitaxel and carboplatin as first line in epithelial ovarian cancer has shown the same efficacy of combination regiments of taxol given weekly plus carboplatin and taxol given every three weeks plus carboplatin. Myelosuppression is less frequency in the weekly group than in every three weeks group. Weekly taxol therapy has mild toxicity and is more suitable for the old and feeble patients. Weekly taxol therapy can be conveniently administered in outpatients department. For post-therapy surveillance position emission tomography (PET) is a best method for detecting recurrence with 83% sensitivity, 80% specificity, 82% accuracy. Treatment of relapsed epithelial ovarian cancer should be individual and palliative. Quality of life should be considered firstly. No drug is of choice in selection of second-line treatment. and primary consideration is toxicity. Five year survival rate for patients with early-stage epithelial ovaran cancer are 80% to 100 depending on the tumor stage and grade. Five year survival rate for patients with advanced disease is 30% to 40% malignant germ cell tumor of the ovary is very sensitive to the chemotherapy. Chemotherapy has improved the survival of patients with malignant germ cell tumor of the ovary dramatically. Survival rate has been increased from 10% to 90% Reproductive function can be preserved for any stage patients with malignant germ cell tumor of the ovary. Primary treatment is surgical and unilateral oophorectomy with preserved reproductive function is considered. PVB and PEB chemotherapy are the treatment of choice for patients with MGCT postoperatively. Courses of chemotherapy are depending on the high risk factors of the tumor and tumor maker levels.Some experimental protocols are under way. Clinical trials using high-dose chemotherapy followed by stem cell transplantation has shown no benefit for epithelial ovarian cancer. Immunotherapy has been found to have some activity in patients with minimal residual disease. Studies are being done with cytokines,tumor necrosis factor, Interferon and IL2. Vaccine trials are under way and gene therapy using adenovirus vectors administered intraperitoneally is currently ongoing, but the results are not yet available.

S7-1

UPDATE OF GYNECOLOGICAL ENDOSCOPY

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Aims: To comprehend updating gynecological endoscopy.
Materials and Methods: To marshal the material of International Society for Gynecological Endoscopy Annual Meeting in recent 3 years and the literatures cited by Medline in recent 5 years.
Results: Laparoscopic hysterectomy, myomectomy and to diagnose as well as to treat gynecological acute abdominal diseases were routine operations already. Laparoscopy was the standard diagnostic & therapeutic method for EMS. To treat gynecological malignant tumor laparoscopically was to

be evaluated. It's a trend to treat earlier stage of adenocarcinoma laparoscopically instead of laparotomy. Laparoscopic surgeries can be performed at any trimester. Gasless laparoscopy fitted those women who had the contraindications of gas laparoscopy. Hydrotransvaginal laparoscopy fitted asymptomatic infertile women who haven't obvious pelvic diseases. Visible trocar reduced the complication of laparoscopy by<0.012%. The outcome of infertility & pregnancy can be improved by the application of hysteroscopy, which have to be the initial and routine examination for infertile women. Part of hysteroscopic examination can be instead of sonohysterography. Hysteroscopy was used when sonohysterography failed only. Endometrial Ablation (EA) had set foot on treatment of pre-adenocarcinoma and earlier stage of adenocarcinoma. After transcervical resection of endometrium the pregnant rate was 2.39% which diagnosis depended on the alert of both patients and doctors. The severe complications of Hysteroscopy became very rare and are avoidable if it is prevent seriously. Some simple, fast and much success non-hysteroscopic EA was created in recent few years.
Conclusions: Laparoscopy and Hysteroscopy are safe and efficacious method to evaluate, diagnose and treat gynecological diseases.

妇科内镜的近代进展
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目的： 了解妇科内镜的近代发展。
方法： 汇集近 3 年国际妇科内镜年会资料及近 5 年 Medline 文献。
结果： 腹腔镜子宫切除、子宫肌瘤剔除及妇科急腹症诊治已成常规术式和诊治子宫内膜异位症的标准方法，应用于妇科恶性肿瘤尚处于评估阶段，治疗早期子宫内膜癌有取代开腹术的趋势。妊娠各期均可进行腹腔镜手术。无气腹腔镜适合有气腹禁忌患者。经阴道注水腹腔镜适合无症状和无明显盆腔病变的不孕患者。可视套管针使并发症下降到<0.012%。宫腔镜的应用可改善妊娠率，应为不孕妇女的初始常规检查。子宫声学造影可替代部分宫腔镜检查，只在失败或不能诊断时再作宫腔镜。子宫内膜去除术已涉足子宫内膜癌前和早期子宫内膜癌的治疗。子宫内膜切除术后妊娠发生率 2.39%，其诊断有赖于医患双方的警惕性。宫腔镜的严重并发症已罕见，如严加预防可能避免。近些年来研发的一些非宫腔镜子宫内膜去除术，为去除子宫内膜提供了简单、快速和更成功的的方法，
结论： 腹腔镜、宫腔镜是安全，和有效的评价和诊治妇科疾病的方法。

