

*Basic and Clinical Research on
Collateral Disease Theory (4)*

络病学基础与临床研究(4)

吴以岭 主编

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·北京·

内容提要

随着中医络病理论及通络药物的研究日趋深入与广泛,引起了国内外医学界的关注。为了交流络病理论的研究成果,2005年始中国中医药学会每年召开一次国际络病学大会。《络病学基础与临床研究(4)》作为第四届国际络病学大会的论文集,汇集论文148余篇,内容涉及“973计划”项目研究、理论研究、实验研究、临床研究和络病学教育等。论文充分显示了络病理论及其应用研究的学术进展,为从事络病理论、临床研究和络病学教学的广大医药工作者提供了丰富的信息。

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前 言

又值金秋时节,第四届国际络病学大会即将在“十朝都会”南京隆重召开,来自美国、中国大陆与台湾、香港、澳门等地专家 700 余人会聚一堂,回顾络病学研究历程,交流学术成果,畅想发展蓝图,必将成为向国内外专家学者展示络病理论、基础与临床研究最新成果的国际盛会。

在国内外致力于络病理论及其应用研究的专家学者共同努力下,络病学学科建设取得重要进展。2008 年 5 月由王永炎院士为组长、张伯礼院士为副组长的专家组认为:“吴以岭教授主持的‘络病理论及其应用研究’系统构建络病理论,初步形成‘络病证治’体系;络病理论指导临床心脑血管病等难治病明显提高了疗效,显示出其重要的临床指导价值;形成络病研究的专家队伍;《络病学》教材作为新世纪高等中医药院校创新教材在全国 20 余家高校开课受到好评,提高临床辨证能力起到积极作用;建立河北省络病重点实验室;取得一批国家省部级重大成果。通过上述工作,为络病学学科建立奠定了坚实基础,具备建立新学科的基本要素,同意推荐“络病学”为中医临床基础学科。”国家中医药管理局根据上述论证意见同意建立“络病学”中医新学科。络病学学科建立是国内外致力于络病研究专家共同努力的结果,回顾过去的 20 多年,络病理论由散在的只言片语记载到形成系统的理论体系,由经验方的应用到疗效确切的现代中药制剂广行于世,由单枪匹马式研究向多学科专家群策群力集体攻关。络脉、络病及通络治法相关的文献由 1988 年的 360 余篇上升到 2007 年的 2690 余篇,成为近年医学界研究的热点,显示了络病学研究近年蓬勃发展之势,对络病学科建立起到了重要推动作用。

围绕络病学学科分支——脉络病研究不断深入,国家 973 计划项目——脉络理论指导血管病变防治的基础研究,经过项目组合力攻关,已顺利通过科技部 973 项目中期评估。该研究以“源于临床、基础研究、指导临床”为指导思想,完成 3469 例血管病变患者临床流行病学调查,以基于熵的复杂系统分析方法建立定性定量、整体与局部相结合的脉络病辨证诊断标准,为建立脉络病动物模型深入开展病理生理学机制研究奠定基础。基于临床流调结果提出“营卫承制调平”假说指导项目开展,建立脉络病病理、证候及病证复合模型,从络气失调引起的络气郁滞和络气虚滞切入探讨血管病变病机演变规律,不同于既往从血瘀、痰浊切入的研究,揭示了络气失调通过全身性神经内分泌免疫网络调节功能紊乱影响血管局部病理损伤,通心络干预血管病变局部病理损伤与西药疗效相当,改善全身性神经内分泌免疫网络功能则明显优于西药。

973 计划项目中开展的通络干预“微血管损伤”为共性机制的三大临床疾病取得显著进展,通心络干预急性心肌梗死介入治疗缺血区微血管及心肌损伤方面取得优于权威西药的突破性进展;由北京阜外医院为组长单位正在开展通心络对急性心肌梗死无再流防治的循证医

学研究,为通心络对急性心肌梗死再灌注治疗后心肌无再流发生率、无再流面积以及心室重构和心脏功能近远期变化的影响提供临床证据;提出脑梗缺血区微血管保护——脑梗死治疗新靶点,证实通心络可保护缺血区微血管结构和功能完整性、减少再灌注损伤、促进治疗性血管的新生、建立有效侧支循环发挥对缺血区微血管保护的作用,对急性脑梗死治疗具有重要临床价值;在通络干预糖尿病并发心肌、肾脏、神经、视网膜病变微血管保护方面取得显著疗效,开辟了这类难治性疾病临床治疗新途径。

