脾虚证患者十二指肠的病理形态及组织化学研究

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内容提要　本文通过光镜、电镜和组织化学方法，对54例脾虚患者及29例非脾虚患者的十二指肠标本进行观察，并与正常者作对比。结果表明：脾虚组的十二指肠炎较多；碱性磷酸酶和酸性磷酸酶在十二指肠绒毛功能部增强，顶部减弱；微绒毛稀疏、缩短；绒毛上皮细胞间隙增宽，杯状细胞、内分泌细胞、隐窝处低分化细胞、上皮内淋巴细胞浸润及固有膜各种炎性细胞均增多；细胞器一般也增多等病理改变，与非脾虚组及正常对照比较，有显著差异($P<0.05\sim0.005$)。提示脾虚组与非脾虚组及两组中慢性胃炎、溃疡病的十二指肠具有不同的病理形态基础。

本文运用现代病理组织学的方法和技术对脾虚证患者十二指肠进行超微结构变化及酶活性的组织化学研究，对脾胃病、证作了进一步的病理形态学探索。今将初步结果报道如下。

资料与方法

一、观察对象：83例胃切除或纤维胃镜活检的十二指肠标本为观察对象，分脾虚及非脾虚组。男64例，女19例。年龄18～72岁，其中30～49岁占43例(51.8%)。病期1个月～34年，其中1个月～9年者45例(54.2%)。另设正常对照10名。

二、辨证和辨病：由中医按证计分，凡食少、无力、面色少华、纳后腹胀、舌淡胖有齿痕、脉细各为1分，大便不实为2分，达5分者为脾虚(主要脾气虚)；有面浮脚肿，形寒肢冷者为脾阳虚；舌质红、口干者为脾阴虚。

83例患者中脾虚证54例（脾气虚41例，脾阳虚11例，脾阴虚2例），占65.1%；非脾虚证29例(气血两虚8例，气阴两虚及肝胃不和各5例，肝郁气滞4例，血虚及阴阳失调各2例，阴虚、阴虚夹热毒、肝火犯肺各1例)。

脾虚组患者经临床、X线钡餐、胃镜、病理等检查确诊为慢性胃炎25例(浅表性22例，萎缩性3例)，溃疡病20例（胃溃疡8例，十二指肠溃疡12例），其它9例(胃癌4例，胃下垂2例，胃后壁息肉合并幽门梗阻，残胃吻合口炎、胰头癌各1例)。非脾虚组慢性胃炎11例(浅表性9例，萎缩性2例)，溃疡病7例(胃溃疡6例，十二指肠溃疡1例)，其它11例（胃癌3例，十二指肠炎及消化不良各2例，胃下垂、慢性胆囊炎、内痔、慢性咽喉炎各1例)。

三、检测方法

1.病理组织学标本制备：脾虚组51例，非脾虚组22例共73例，取材均为十二指肠第一、二段，冷丙酮固定，石蜡包埋，HE染色，光镜下观察。参照有关文献[1~3]规定，观察指标如下：（1）十二指肠绒毛及隐窝变化；（2）绒毛顶部上皮细胞（脱落带）的变化：观察5个绒毛顶部，计数其中最多一个的上皮细胞变性、坏死、脱落、核固缩数；（3）肠隐窝(增生部)细胞分裂相：10个高倍视野中所见核分裂数；（4）杯状细胞计数：计数5个绒毛由隐窝绒毛结合部向上延伸到顶部的杯状细胞，算出每个绒毛的杯状细胞平均数；（5）上皮细胞内淋巴细胞浸润：计数5个绒毛，算出每个绒毛上皮内淋巴细胞浸润程度(分五级：稀

少±，散在＋，弥漫＋＋、成堆＋＋＋、淋巴滤泡＋＋＋＋)、血管，间质情况。

另参照几.别尔林等及全国胃癌防治研究协作组病理组1978年所订胃及十二指肠粘膜病理诊断标准[4,5]，规定十二指肠粘膜变化为：无异常、功能障碍及炎症(浅表性、弥漫性、萎缩性) 3类。

2.组织化学标本制备：脾虚组46例，非脾虚组25例共71例的十二指肠标本2～4 mm厚，冷丙酮固定，石蜡包埋，切片(6～8 μm厚)，分别作碱性磷酸酶(AKP)和酸性磷酸酶(ACP)组化测定，光镜观察。应用钙钴法[6]显示十二指肠绒毛上皮纹状缘的AKP活性，反应部位为硫化钴黑色沉淀。应用铅法[6]显示十二指肠绒毛上皮细胞内ACP活性，反应部位为硫化铅黑色沉淀。两者反应程度基本一致，分6级：深黑色＋＋＋＋，黑色＋＋＋，棕黑色＋＋，棕色＋，棕黄色±，无色－。