S8-1
BASIC RESEARCH ON ENDOMETRIOSIS IN CHINA
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Objective: The purpose of our study was to determine the roles of ICAM-1, E-cadeherein, MMPs, VEGF and TSP-1 in the development of endometriosis.
Materials and methods: The endometriosis patients were compared with randomly selected control women with respect to serum ICAM-1 level and E-cadeherein level. We also examined MMP-9, TIMP-1, VEGF and TSP-1 mRNA expression in different endometriosis lesions and that in endometrium of control women.
Results: Both the serum ICAM-1 level and serum E-cadeherein level in endometriosis patients are higher than those of control women. The expression intensity of MMP-9 mRNA in endometriosis lesions is greater than that of normal endometrium; on the contrary, the intensity of TIMP-1 mRNA in endometriosis lesions is less than that of control. There is no significant difference between endometriosis patients and the control group with respect to the positive rate of VEGF mRNA expression, but the expression intensity of the former is much higher than that of the latter. Both the positive rate of TSP-1 mRNA expression and its intensity in endometriosis patients are lower than those of the control group.
Conclusions: Our data supported the 'AAA' model and the three phases in the pathogenesis of endometriosis. In attachment phase, the destruction of cadeherein molecule may result in the separation of homogeneous cells, and ICAM-1 is an important attachment molecule. MMPs are of the most importance in the process of aggression. VEGF and TSP-1 play an important role in the phase of angiogenesis. However, endometriosis is still a bewildering disease, and the future task is to determine the number and location of genes responsible for endometriosis.

子宫内膜异位症发病的“在位内膜决定论”
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郎景和

作为内异症发病主导理论的 Sampson 经血逆流种植学说的重要缺憾是无法解释 80%-90%的妇女有经血逆流现象，但仅有 10%-15%的妇女罹患内异症。因此，模型建立、临床循证和科学解释，甚至修正完善这一学说对真正认识内异症发生以及有效防治是非常重要的。
从病理生理学而言，经血逆流之，内膜细胞种植要具备四个条件，即：①子宫内膜细胞必须通过输卵管进入腹腔；②经血碎片中的细胞必须是活的；③细胞必须有能力种植到盆腔器官组织上；④内异症在盆腔的分布解剖必须与脱落细胞的种植原理一致。所以，脱落的内膜 细胞须突破盆腹腔的 3 道防线：❶腹水或腹腔液；❷腹腔细胞，主要是巨噬细胞和自然杀伤细胞（NKC）；❸腹腔细胞外基质（ECM）。在这过程中，黏附、侵袭和血管形成是病理过程的 3 个主要步骤，所谓“3A 模式”（Attachment, Aggression, Angiogenesis），以此完成逆流内膜细胞在盆腹腔腹膜、器官和组织的种植、生长，并随激素影响发生出血以及炎性反应、免疫反应等变化，从而形成内异症病变及发生盆腔痛、不育等临床表现。
先前较多的研究基本集中在内异症病变的各种生物学特征、免疫学反应等方面，而发生这些变化的内在因素或始动原因则较少被注意和认识。作者的研究证明子宫在位内膜的生物学特质在内异症发病中起重要，甚至决定作用。研究证实，内异症患者和非内异症妇女的在位内膜之黏附、侵袭和血管形成能力均有明显差异，增强的粘附、侵袭和血管形成能力使其易于发生内异症。作为重要的前列腺素合成限速酶的环氧合酶-2（Cyclooxyenase-2,Cox-2）能增加侵袭性、诱导血管形成，在内异症患者的在位内膜，其表达亦明显增高，使之有助于内膜细胞之黏附与侵袭。RANTES(Regulated on activation normal T cell expressed and secreted，正常 T 淋巴细胞表达和分泌的受激活调节因子)可使单核巨细胞游出，激活，发生免疫异常，发生黏附和血管形成，促成内异症；而内异症在受到 RANTES 之影响，又正反馈地提升 RANTES。这一“链式反应”在

内异症患者的在位内膜表现十分明显。参与雌激素转化的芳香酶 p450 在内异症患者的在位内膜亦呈高表达状态。另一些支持“在位内膜决定作用”的是基因差异、蛋白质组学及猕猴动物研究。用 Fluro-DDPCR 检测内异症患者和正常妇女在位内膜有差异基因表达；蛋白指纹图谱分析，即用表面增强激光解析离子化飞行时间质谱技术（SELDI-TOF-MS），发现有差异蛋白质峰。成功的猕猴动物模型建立不仅说明经血逆流可以导致内异症，更说明在位内膜是决定因素，而免疫反应是继发的，或者免疫应答，或者免疫耐受。局部环境及激素状态是影响因素。在位内膜在发病中的研究有助于建立预防和治疗的新策略，如对在位内膜的干预，或者对内异症的早期和微创诊断。

