

*Basic and Clinical Research on
Collateral Disease Theory*

络病学基础与临床研究

吴以岭 主编



中国科学技术出版社

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前 言

络病理论是中医理论体系的独特组成部分,是研究络病发生发展及其辨证治疗规律的应用理论,络病是广泛存在于多种难治性疾病中的病理状态,络病学是研究络病理论及其应用的临床学科。系统研究络病发病、病机、辨证、治疗,创建络病学学科,对于推动中医学术发展、提高现代多种难治性疾病诊疗水平,具有重要学术价值。由于中医学术发展史上重经轻络、络脉庞大繁杂以及历史条件的限制,络脉及络病理论未受到充分重视和深入研究,亦未形成系统理论体系,历代不少有识之士均疾呼加强络脉及络病研究,清代医家喻嘉言说:“十二经脉,前贤论之详矣,络脉却未之及,亦缺典也”,清代名医叶天士也说:“遍阅医药,未尝说及络病”,“医不知络脉之法,所谓愈究愈穷矣。”可惜的是叶天士所批评的现象在其身后 200 余年并未引起充分重视,络病理论始终未能形成完整的理论体系,亦未发展成独立的络病学学科,因此创新发展络病理论是历史赋予当代中医药工作者的重大课题。

为推动建立络病学学科,我们自 20 世纪 80 年代初开始对络病学说进行了系统研究,并于 2000 年承担了国家中医药管理局课题——络病理论及其应用研究。该课题研究中提出络病研究理论框架——“三维立体网络系统”,从络脉与经脉时空差异性切入研究络脉与络病理论,提出“气络—NEI 网络”与“脉络—血管系统病”新概念,探讨络病发病、病机、辨证及治疗,初步建立“络病证治”,首次在中医学术发展史上形成系统络病理论。运用络病理论指导临床难治性疾病治疗研究,完成国家级及省部级课题 6 项,研制出络病理论指导下治疗心脑血管病、神经肌肉类疾病等系列创新中药。2004 年 11 月,国家中医药管理局组织国内著名医学专家对该课题进行了鉴定,与会专家认为:“该项研究按照中医学术自身发展规律对络病学说进行了全面系统研究,初步建立‘络病证治’体系,首次形成系统络病理论,为络病学学科建立奠定理论基础,属国内外创新性科研成果。”在此基础上出版了系统论述络病理论的专著《络病学》。

近年,由于络病理论研究及其指导难治性疾病治疗取得的显著进展,特别是络病理论代表方通心络胶囊广泛应用于临床取得显著疗效,于 2000 年获得国家科技进步二等奖,引起医学界广泛关注,使络病学成为近年学术界关注的热点和焦点。通心络胶囊对“脉络—血管系统病”共性病理环节作用研究,佐证了络病理论的科学价值。在络病理论研究过程中,形成了包括中医、西医、中西医结合、生物学、物理学等多学科专家在内的专家群体,于 2004 年 12 月成立了国家级二级学会——中华中医药学会络病分会。一年来在学会全体委员共同努力下,各地专家对络病理论进行了深入研究,建立了国内首家省部级络病重点实验室——河北省络病实验室;《络病学》教材也通过国家中医药管理局组织的专家审定,2006 年在高等中医药院校本科班、硕士及博士班开设络病学课程;络病理论及通心络胶囊研究列入国家自然科学基金项目,“络病理论指导血管病变防治的基础研究”列入国家 973 计划项目。

络病学也引起国外医学界的关注。络病理论与通心络胶囊的研究论文参加 2005 年北美心脏病年会及欧洲心脏病年会；美国德克萨斯州心脏病研究中心耿永健教授对络病理论及通心络胶囊进行的实验研究已取得良好结果；美国东卡大学医学院共同申报络病理论及通心络胶囊的美国传统医药基金项目；美国哈佛大学医学院麻省总医院张群豪教授 2004 年开始在美国最早的中医学院开设络病学课程，并于 2005 年筹备络病学小组，成功把络病学尤其是络病理论代表方通心络胶囊纳入哈佛大学医学院医师继续教育课程；通心络胶囊作为药品成功在韩国注册上市，络病理论及通心络胶囊的确切疗效引起韩国医学界的重视。国外专家莅临大会做学术报告必将促进络病学在国外的传播。