3.透射电镜标本制备：脾虚组17例，非脾虚组7例，正常2例。取26例的十二指肠标本经5％戊二醛和1％四氧化锇双固定，环氧树脂618包埋，LKB2088V型超薄切片机切片，2％醋酸铀及枸橼酸铅电子染色，荷兰P-hilips—400型透射电镜观察。

结　果

一、光镜检查：脾虚组51例，非脾虚组22例。

1.肠绒毛和隐窝、绒毛顶部上皮细胞以及隐窝区细胞分裂相：脾虚组的肠绒毛和隐窝无变化32例，变形及/或减少18例，未检1例；非脾虚组依次为20例、2例，两组相比差异显著($X^2=5.51$，$P<0.05$)。脾虚组绒毛顶部上皮变形、坏死、脱落0个10例，1～3个10例，4～12个30例，未检1例；非脾虚组依次为14例、4例、4例，两组相比差异非常显著($X^2=14.33$，$P<0.005$)。脾虚组隐窝区细胞分裂相0个22例，1个以上29例；非脾虚组依次为17例、4例、未检1例，两组相比差异显著($X^2=8.57$，$P<0.05$)。且另见10例脾虚证患者的隐窝细胞增生成栅状。正常标本具正常十二指肠绒毛及其顶部、隐窝及其分裂相的形态[4,5,7]。

2.杯状细胞计数及上皮细胞内淋巴细胞浸润：脾虚组杯状细胞小于15个21例，大于16个28例，未检2例，非脾虚组依次为20例、1例、1例，两组间差异非常显著($X^2=15.35$，$P<0.005$)。脾虚组上皮内淋巴细胞浸润小于15个20例，大于16个29例，未检2例；非脾虚组依次为19例及2例、1例，两组间差异非常显著($X^2=14.69$，$P<0.005$)。正常情况此两指标数皆应小于15个。

3.固有膜炎性细胞浸润：脾虚组的淋巴细胞浸润＋以下2例，＋＋以上49例；非脾虚组分别为9例、13例，两者间差异非常显著($X^2=16.43$，$P<0.05$)。脾虚组浆细胞浸润＋以下25例，＋＋以上26例；非脾虚组分别为17例、5例，两组间差异显著($X^2=5.02$，$P<0.05$)。脾虚组嗜酸粒细胞浸润±以下34例、＋以上17例；非脾虚组分别为21例、1例，两组间差异非常显著($X^2=6.86$，$P<0.01$)。脾虚组还见纤维增生15例(29.4%)，固有膜瘀血、水肿27例(52.9%)及粘膜肌增厚，十二指肠腺增生，巨噬细胞浸润等变化。正常者淋巴细胞浸润低于＋＋，浆细胞低于＋，嗜酸粒细胞低于±。

4.十二指肠粘膜变化：脾虚组粘膜无异常5例，功能障碍9例，炎症(浅表性、弥漫性、萎缩性)37例；非脾虚组依次为17例、1例、4例，两组相比，脾虚组的十二指肠炎显著多于非脾虚组($X^2=34.68$，$P<0.005$)。

二、组织化学测定：脾虚组AKP、ACP分别为46例、40例；非脾虚组依次为25例、23例。

脾虚组肠绒毛功能部纹状缘AKP＋＋＋以上37例，＋＋6例，＋3例；非脾虚组依次为5例、14例、6例，两组相比，脾虚组活性增强非常显著($X^2=24.57$，$P<0.005$)。脾虚组肠绒毛顶部纹状缘AKP＋＋以上19例，＋27例，非脾虚组依次18例、7例，两组相比

(图1，2)，脾虚组活性减弱显著 ($X^2=14.47$，$P<0.005$)。脾虚组绒毛功能部上皮细胞内ACP＋＋＋以上31例，＋＋3例，＋6例；非脾虚组依次2例、12例、9例，两组相比，脾虚组活性增强非常显著($X^2=25.52$,$P<0.005$)；脾虚组绒毛顶部上皮ACP＋＋14例，＋26例，非脾虚组依次14例、9例，两组相比(图3,4)，脾虚组活性减弱显著($X^2=3.95$，$P<0.05$)。正常组AKP、ACP以＋＋为多。