S10-1

VARIATION AND RECONSIDERATION OF SURGICAL MANAGEMENT IN CERVICAL CANCER –CLINICAL ANALYSIS ON 1342 CASES

Cao Zeyi, Peng Zhilan, Liao Qinping, Chen Chunling, Wang Ping

Objective: To study 33 years experience of surgical treatment of cervical cancer. Clarify the changes of the indication of Radical Hysterectomy during last decades and discussion of improvement of the surgical procedure.

Methods: Retrospect analysis use WCUMS 2nd hospital and BUMC women's hospital 1968~2001 (divided into 3 phases A, B, C) 1342 cases whom had Radical Hysterectomies.

Results: Since 1960s the incidence of cervical cancer becomes younger and younger. The average age was 53 years old in 1960s, and 1990s was 42 years old. The squrmous cancer and the gland cancer were 8:1 in 1960s to 4:1 in 1990s. The younger patients more concern that after treatment to keep their ovarian and vaginal function. In phase C to treat most stage Ⅰb2~Ⅲ cases chemotherapy first than follow to surgical procedure. We found the operation time, hemorragh during operation and the complication after surgery was much better than the phase A. The 5 years survival was increased.

Conclusion: Younger patients of cervical cancers should be chosen surgical treatment first or after chemotherapy and suggested to improve the surgical technique of radical hysterectomy is necessary.

子宫颈癌手术治疗的变迁和思考（附 1342 例临床病理的分析）

曹泽毅 彭芝兰 廖秦平 陈春玲 王平

子宫颈癌是我国妇科恶性肿瘤的常见病，迄今仍为第一位。近 50 年来，我国妇科肿瘤学界对子宫颈癌的诊断，治疗和预防有了巨大的进展。放射治疗和手术治疗子宫颈癌已广泛采用而且取得很好的疗效，特别是子宫颈癌广泛性切除术已经普及到全国各大医院，对早期宫颈癌的治疗起到重要的作用[1, 2, 3]。各地对宫颈癌的手术治疗各有特点，今年国内外在手术技术上也有不少改变和发展[4, 5, 11, 12]，由于华西医科大学附属二院和北京大学妇产儿科医院进行的手术方式步骤相近，在不同阶段的改进也相同。现就华西附二院和北医妇儿医院 1968 年至 2001 年至今手术治疗宫颈癌 1342 例的阶段变迁（改进）和发展，进行综合分析讨论。

目的： 总结分析 30 多年手术治疗宫颈癌的临床经验，明确手术适应症的变化及探讨手术方式的改进。

方法： 从华西医大附二院、北大医院妇儿医院两院 1968~2001 年间分 3 阶段对 1342 例宫颈癌手术治疗患者进行回顾性分析。

结果： 30 年来宫颈癌的发病年龄明显年轻化，由 1960 年代平均 53 岁降到 1990 年代平均 42 岁。病理类型的变化，鳞、腺癌比由 8：1 到 4：1。第 3 阶段对Ⅰb2-Ⅲ患者多用化疗后手术，并不增加手术危险。对比各阶段手术时间缩短（P<0.005）；出血减少（P<0.005）；手术合并症减少。5 年存活率有所提高。

结论： 年轻患者应首选手术治疗或化疗后手术，并需进一步改进手术操作技术。

S10-2

MANAGEMENT OF CERVICAL CARCINOMA

Dr. Bernd-Uwe Sevin

This presentation will discuss current concepts in the surgical treatment of cervical cancer.

Emphasis will be placed on the rationale and recommendation for conservative versus radical surgeries. A detailed multivariate survival tree analysis (Segal/Block) of prognostic risk factors such as cell type, depth of invasion, lymph-vascular space invasion and lymph node metastases will be discussed.

Indications for fertility maintaining conservative treatment will be discussed as well.

For patients treated with radical hysterectomy, who are at risk for recurrent disease, postoperative radiation and chemotherapy will be addressed.

For patients with more advanced disease, the data that led to the current standard of chemo-radiation will be presented. Controversies in the management of stage I B2 cancers will be discussed as well.

S10-3

THE ROLES OF CYTOLOGY, HR-HPV TEST AND COLPOSCOPY/PATHOLOGY IN THE SREENING OF CERVICAL LESION

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Cervical Cancer is the second high incidence disease in the gynecological cancers in the world. About 100,000 new cases are diagnosed in China annually, which are the 1/5 of the world.

Objective: This study was performed to systematic investigate the roles of the cytology, HR-HPV test and colposcopy/pathology in the screening for the patients with cervical lesion.