“首届国际络病学大会”是络病学在国内外受到广泛关注的背景下召开的一次国际性的络病学术大会。来自国内外学术界的 500 余名专家学者会聚北京，就络病学的基础与临床研究开展广泛的学术交流。与会代表为大会准备的参会论文达 100 余篇，包括络病学理论探讨、实验与临床研究文章，反映了络病学最新的学术研究进展。

我们将论文汇编成书，值此该书即将付梓出版之际，向关心与支持络病分会工作的国家中医药管理局、中华中医药学会领导，向在百忙之中亲自审阅本书的王永炎院士，向为本书题词的著名医学专家路志正教授、颜德馨教授、陈灏珠院士、陈可冀院士，向所有致力于络病学研究的国内外专家学者表示衷心的感谢！

吴以岭

2005 - 10 - 14

PREFACE

The collateral disease theory (CDT) is a particular component part of the traditional Chinese medicine system, which is the application theory for studying the occurrence, development and treatment of collateral disease that is a kind of pathological state presenting among many refractory diseases. The collateral subject is a clinical subject engaged in the study and application of the collateral disease theory, including a systematic research about the occurrence, pathogenesis, differentiation of syndromes and treatment of collateral disease. Therefore, the establishment of the subject of collateral disease will be of important academic value in promoting the academic development of the traditional Chinese medicine and enhancing the diagnostic and therapeutic levels for many modern refractory diseases.

In the academic development history of traditional Chinese medicine, the collateral and collateral diseases theory were not paid much attention to, and were not studied deeply so as to be not formed into a systematic theory because of the huge scale of the collateral system, limitation of historical conditions and the viewpoint of taking meridian seriously while looking down on collateral. In the past dynasties many men of insight appealed for paying much attention to the study of collateral and collateral diseases. YU Jiayan, a famous medical expert of Qing dynasty, remarked: "the twelve meridians and vessels had been carefully studied by ancient scholars of virtue and capability and there were lots of publications about it, however, the study of collateral was not carried out and there were few books and record about it". YE Tianshi, another outstanding medical expert of Qing dynasty, once said: "I had read through all the medical books and didn't find out any statement about collateral disease", and "if we didn't know how to cure collateral disease, the more we searched for other ways of treatment the more we would be confused". It's regrettable that about 200 years after YE Tianshi passed away the phenomenon that he criticized hasn't been paid much attention to yet, and the collateral disease theory hasn't been developed into complete theoretical system and is still far away from an independent subject of collateral disease. Therefore, it's a challenging historical mission for the contemporary herbalist doctors to bring innovation and development to the collateral disease theory.

In order to accelerate the process of establishing the subject of collateral disease, we have been carrying on a consistent study about collateral diseases since 1980's. In the year 2000, we undertook the subject-The study of collateral disease theory and its application-from the State Administration of Traditional Chinese Medicine (SATCM). In the study, a theoretical frame was brought forward-three dimensional stereoscopic network system. According to time-space difference between collateral and meridian, the collateral disease theory has been studied, and the new concept of "qi collateral-NEJ net" and "collateral-vascular system diseases" is proposed to investigate the occurrence, pathogenesis, differentiation of syndromes and treatment of the collateral disease, as a result, "collateral diseases are treated based on differentiation of syndromes" is established initially and the systematic collateral disease theory is formed for the first time in academic development history of traditional Chinese medicine. Through applying the collateral disease theory to direct the treatment study on refractory diseases, we have completed 6 academic research subjects of national and provincial scale and have developed new traditional Chinese medicines for treating cardiovascular disease and neuromuscular disease. In November 2004, the SATCM invited a group of famous medical experts to give an evaluation to the research subject of "The study of CDT and its application". All the experts agreed that according to the development rule of traditional Chinese medicine this study has covered a completely systematic research of the CDT, and the initial stage of "treatment of collateral disease based on differentiation of syndromes" has been successfully established. They all agreed that a systematic CDT has been formed for the first time, which has laid the foundation for establishing the collateral disease subject. Therefore, the study is a remarkable scientific research achievement in the field of medicine. Afterward, the monograph to expound CDT

systematically, 《*Collateral Disease Theory*》 was published.