三、电镜观察：脾虚组17例，十二指肠

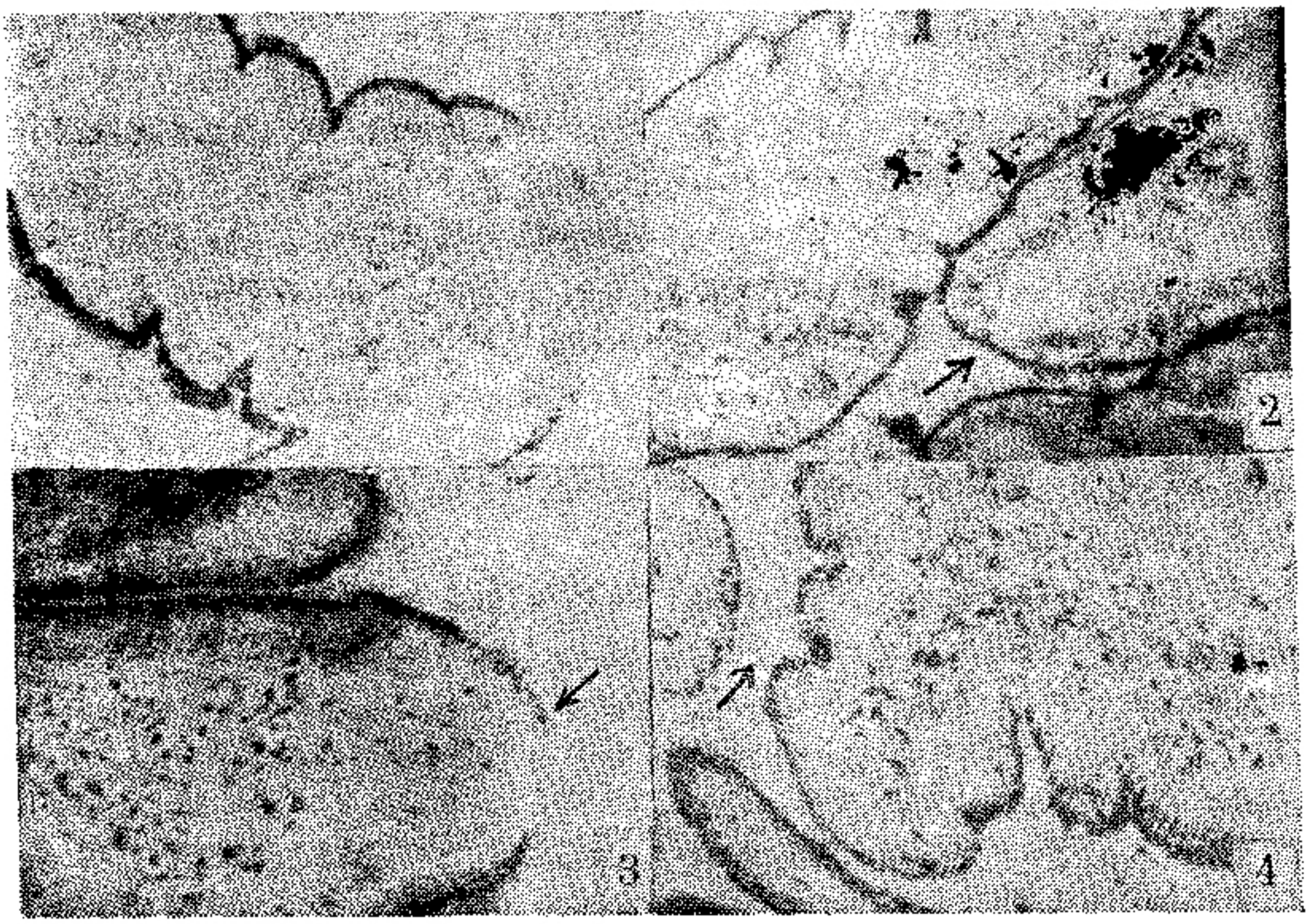

图1 脾虚患者十二指肠绒毛功能部纹状缘AKP活性增强＋＋＋，顶部活性减弱±↑ ×600 图2 非脾虚患者绒毛功能部及顶部AKP活性均正常＋＋↑ ×600 图3 脾虚患者十二指肠绒毛功能部上皮内ACP活性增强＋＋＋，顶部活性减弱±↑ ×600 图4 非脾虚患者绒毛功能部及顶部ACP活性均正常＋＋↑ ×600