Methods: From Oct.2003 to Dec.2004, the patients in the Gynecological Department of Peking University People's Hospital were enrolled in this study. Diagnosed by Liquid-based Cytology test, 1436 cases with abnormal cytology were also performed a HR-HPV test by Hybrid Capture II. To compare the different methods used in the screening of cervical lesion, the Liquid-based Cytology, HR-HPV test and colposcopy/pathology analysis were performed parallelly in 1476 cases. The average age was 35.6 yrs in this study population.

Results: 1436 cases with abnormal cytology included 939(65.4%) cases with ASC, 389(27.1%) cases with LSIL

and 108(7.5%) cases with HSIL. The ratios of HR-HPV positive infection among these groups with different cytological diagnosis were 28.6% (269/939), 74.0% (288/389) and 88.0% (95/108), respectively. High ratio of HR-HPV infection was positively associated with the aggravation of cervical lesion (p<0.01). In the 1476 cases, compared with the final pathological diagnosis, the ratio of HR-HPV positive infection were increasing with aggravation of cervical lesion: 36.6% (444/1214) in cervicitis; 84.3%(70/83) in CIN-I; 90.0% (54/60) in CIN-II; 95.8% (69/72) in CIN III and 100% (17/17) in early invasive cancer. In the patients with Cyto(-)/HR-HPV(-) or Cyto(-)/HR-HPV(+), no case was diagnosed with CIN-I or higher than CIN-I by pathology. Moreover, in the patients with Cyto(+)/HR-HPV(-), 22 cases (3.1%, 22/714) were diagnosed with ≥ CIN-I (including CIN-I 13,CIN-II 6,CIN-III 3). However, in the patients with Cyto(+)/HR-HPV(+), 210 cases (35.6%, 210/590) were diagnosed with ≥ CIN-I (including CIN-I 70,CIN-II 54,CIN-III 69 and early invasive cancer 17). In the patients with abnormal cytology, compared with the HR-HPV negative group, the HR-HPV positive group is significantly associated with the CIN (p<0.001).

Conclusion: Combined analysis of Cytology, HR-HPV test and colposcopy provide very helpful information for the screening of cervical lesion. HR-HPV analysis significantly improved the diagnostic accuracy of cervical lesion in the patients with abnormal cytology.

细胞学、高危型人乳头瘤病毒、阴道镜及病理学检查在宫颈病变筛查中的意义

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宫颈癌在全球居女性恶性肿瘤居第二位。在中国每年约有10万新发病例，占世界发病率五分之一。做为宫颈癌高发国家，中国妇产科医师面临艰巨的任务。

目的：本研究应用超薄液基细胞学、高危型HPV-HC2检测、阴道镜及并病理学检查，对在医院就诊患者进行宫颈病变的早期筛查，探讨以上方法筛查宫颈病变的临床意义。

方法：对2003年10月到2004年12月间，在北京大学人民医院妇科就诊的1436例细胞学异常患者进行了高危型HPV检测。对1476例就诊患者进行了超薄液基细胞检查、高危型HPV HC2检测，阴道镜及病理学检查。以上患者平均年龄35.6岁。

结果：(1) 1436例细胞学异常者中，细胞学为ASCUS 939/1436例(65..4%)，LSIL 389/1436例(27.1%)，HILG 108/1436例(7.5%)；高危型HPV检测结果显示随着宫颈细胞学级别的升高，HPV阳性率也升高，组间相比$P<0.01$。(2)对1476例患者全部进行了超薄液基细胞学、高危型HPV-HC2检测、阴道镜及并病理学检查显示，高危型HPV随宫颈病变加重，阳性率升高：宫颈炎36.6%(444/1214)；CIN-I 84.3%(70/83)；CIN-II 90.0% (54/60)；CIN III 95.8% (69/72)；早期浸润癌100% (17/17)。在细胞学正常/HPV阴性者108例中，或细胞学正常/HPV阳性者64例中均未发现宫颈病变；在细胞学ASCUS以上/HPV阴性者发现宫颈病变22/714例(3.1%)，包括CIN-I 13例,CIN-II 6例,CIN-III 3例；在细胞学ASCUS以上/HPV阳性者发现宫颈病变210/590例(35.6%)，包括CIN-I 70例,CIN-II 54例,CIN-III 69例，早期浸润癌17例；后两者相比有显著差异(p<0.001)。