In recent years, the CDT has been developing rapidly and the application of the CDT has achieved an outstanding progress on treating refractory diseases—especially the therapeutic effect of the Tongxinluo capsule (TXLC). As a representation of the CDT, the TXLC has been widely used in clinical treatment and got the National Scientific Progress Award of Second-Class in 2000. Therefore, which has drawn a broad attention in the field of medicine and the CDT has become a upsurge and focus in the academic field. The study of the effect of TXLC on the generality pathological link of “collateral-vascular system diseases” identified assistantly the scientific value of CDT. The experts from many fields have participated in the study of CDT including traditional Chinese medicine, western medicine, the integrated traditional and western medicine, biology and physics etc. In December 2004, a national second-class medical association was established—The Collateral Disease Branch of the China Association of traditional Medicine (CATM). In the last one year under the joint efforts of the whole committee members of the branch, the experts from different districts have studied CDT deeply and established the first provincial and ministerial class collateral disease key laboratory—Hebei Provincial Collateral Disease Laboratory. The teaching material of 《*Collateral Disease Theory*》 has been revised by the experts organized by SATCM. In 2006, 《*Collateral Disease Theory*》 will be taught as a subject to undergraduate and graduate students including doctoral students in medical colleges. The CDT and the study about TXLC have been placed on the project of National Nature Science Fund and “basic study on the prevention and treatment of vascular diseases according to CDT” has been placed on National 973 Planning Project.

CDT has drawn much attention of many medical associations from abroad. The research papers of the CDT and the TXLC were discussed by experts in the 2005 Annual Scientific Session of American College of Cardiology (ACC) and 2005 Annual Congress of European Society of Cardiology (ESC). Professor GENG Yongjian who works at the Heart Disease Center of Texas has got some good research result on the experiment of the CDT and the TXLC. Now we are applying for the Fund of American Traditional Medicine for the CDT and the TXLC with the Medical School of East Carolina University together. ZHANG Qunhao, professor of Harvard University, began to teach course of collateral disease in the earliest Traditional Chinese Medicine College in America in 2004 and he introduced the CDT, especially the TXLC, as a course to the continuing medical education in the Medical College of Harvard University. Furthermore, the TXLC has been registered as a routine medicine in Korea. The definite therapeutic effect of TXLC has brought to Korea medical field's attention. In the conference these academic reports made by the experts coming from abroad must promote the propagation of CDT in abroad.

Under widespread attention in home and abroad, the First International CDT Conference will be held in Beijing. More than 500 medical experts from China, America and Korea will attend this conference and they will have an extensive communication about CDT and its clinical application. These experts have prepared about 100 research papers including theoretical investigation about CDT, experimental and clinical research which reflected the latest development and achievement of CDT.

Now we have compiled these papers into a book. Before the publication of this book, we wish to convey our hearty thanks to the leaders of SATCM and CATM for their concern and support, to Academician WANG Yongyan who checked and approved this book personally during his busy work, to the famous medical experts, Professor LU Zhizheng, YAN Dexin and Academician CHEN Haozhu, CHEN Keji, to all the medical experts from home and abroad for their great contributions to the study of CDT.