绒毛顶部的吸收上皮微绒毛有明显的退行性变，呈现稀、短，分布不均。十二指肠吸收上皮的细胞间隙呈不同程度增宽，尤以细胞基部为甚；但细胞连接（紧密连接，中间连接，桥粒)一般完好无损。上皮内淋巴细胞浸润显著，可见其穿越基膜，甚至通过紧密连接入肠腔，上皮基膜略增厚。吸收上皮细胞器均见明显改变，绒毛顶部上皮细胞器一般表现退化，尤见线粒体肿胀、空泡化；绒毛功能部以下的上皮细胞质中游离核蛋白体、线粒体、内质网、高尔基复合体及溶酶体等一般表现为增生。增生性变的上皮细胞核及胞体明显伸长，呈现栅栏状结构，杯状细胞的分泌颗粒一般增多，呈现分泌亢进现象。固有膜结缔组织瘀血、水肿，淋巴细胞、浆细胞、肥大细胞及酸性粒细胞增多，十二指肠腺亦增生，分泌活跃。此外，内分泌细胞较多及隐窝处出现较多的含核蛋白体丰富的低分化细胞。

非脾虚组7例肠微绒毛基本正常或比正常排列稍稀，上皮细胞间隙基本正常，吸收上皮细胞器接近正常。上皮内淋巴细胞、杯状细胞、低分化细胞及内分泌细胞以及固有膜内淋巴细胞、浆细胞、嗜酸粒细胞等均少于脾虚组，比正常组稍多。正常标本2例如正常十二指肠粘膜超微结构特征。

四、脾虚组、非脾虚组中相应疾病（慢性胃炎、溃疡病）病理观察：以十二指肠粘膜变化(正常、异常)及组化（酶活性＋＋为正常、

+++及+为异常)为主要指标，按四格表精确检验简化法对比如下：慢性胃炎：脾虚组25例，非脾虚组11例；溃疡病：脾虚组20例，非脾虚组7例，以十二指肠粘膜变化；肠绒毛功能部纹状缘AKP；绒毛顶部纹状缘AKP；绒毛功能部上皮细胞内ACP；绒毛顶部上皮ACP等指标分别相比，差异皆显著（$P<0.05$）。电镜观察符合于脾虚组、非脾虚组的不同超微结构变化。

讨　论

十二指肠是胃液、胆汁、胰液及十二指肠液汇合之处，有大量绒毛吸收上皮的微绒毛，其表面富有水解酶的糖衣，它和细胞连接共同起着防护粘膜的屏障及消化吸收营养物质的重要作用，且有肠道内分泌细胞，可广泛影响物质代谢过程[5,8]。脾虚组(包括慢性胃炎、溃疡病，下略)绒毛变平或损伤多，微绒毛稀疏和脱落多，因而消化、吸收功能不良与非脾虚组(及其慢性胃炎、溃疡病，下略)、正常相比，差异均显著。绒毛顶部上皮变性、坏死多，隐窝区细胞分裂相多，绒毛功能部AKP和ACP活性增强等与非脾虚组及正常相比也多而明显，说明十二指肠顶部上皮不是正常的恒定更新，而是衰老、损伤、再生加快。绒毛顶部AKP、ACP活性降低，纹状缘减少，细胞器减少，细胞间隙增宽，基底膜增厚等使消化吸收及物质交换和屏障作用有所障碍，由于营养物质缺乏，引起上皮细胞萎缩及其单位膜完整性破坏以及脂质沉淀，又可使微绒毛减少，纹状缘酶损失，核糖核酸蛋白质和粗面内质网减少以及细胞器肿胀等，进一步降低消化吸收及屏障作用，从而易引起免疫反应异常及炎症[9]。绒毛功能部大部吸收上皮细胞器增生，杯状细胞及其分泌颗粒、内分泌细胞均增多，可能是绒毛受损后代偿性反应加强所致。上皮内和固有膜淋巴细胞浸润多，浆细胞、嗜酸粒细胞、肥大细胞多、瘀血、水肿、纤维增生也多，是一种慢性或变态反应性炎症，与以往报道述及脾虚证的病理组织学表现是一致的[11,12]。总之，脾虚组在十二指肠的病理表现主要是不同程度的十二指肠炎及功能障碍的组织学和超微结构改变。