结论：在进行宫颈病变的早期筛查中，联合进行细胞学、高危型HPV-HC2检测、阴道镜及病理学检查非常有意义，尤其对细胞学异常及HPV阳性者应重点筛查。

SII-1

FUTURE DIRECTIONS IN OVARIAN CANCER: NEW AGENTS, SCREENING AND PREVENTION

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There has been little overall improvement in survival for patients with ovarian cancer despite the development of more effective chemotherapy regimens. Current therapy consists of six cycles of paclitaxel plus carboplatin. Based on the high activity of new two- and three-drug combinations, a series of prospective randomized trials are in progress to evaluate whether three-drug combinations, such as gemcitabine plus carboplatin plus paclitaxel or encapsulated doxorubicin plus carboplatin plus paclitaxel, can improve survival compared to treatment with the standard two-drug combination. At present, there is no evidence that any combination is superior to the two-drug combination of carboplatin plus paclitaxel. A series of novel cytotoxic agents are being studied in ovarian cancer, including TLK286, yondelis, pemetrexed, and epothilones. In addition, new molecular-targeted therapies are being evaluated in ovarian cancer. Inhibitors of epidermal growth factor receptor (EGFR) have been shown to have activity in ovarian cancer with erlotinib producing an 8% response rate. Phase II trials of the monoclonal antibody cetuximab are currently in progress. Bevacizumab is a monoclonal antibody targeting vascular epithelial growth factor (VEGF). In a Gynecologic Oncology Group (GOG) trial, bevacizumab was shown to produce responses in 17% of patients with recurrent ovarian cancer. Currently, the GOG is performing a trial of bevacizumab in combination with paclitaxel and carboplatin in patients with previously untreated advanced ovarian cancer. Other biological agents, such as rituximab and endostaurin, are also undergoing clinical evaluation in ovarian cancer. Numerous screening strategies are also being studied in an effort to identify women with earlier stage disease when it is much more curable. Multiple novel biomarkers as well as proteomic assays are being evaluated based on encouraging preliminary results. At this point, no screening test has been shown to impact upon morbidity and mortality from this disease. Prevention studies are focused on using hormones, COX-2 inhibitors, and fenretinide. Clinical studies of fenretinide are still in progress by the GOG. Molecular studies are in progress to better identify high-risk individuals who may be candidates for additional prevention studies.

SII-2

A NOVEL TARGETING THERAPY FOR OVARIAN CANCER THROUGH LUTEINIZING HORMONE RECEPTOR (LHR) USING A HECATE-CHORIONIC GONADOTROPIN (CG)-β CONJUGATE

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Objectives: The development of targeted antitumor drug delivery systems based on certain carrier molecules and their specific binding sites in tumor tissues has a great potential for cancer treatment. Based on such an approach, Lytic peptide Hecate, a fusion protein of a 23–amino acid and a 15–amino acid (81-95) fragment of the human CGβ chain were conjugated in order to form a novel anticancer drug which could induce selectively the destruction of ovarian cancer cells expressing LHR *in vitro* and *in vivo*.
Materials and Methods: We analyzed the molecular mechanisms underlying the cell death induced Hecate–CGβ conjugate, its antitumoral efficacy and the endocrine consequences in a transgenic (TG) mouse model bearing the inhibin α-subunit promoter (inhα)/Simian Virus 40 T-antigen (Tag), that develops LHR expressing granulosa cell tumors with 100% incidence. Wild-type control littermates and TG mice presenting with gonadal tumors, and, were treated either with Hecate or Hecate-CGβ conjugate.
Results: We found that the evaluation of inhibition potential of the Hecate-CGβ conjugate to LHR and also that the Hecate-CGβ conjugate selectively and in a dose-dependent manner kills cells possessing LHR in lower concentrations compared to the Hecate alone and that the cytotoxic effect strongly correlates with the number of LHR. The hecate conjugate drug showed to be highly effective for treatment of human ovarian epitheliam carcinoma cell xenografts and also *in vitro*. Hecate-CGβ conjugate treatment was effective in reducing significantly the testicular and ovarian tumor burden (tumor volume/body weight), whereas no change in ovarian, but concomitant increase in testicular volumes was observed during Hecate treatment. Increase in serum LH and a drop in progesterone (produced by the tumors), in Hecate-CGβ conjugate treated mice, in comparison with TG sham and Hecate treated groups, emphasized the positive treatment results. A rapid and cell-specific membrane permeabilization of LHR expressing cells *in vitro* after the Hecate-CGβ conjugate treatment suggested a necrotic mode of cell death, without activation of apoptosis, as determined by flow cytometry, caspase-3 activation, and by the pan-caspase inhibitor Z-VAD treatment.
Conclusions: Hecate-CGβ conjugate provides a novel specific lead into ovarian cancer therapy by targeted destruction of LHR expressing tumor cells.