应用络病理论指导心律失常治疗研究,指出心之气络络虚不荣与心脏传导系统、心肌细胞自律性及自主神经功能失常相关性,以“荣养气络”药研制的参松养心胶囊获2007年中华中医药学会科学技术一等奖。实验研究证实参松养心胶囊对心室肌细胞钠、钙通道和多种钾通道具有明显阻滞作用,使其既能广谱抗心律失常,又能避免心律失常副作用,为治疗快速性心律失常提供了实验依据。同时又能增强心脏起搏电流,改善窦房结恢复时间、房室传导时间,起到治疗缓慢性心律失常作用,显示其整合调节干预心律失常的独特优势。由南京医科大学第一附属医院、北京阜外医院、北京朝阳医院为组长单位,国内36家医院参与的参松养心抗心律失常循证医学研究已全部结束,研究结果表明参松养心胶囊治疗非器质性早搏优于安慰剂,治疗器质性早搏优于西药慢心律;对病窦、慢快综合征、房室传导阻滞等缓慢性心律失常疗效确切,填补缓慢性心律失常西药治疗空白;治疗房颤与西药心律平相当,安全性优于心律平。参松养心胶囊是目前唯一一个经循证医学验证疗效确切的抗心律失常中成药,其快慢均治的整合调节作用对提高目前心律失常药物治疗水平具有独特优势。

络病学研究专家队伍建设和高层次人才培养工作也取得显著成效,继中华中医药学会络病分会建立起160多名多学科专家群体,北京、上海、广东、江苏、吉林等多省市相继建立省级络病专业委员会,推动了全国范围内络病学术研究高层次专家队伍建设。召开第三届络病学教学研讨会,加强络病学教学工作和师资培养,教学院校与选修人数持续增加,使络病学教学与本科、硕士、博士等高层次中医药人才培养密切结合。

络病学国际合作与交流取得重要进展,《络病学》英文版正式出版,正与美国、荷兰、澳大利亚协商开课事宜。与美国贝勒医学院王兴利教授合作的国际科技合作项目——通心络对心血管系统的保护作用及分子机制研究,揭示了通心络通过AMPK信号通路介导的硫氧还蛋白抗氧化系统激活,减少软脂酸引起的内皮细胞凋亡的分子机制,研究结果已发表于SCI收录杂志。与美国杰克逊实验室合作的另一国际科技合作项目——肌萎灵冻干粉对肌萎缩侧索硬化转基因小鼠作用研究,显示气络理论指导研制的肌萎灵冻干粉延长转基因小鼠存活时间与力如太相当,延缓瘫痪症状出现时间明显优于力如太,该项目深入进展对于络病学分支——气络理论发展具有重要推动作用。

本次国际络病学大会收到论文集148篇,反映了最近一年来络病理论研究、基础研究、临床研究、教学研究等诸多方面的最新进展,对于了解络病学科发展情况具有重要参考价值。经过专家审议,我们将参会论文汇编为《络病学基础与临床研究(4)》,希望能为络病理论深入研

究提供启迪与思路。值此会议召开之际,我们向关心和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,向多年来一直支持络病学研究的邓铁涛教授、颜德馨教授、路志正教授、朱良春教授、陈灏珠院士、王永炎院士、陈可冀院士、高润霖院士、李连达院士、张伯礼院士等表示衷心感谢!向参与承办此次会议的中华医学会心电生理和起搏分会、国家中医药管理局台港澳交流合作中心、江苏省中医药学会、南京中医药大学、南京医科大学第一附属医院等单位表示衷心感谢!向所有致力于络病学研究的海内外专家表示衷心感谢!

吴以岭

2008年10月28日

PREFACE

The fourth International Collateral Disease Conference will be held in the “Capital of Ten Dynasties”-Nanjing in the fruitful golden season. The 700 experts come from America, China-mainland, Taiwan, Hong Kong, Macao will flock together to review the research course on Collateral Disease, exchange academic achievements, plan cheerfully the development blueprint, therefore, which must be an international pageant for showing the latest research achievements on the study of Collateral Disease Theory, basic and clinical researches.