通心络抑制 IL-1 β 介导的小型家猪冠状动脉痉挛的作用及机制

(正文见 100 页)

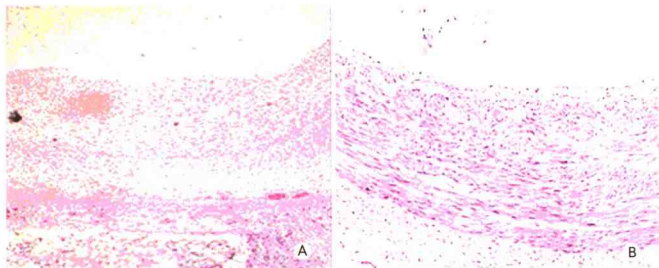


图2 2组手术处理血管段病理改变($\times 10$)

对照组(A)明显内膜增生,单核细胞浸润,平滑肌内膜下迁移,通心络组(B)轻度内膜增生,较对照组明显减轻

通心络胶囊对局灶性脑缺血大鼠半暗区 GAP-43 和突触素表达的影响

(正文见 119 页)

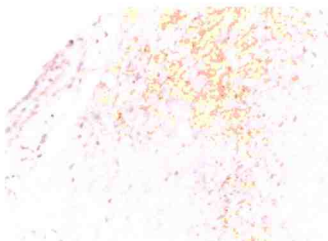


图1 1W时自然恢复组 GAP-43 的表达(SABC $\times 200$)



图2 1W时通心络组 GAP-43 的表达(SABC $\times 200$)

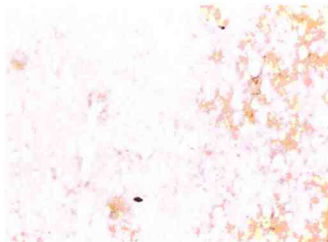


图3 2W时自然恢复组 Syn 的表达(SABC $\times 200$)

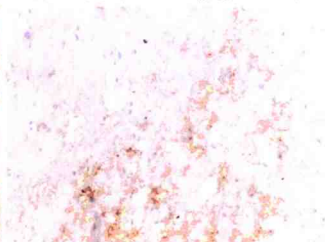


图4 2W时通心络组 Syn 的表达(SABC $\times 200$)

通心络超微粉对大鼠脑缺血再灌注后血脑屏障损伤的保护和S100B蛋白血清水平的影响

(正文见 105 页)

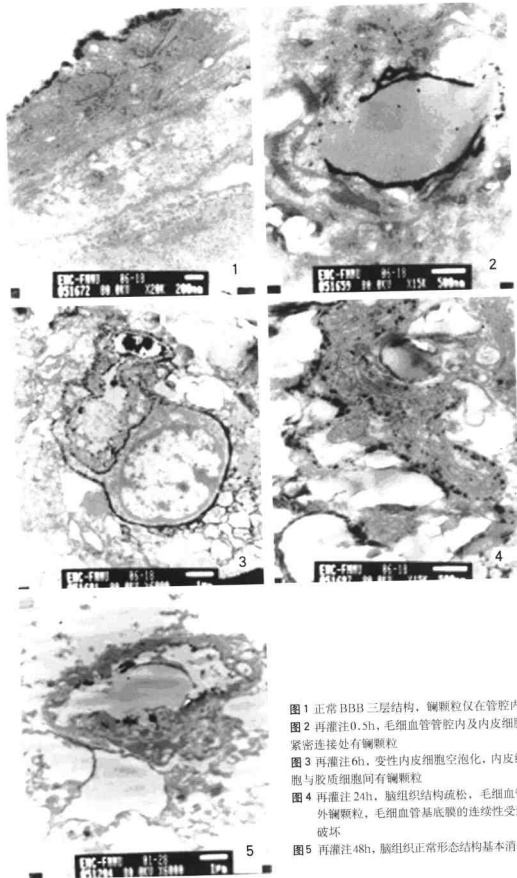


图1 正常BBB三层结构, 髓颗粒仅在管腔内
图2 再灌注0.5h, 毛细血管管腔内及内皮细胞紧密连接处有髓颗粒
图3 再灌注6h, 变性内皮细胞空泡化, 内皮细胞与胶质细胞间有髓颗粒
图4 再灌注24h, 脑组织结构疏松, 毛细血管外髓颗粒, 毛细血管基底膜的连续性受到破坏
图5 再灌注48h, 脑组织正常形态结构基本消失

通心络胶囊对脑梗死大鼠脑皮质血管新生和皮层神经元凋亡的影响

(正文见115页)