S12-1

LARGEST REPORTED FALLOPIAN TUBE CYSTADENOFIBROMA: A CASE REPORT AND ANALYSIS OF THE PUBLISHED ARTICLES

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Aim and Objectives: To report the largest fallopian tube cystadenofibroma and review the literature.
Background: Primary tumours of the fallopian tube, both benign and malignant, are extremely uncommon. The majority of benign tubal tumours are little more than interesting pathologic curiosities and generally incidental findings at the time of pelvic surgery. Nonetheless, some have important clinical significance.
Materials and Methods: We report a case of papillary cystadenofibroma of fallopian tube in early pregnancy, in a 21year old patient presented to us initially with threatened miscarriage. Ultrasound revealed large right adnexal multicystic mass of 7x10x6cm size. She underwent emergency laparotomy and right salpingectomy.
Results: Histology revealed this as benign papillary cystadenofibroma of fallopian tube.
Summary / Conclusion: To the best of our knowledge, this is the largest cystadenofibroma of the fallopian tube published in the literature and it weighed 300.

S12-2

DIAGNOSIS OF OVARIAN CANCER USING DIFFERENTIALLY EXPRESSED PROTEIN PATTERN IN SERUM

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Objective: To develop a diagnostic model of ovarian caner with analyzing differentially expressed protein in serum and evaluate its clinical significance.
Methods: 64 cases of patients with ovarian cancer, 61 cases of age-matched controls were tested by SELDI-TOF-MS and WCX2 ProteinChip technology, and set up a primary diagnosis model of ovarian cancer by Biomarker Wizard and Biomarker Patterns Software. This model was further valuated by blind test. Meanwhile, the serum levels of CA_{125} were detected in the same samples and the differences of these two methods were compared with.
Results: 4 protein peaks(6195、6311、6366 and 11 498 m/z)were significantly different between ovarian caner and controls, the diagnostic sensitivity, specificity and positive predictive value were 89.3% (25/28), 90% (18/20) and 92.6%(6 samples with early stage were all distinguished correctly), compared with 60.7% (11/28), 40.0% (8/20) and 58.6% respectively for CA_{125} for the same samples (3 of 6 samples with early stage were successfully distinguished). The diagnostic values of these 2 methods were significantly different ($P < 0.05$).
Conclusion: High sensitivity and specificity achieved by this diagnostic pattern showed great potential for early diagnosis of ovarian cancer.
Keywords: Ovarian cancer; Surface enhanced laser desorption/ionization time-of-flight mass spectrometry; Diagnosis; Proteomics

卵巢癌患者血清差异表达蛋白诊断模型的研究

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目的：通过分析卵巢癌血清蛋白表达谱的变化建立差异表达蛋白诊断模型，初步探讨其临床应用价值。
方法：应用表面增强激光解吸电离飞行时间质谱(SELDI-TOF-MS)及其配套蛋白质芯片，检测64例卵巢癌患者和61例年龄匹配的对照组血清，获得其蛋白指纹图谱，应用Biomarker Wizard和Biomarker Patterns软件分析卵巢癌差异蛋白并建立诊断模型。通过盲法分析进一步验证该诊断模型。同时对相同标本进行CA_{125}检测，并对两种诊断方法进行比较。
结果：卵巢癌和对照组血清蛋白质在质荷比(m/z)为6 195、6 311 、6 366和11 498等4处有显著差异。应用该4个差异表达蛋白构建的诊断模型，其盲法预测的敏感性、特

异性、阳性预测值分别为 89.3%（25/28）、90%（18/20）、92.6%，其中 6 例Ⅰ期样本全部预测正确；相对应的 CA_{125} 检测值分别为 60.7%（17/28）、40.0%（8/20）、58.6%，其中 6 例Ⅰ期样本有 3 例预测正确。两种方法敏感性、特异性的差异均有统计学意义（P<0.05）。

结论：该方法敏感性和特异性高，有望应用于卵巢癌的早期诊断。

S12-3

DIFFERENTIAL EXPRESSION OF ALTERNATIVELY SPLICED OF HLA-G ISOFORMS IN OVARIAN CANCER

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Aims: It has recently been reported that HLA-G involved in cancer immune escape, however, it is not known which of the membrane bound (HLA-G 1-4) and soluble (HLA-G 5-6) alternatively spliced forms play the key role in the development of ovarian cancer. So we investigated the mRNA expression of the 6 HLA-G mRNA isoforms in ovarian cancer tissues and normal ovaries.

Methods: The mRNA Levels of HLA-G isoforms were detected in 18 of normal ovary and 70 of ovarian cancer, among which 44 were primary and 16 were recurrent ovarian cancer. Semiquantitative RT-PCR method was used and the expression level was also analyzed by SPSS with the clinical pathological results.