Under many multi-subject experts' efforts on Collateral Disease theory from home and abroad, Collateral Disease subject has achieved important progression. In May, 2008, the expert team composed by academician Wang Yongyan as director and Zhang Boli as vice-director considered that the “Study on Collateral Disease theory and its application” chaired by professor Wu Yiling has constituted systematically Collateral Disease theory and preliminarily formed the system of “Collateral Disease treated according to its symptoms”; the efficacy for cardio-cerebrovascular diseases has been increased obviously under the guidance of Collateral Disease theory, which showed its important directive significance in clinic; formation of experts team in the study of Collateral Disease; *Theory of Collateral Disease* has been used as New Century Creative Textbook for higher TCM collage in over 20 universities countrywide, and that is also highly appreciated, which has a positive effect for enhancing the ability of clinical differentiation of syndrome; Hebei Provincial Key Laboratory for study of Collateral Disease is established; many great achievements of provincial and ministerial rank. Through the efforts mentioned above, to have established stable basis for Collateral Disease subject, and which has the basic factors for setting up new subject, we agree to recommend “Theory of Collateral Disease” to be the basic subject of TCM clinic”. According the demonstration suggestion mentioned above State Administration Bureau of Traditional Chinese Medicine agreed to establish the new subject of TCM-“theory of Collateral Disease”. The establishment of Collateral Disease subject is the result of the joint efforts of the experts who devote themselves to the study of Collateral Disease. To review the last 20 years, theory of Collateral Disease has become systematic theory system from non-complete records, from the application of experienced medicament to the modern TCM with definite efficacy being used worldwide, from individual type study to the multi-subject experts studying together. The literatures about collateral, Collateral Disease and related ones with the therapy of promoting collateral have been enhanced from 360 articles in 1988 to 2690 articles in 2007, which has become the research heat point in medical field in recent years and showed the trend of flourishing development in last years, and had the important promotion effect for the establishment of Collateral Disease subject.

With the further study of collateral disease that is the branch of Collateral Disease subject, national 973 project “The Basic Research on the Prevention and Treatment of Vascular Disease under the guidance of the Collateral Disease Theory” has been approved for the middle-period appreciation by the efforts of expert team. The study, based on the directive point “coming from clinic, basic research, directing clinic”, has finished the clinical epidemiological investigation in 3469 patients with vascular pathogenesis, using the complicate system analysis method based on entropy to build the syndrome differentiation diagnostic standard of combination the whole and part, the quality and quantity identification, laid the foundation for establishing the animal model with collateral disease to research further the mechanism of pathophysiology. Based on the result of clinical epidemiological investigation, to put forward the hypothesis “Yingweichengzhitiaoping” to direct the development of subject, to set up the complex model of pathology of collateral disease, syndrome and symptoms, to investigate the evolvement regulation from the stagnation of Luo qi and deficiency of Luo qi caused by the disturbance of Luo qi, which is different from conventional study from blood stasis and phlegm obstruction, therefore, revealed the disturbance of Luo qi could affect vessel local pathological lesion through the disturbance of systemic neuroendocrinoimmunologic network regulation. The therapeutic effect of Tongxinluo by the intervention of vessel local pathological lesion is similar to that of western medicine, while the effect of improving systemic neuroendocrinoimmunologic network function is superior to that of western medicine.

The research on the common mechanism of Tongxinluo in the convention of "microvascular lesion" for three important clinical diseases in National 973 project have got obvious progress, The intervention therapy of Tongxinluo for microvascular and myocardial lesion due to myocardial infarction have achieved breakthrough progress that is superior to that of authoritative western medicine; the units led by Beijing Fuwai Hospital are conducting the evidence-based Medicine for the prevention and treatment of no-reflow in acute myocardial infarction by Tongxinluo, which will provide the experimental clinical basis for the occurrence rate of myocardial no-reflow, the area of no-reflow, reconstitute of myocardium and the changes of cardiac function at recent and long-term period after treatment of Tongxinluo reperfusion therapy for acute myocardial infarction; put forward the new treatment target of microvascular protection at ischemic area of cerebral infarction-treatment for cerebral infarction, which identified that Tongxinluo could prevent the integrity of microvascular structure and function, relieve reperfusion lesion, promote the reoccurrence of therapeutic vessel, set up effective side-way circulation to protect micro-vessel in ischemic area, which had important clinical significance in the treatment of acute myocardial infarction; that had obvious therapeutic effect in the convention of Tongxinluo on diabetes mellitus complicated with the pathological changes in myocardium, kidney, nerve, retina and protection of micro-vessel, and find the new way to treat this kinds of difficult and complicated diseases.