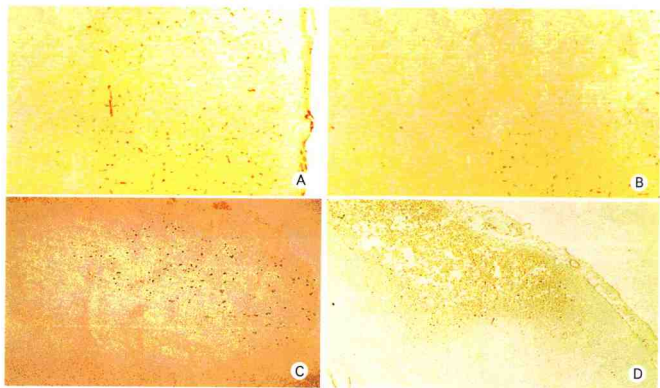


图 2 组缺血后缺血皮质VEGF因子、VEGF 阳性细胞表达

A为通心络组缺血大鼠缺血侧皮质VEGF染色,B为对照组VEGF染色,通心络治疗组VEGF因子阳性表达增加,C通心络组大鼠缺血皮质VEGF表达,D为对照组皮质VEGF表达,可见通心络组VEGF阳性细胞明显增多

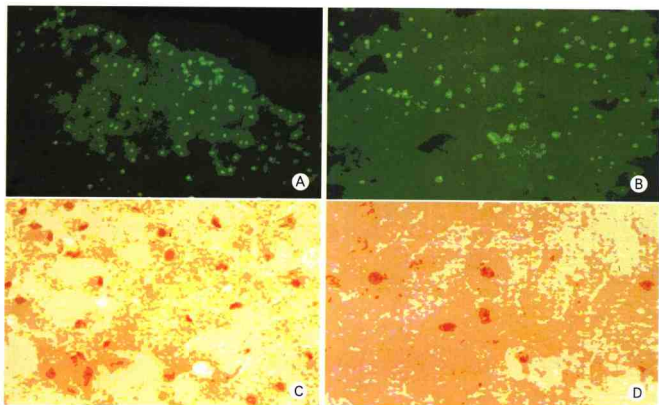


图 3 脑缺血后缺血皮质 TUNEL 阳性神经元

A为对照组,B为通心络组,可见通心络组TUNEL阳性细胞明显减少,C为对照组缺血皮层caspase-3,D为通心络组缺血皮层,可见caspase-3阳性细胞计数明显减少

络方剂对STZ诱导的糖尿病大鼠模型肾脏作用的形态学观察

(正文见137页)

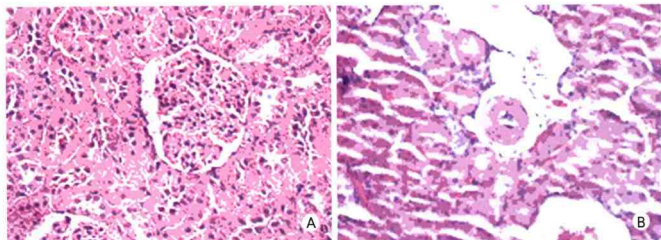


图1 3组肾脏组织HE染色病理变化

A 正常对照组, B 糖尿病组, C 络方剂组

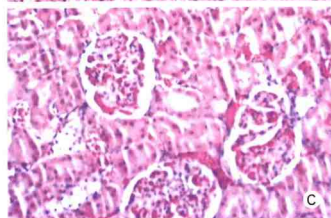


图2 3组肾皮质透射电镜观察变化

A 正常对照组肾小球, 肾小球毛细血管内皮细胞呈扁平状, 核小浓染, 基底膜均匀一致, 足细胞核大可见较深褶皺, 足突紧凑, 分布一致。
B 糖尿病组肾小球, 肾小球基底膜弥漫性均匀增厚, 系膜区电子致密物沉积, 基质明显增多。
C 络方剂组肾小球, 肾小球基底膜无增厚, 系膜区无基质增生, 其超微结构接近正常