Results: The total isoforms of HLA-G were increased in recurrent ovarian cancer. We found that all the ovarian cancer tissues and the normal ovaries have HLA-G mRNA expression. The HLA-G isoforms expressed differently in both normal ovaries and ovarian cancer. The mRNA of the total HLA-G isoforms in the tissues of normal ovary, primary ovarian cancer and recurrent ovarian cancer were as follows: G0: 11.49±7.42, 11.13±6.04 and 16.61±8.51, respectively. The difference was significant between the recurrent tissues and the other two types of normal tissues and primary ovarian cancer. The mRNA of G1-G6 in the normal ovary, primary cancer and recurrent cancer tissues were as following: G1:1.79± 1.12, 3.37±1.64, 4.83±3.05; G2: 6.96±4.51, 7.34±4.62, 7.46±3.82; G3: 8.61±4.55, 9.44±5.75, 10.78±3.81; G4:0.79±0.25, 1.09±0.74, 3.56±3.20; G5:0.43 ±0.54, 0.89±1.47, 1.61±2.14; G6: 6.91±6.10, 6.68±4.45, 8.75±5.46. the difference were significant in G1, G4 and G5, ($p<0.05$). However, the mRNA level was increased in the recurrent ovarian cancer tissues in G1, G4, G5, G6 and the total isoforms G0 ($p<0.01$).

Conclusion: The membrane isoforms of G1, G4 and the soluble isoforms of G5, G6 were most important for developing of primary and recurrent ovarian cancer through elevating their mRNA level. It suggested that overexpression of HLA-G or its specific isoforms may contribute to the immune escape and associated with ovarian cancer and its recurrency.

S13-1

CONTROVERSIES ABOUT PAIN RELIEF FOR LABOR

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Background: Many women want pain relief for labor. However, there is some evidence that pain relief for labor may interfere with the progress of labor. Systemic analgesics, such as inhalation nitrous oxide or parenteral narcotics, provide some, but not complete relief. Parenteral narcotics cross the placenta and may adversely affect the fetus. Regional anesthetic techniques each have specific problems. Pudendal blocks are technically difficult. Paracervical blocks cause fetal bradycardia and pose the risk of inadvertent injection into the fetal head. Epidurals, spinals and the combine spinal-epidural give excellent pain relief but some studies suggest they slow the progress of labor or increase the cesarean section rate.

Hypothesis: Epidurals, spinals or the combined epidural/spinal can provide adequate pain relief without interfering in the progress of labor, if a low dose of anesthetic drugs is used.

Results: Several studies will be presented that show how using a low dose anesthetic technique can provide excellent pain relief for labor and not prolong labor, cause fetal distress or increase the incidence of cesarean section. Several studies suggest that providing pain relief for labor can lower the cesarean section rate and improve maternal satisfaction. One particular technique the "Walking Epidural" will be described in detail. This technique provides excellent anesthesia and does not interfere with the normal painless sensations of labor or the ability to valsalva and push the baby out. With a walking epidural, the women in labor will have complete pain relief but she will feel normal enough that she will be able to walk if she chooses.

S13-3

MEDICAL ABORTION

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With the introduction of the anitprogestin, mifepristone, medical abortion has become a reality. Various studies have shown that the combination of mifepristone with a prostaglandin analogue is an effective method for termination of pregnancy up to 63 days of pregnancy with a complete abortion rate of over 95% in many series. The dose of mifepristone can be reduced to 200 mg without loss of efficacy. The prostaglandin most commonly used now is misoprostol which is orally active, stable at room temperature and cheap. Vaginal administration of misoprostol is more effective than oral administration. There is recent evidence that sublingual administration of misoprostol is as effective as vaginal administration. Comparative studies have shown that the complete abortion rate for surgical abortion is higher than that of medical abortion but the incidence of administration of antibiotics is higher with surgical abortion. Both surgical and medical abortions were well accepted by women especially if it is the method they have chosen. Recent studies have shown that the combination of mifepristone and misoprostol can also be used to terminate pregnancies between 63 to 84 days. In the second trimester, the combination of mifepristone and a prostaglandin analogue is also a very effective method for termination of pregnancy. Mifepristone is more effective than laminaria tent in shortening the induction-abortion interval. Misoprostol has also been shown to be more effective than

gemeprost for termination of pregnancy in the second trimester.

S14-1

SURGICAL MANAGEMENT OF OVARIAN CARCINOMA

Dr. Bernd-Uwe Sevin

This presentation will discuss the current surgical procedures applied in the multi-modal treatment of ovarian cancer, combining surgery and chemotherapy of primary and recurrent disease.

Issues addressed include surgical staging, conservative (fertility maintaining) surgery, tumor debulking as well as interval debulking.

Tumor debulking, (cytoreductive surgery) reducing tumor volumes to minimal residual disease has been shown to be instrumental in improving response to chemotherapy and disease free survival. The concept is rational because primary ovarian cancer has a response rate to current chemotherapy regimen of over 75%. Tumor debulking in advanced ovarian cancer may include radical oophorectomy, omentectomy, bowel resection, splenectomy and therapeutic lymph node dissection.