The theory of Collateral Disease guided the treatment research of arrhythmia shows that correlation between deficiency of Qi collaterals of heart and heart conducting system, myocardial cell autorhythmicity, autonomic nerve malfunction. Shensongyangxin capsule developed according to Chinese herb of Rongyangqiluo awarded science and technology Award of first class of Chinese Academy of Combination of Traditional Association of the Integration of Traditional Chinese with Western Medicine. Experimental results confirmed that Shensongyangxin capsule has obvious blockage effect on sodium channels, calcium channel and several potassium channels in ventricular muscle cell, and broad-spectrum anti-arrhythmia, avoids side effect of arrhythmia. Experimental results provided evidence on the treatment of tachyarrhythmia. Shensongyangxin capsule can enhance cardiac pacing current, improve sinoatrial recovery time and atrioventricular conduction time and has unique dominance on integrated regulation and intervention of arrhythmia. Study of evidence-based medicine for Shensongyangxin capsule anti-arrhythmia have been already finished by First Hospital Affiliated to Nanjing Medical University, Beijing Fuwai Hospital and Beijing Chaoyang Hospital as director unit composed by 36 hospitals. The results indicated that effect of Shensongyangxin capsule on non-organic premature was superior to placebo, effect of Shensongyangxin capsule on organic premature was superior to Mexiletine. Shensongyangxin capsule has definite effect on Disease hole, brady-tachy arrhythmia syndrome, brady arrhythmia with atrial ventricular block. Shensongyangxin capsule fills vacancy of western medicine on slow arrhythmia. There was no difference between Shensongyangxin capsule and Propafenone on atrial fibrillation. Shensongyangxin capsule was safer than Propafenone. Shensongyangxin capsule was unique anti-arrhythmia Chinese patent medicine authenticated by evidence-based medicine. It has distinctive predominance on the treatment of arrhythmia.

Construction of expert group on studying the theory of Collateral Disease and high-level personnel training have got a marked effect. With Collateral Disease branch of Chinese Academy of Combination of Traditional Association of the Integration of Traditional Chinese with Western Medicine was build up including more than 160 subjects experts, Collateral Disease special Interest Committees of Beijing, Shanghai, Guangdong, Jiangsu, Jilin were Build consecutively. They are promoting construction of high-level experts groups in China for studying Collateral Disease. Holding the Third Collateral Disease Teaching seminar, enhancement of the teaching job and teachers cultivate and continually increasing of teaching universities and a number as an elective course have made teaching of Theory of Collateral Disease closely to combine with high-level traditional Chinese medicine personnel training such as regular college course, Master, doctor.

International cooperative on Collateral Disease has got a important progress *Theory of Collateral Disease* English version was formally published. Matters concerned giving a course was consulted with USA, Holland, Australia. Protection and molecular mechanism of Tongxinluo on cardiovascular system, which was a international scientific research cooperative project with Professor Wang Xingli, Baylor Medical College showed that Tongxinluo decrease hexadecanoic acid -

induced Apoptosis of endotheliocyte with activation of anti-oxidation by AMPK Signal pathway-Mediated thioredoxin. Report of studying result has been already published a magazine includes SCI. Effect of Jiweiling freeze-dried powder on transgenic mice with amyotrophic lateral sclerosis (ALS) show that Jiweiling freeze - dried powder developed under the guide of theory of qi and collaterals can prolong survival time of transgenic mice as long as Rilutek Jiweiling freeze-dried powder was superior to Rilutek on delay emergence time of palsy, Progress in depth of the project has Important push effect on the development of theory of qi and collaterals.

This International Collateral Disease Conference received 148 papers; these included the latest progress of theoretical study, basic study, clinical study, and teaching study on Collateral Disease for a year. These have important reference value on understanding development of Collateral Disease subject. All the papers that were considered by experts would be compiled *Basic and Clinical Research on Collateral Disease*(4). We hope this compile to provide edification and train of thought for studying Collateral Disease deeply. At the time of having meeting, we should be thankful to the leaders of State Administration of tradition Chinese Medicine, Chinese Academy of Combination of Traditional Association of the Integration of Traditional Chinese with Western Medicine. We should express our appreciation to those noble-minded predecessors in medicine field. They are Professors Deng Tietao, Yan Dexin, Lu Zhizheng, Zhu Liangchun, and academician Chen Haozhu, Wang Yongyan, Chen Keji, Gao Runlin, Li Lianda, and Zhang Boli. We also should thankful to Cardiac Pacing and Electrophysiology branch, Chinese Medical Association, Taiwan, Hong Kong and Macao liaison the center of State Administration of tradition Chinese Medicine, Jiangsu Provincial Association of tradition Chinese Medicine, Nanjing University of tradition Chinese Medicine, First Hospital Affiliated to Nanjing Medical University. We should express our appreciation to experts and scholars and those who dedicate themselves to the theory of Collateral Disease.

WU Yiling
October 28, 2008

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