根据中医学有关脾胃的论述，脾胃可理解为消化系统为主的多器官、多系统的综合功能单位，本文观察也说明脾虚证是以消化道形态功能改变为病理基础的，与非脾虚证有本质区别，但两者间也可有传变。

本文脾虚证常见者为脾胃不和、脾胃气虚证两类，前者如食少、纳后腹胀、大便不实等，也是现代医学消化系疾患常见的症状群；后者如面色少华、无力、舌淡胖有齿痕、脉细等可能是消化吸收障碍、营养不良后影响到全身各器官系统而产生的病变。

从脾虚与非脾虚组总体及其中主要疾病(慢性胃炎、溃疡病)相比，其十二指肠均有不同变化的病理基础，故脾虚患者以同证的“异病同治”是有一定物质依据的。

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Therapeutic Effects and Mechanism in Treating 3 Kinds of Thrombotic Diseases with Mailuonin (脉络宁) Injection

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Mailuonin (MLN) is a compound preparation of medicinal herbs. The main drugs of this preparation are *Scrophularia ningpoensis, Achyranthes bidentata* and other two drugs, which has a good therapeutic effect and no apparent side-effect. Results: (1) 82.8% (130/157) of thromboangiitis obliterans patients belonged to III phase, clinical cure and markedly effective of which amounted to 148 cases, 94.25%. (2) 73 cases of deep vein thrombosis of lower limb, the total number of their clinical cure and markedly effective were 61 cases, 83.8%;12 cases improved, 16.4%.(3)52 cases of cerebrothrombosis: Course of disease of 39 cases was within 6 months, the rate of basic cure and markedly improved were similar to 35 cases of the control group treated with low molecular dextran. 11 cases' courses were over 1 year; they obtained satisfactory effect also, which denotes that MLN is effective in treating sequelae of cerebro-thrombosis as well. The mechanisms of MLN were as follows: (1)It might increase the activity of fibrinolysis and the electrophoresis of erythrocytes and thrombocytes, reduce the blood viscosity and lower the coagulability tendency, which showed that the MLN has the function of anticoagulation and anti-thrombosis. (2) After treatment the ratio of serum cGMP/cAMP was raised, which means the production of cholinergic effect. The biochemical and pharmacological experiments revealed that MLN caused excitation of histamine and cholinergic receptors as well as the inhibition of adrenergic receptors, consequently vasodilation and increase of blood flow occurred. At the same time, it normalized the disturbance of patient's nailfold microcirculation.

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A Pathomorphological and Histochemical Study in the Duodenum of Spleen Deficiency Patients

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In this paper 54 Spleen deficiency (SD) and 29 non-SD patients' duodenal specimens (including chronic gastritis and peptic ulcer of both groups) obtained during gastrectomy or fibrogastroscopical mucosal biopsy were observed with light-, electronmicroscope and histochemical assay. The finding were compared with the control group. The results obtained were as follows: (1) Under light microscope, the changes in intestinal villi and Lieberkühn's glands, the necrosis, deformation and sloughing of the epithelium of villi-tip, the mitosis in Lieberkühn's glands, the count of goblet cells, the migration of lymphocytes into the intestinal epithelial cells and inflammatory cells in the lamina propria as well as the aspect of duodenitis (superficial, diffuse, atrophic) in the group of SD cases were increased significantly, $P<0.05\sim0.005$. (2) Histochemically, the AKP and ACP activity in the functional region of intestinal villi were increased and their activity decreased in the villi-tip. It was significantly different from normal and non-SD group ($P<0.05\sim0.005$). (3) Under electronmicroscope, less number of microvilli at the cell apex could be seen, the organelles in the functional region of intestinal villi epithelium were increased, the intercellular space was wider, the base membrane thicker, and the endocrine cells and low-differentiated cells in mucus layer, the mast cells, plasma cells and acidophilic cells were all increased and significantly different from those of normal and non-SD group.

In short, the pathological base of SD patients' duodenum is due to various degree of morphological changes of inflammation and dysfunction. SD syndrome in this paper usually consists of two types: Spleen-stomach type and Qi (气) deficiency type; the former seems to be the primary pathological change of SD. When the digestive and absorptive disturbance followed by malnutrition, pathological change in other systems of the body would occur, resulting in Qi deficiency syndrome. Therefore, this paper provides a modern pathological basis for "treating different diseases with the same method" in SD syndrome.

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