Surgery for recurrent ovarian carcinoma will be highly individualized and will depend on the length of the disease free interval (DFI) between primary treatment and recurrence. After a DFI of more than 6 – 12 months tumor debulking again is beneficial only if minimal residual

S16-1

Advance of PCOS diagnosis and treatment

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Polycystic ovary syndrome (PCOS) affects 5%~10% of reproductive aged women and is characterized by polycystic ovaries, hyperandrogenism and chronic anovulation. Although the underlying pathophysiology of PCOS remains unknown, attention has centered upon primary defects in the hypothalamic–pituitary axis, ovarian function, and insulin secretion and action. Hyperandrogenemia, LH hypersecretion, insulin resistance, and compensatory hyperinsulinemia are common biochemical features of PCOS.

To explore the parent's phenotypes in the families of the Chinese women with polycystic ovary syndrome (PCOS), we collected the Clinical data by questionnaires from 139 parents of women with PCOS and from 137 parents of controls with normal menses. It was compared for the distribution of mother's irregular menses, father's premature balding and parent's hypertension among parents of the PCOS group and of the controls. A multiple Logistic regression model was applied for more detailed analysis. The result showed that the prevalence of mother's irregular menses, father's premature balding and father's hypertension were significantly higher in PCOS group (38.1%, 19.4% and 30.9%, respectively) than in the controls (3.6%, 5.1% and 16.1%, P<0.01, respectively). The prevalence of mother's hypertension was higher in the PCOS group (23.0%) than in the controls (13.9%), but had no significance (P=0.06). When mother's irregular menses, father's premature balding and father's hypertension were entered the Logistic regression model, all the OR values were still much higher than 1, P<0.005. The partial regression coefficients of the three-predictor variables changed little when they entered the model in turn. The partial regression coefficients for father's age as a possible confounding factor was very small when it entered the model, P>0.05. The differences between maximum –2log likelihoods used to evaluate the role responsible for the incidence of PCOS in their daughters indicated that: mother's irregular menses > father's premature balding > father's hypertension. So in addition to mother's irregular menses and father's premature balding, father's hypertension may be also an independent phenotype in families of Chinese women with PCOS.

To explore the gene differential expression pattern of Chinese polycystic ovary syndrome, we performed microarray analysis of gene expressions of PCOS granulosa cells to identify differentially expressed genes in PCOS patients. Granulosa cells from five PCOS cases and five normal cases were obtained during oocyte retrieval from women undergoing IVF. As compared with normal human ovarian granulosa cell, forty-six genes were screened out, 25 genes were up-regulated, and 21genes were down-regulated in PCOS. These differentially expressed genes are involved in various biologic functions, such as regulation of fatty acid metabolism, cell-cell signal transduction, immune and inflammatory response, reflecting the complexity of clinical manifestations of PCOS. Our analysis revealed that PCOS granulosa cells have a gene expression profile that is distinct from normal granulosa cells. The genes of FABP4 and CD36 are most important among these. Our study will further our understanding of the pathogenesis of PCOS and help us to identify new targets for future studies and for the development of new therapeutic interventions.

For decades there always be disputed about its diagnostic criteria. In 1999, NIH published its criteria: (1) Chronic anovulation, (2) Clinical and/or biochemical signs of hyperandrogenism, and had excluded other aetiologies. (3) Polycystic ovaries. The diagnose should be done in case of the above items coexistence.

Up till the year 2003 the consensus in diagnosis of PCOS was mainly based on a majority opinion rather than on clinical trial evidence by ESHRE/ASRM. The criteria include: (1) Oligo- and/or anovulation, (2) Clinical or biochemical signs of hyperandrogenism, (3) Polycystic ovaries. Exclusion of other aetiologies (eg. Cushing's disease, congenital adrenal hyperplasia, androgen-secreting tumors, exogenous androgen exces). The diagnose should be done if two of three is accordance. PCO is nowadays defined as the presence of 12 or more follicles in each ovary measuring 2–9 mm in diameter, and/or an increased ovarian volume (N10 mL). Follicle distribution seems not of any value as is stromal echogenicity and the subjective appearance of PCO. The measurement of ovarian volume constitutes a good substitute for stromal echogenicity. Only one ovary fitting this definition is sufficient to define PCO.

多囊卵巢综合征的诊断和治疗进展

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多囊卵巢综合征是生育年龄妇女常见的一种复杂的内分泌及代谢异常性疾病，以雄激素过多及长期无排卵为特征。它不仅是慢性无排卵、多毛症和高雄激素血症最常见的原因，也和胰岛素抵抗、高胰岛素血症、糖耐量异常、异常脂血症和II型糖尿病密切相关。过去临床治疗的重点常放在育龄妇女的闭经和不孕上，而近年来，PCOS 患者