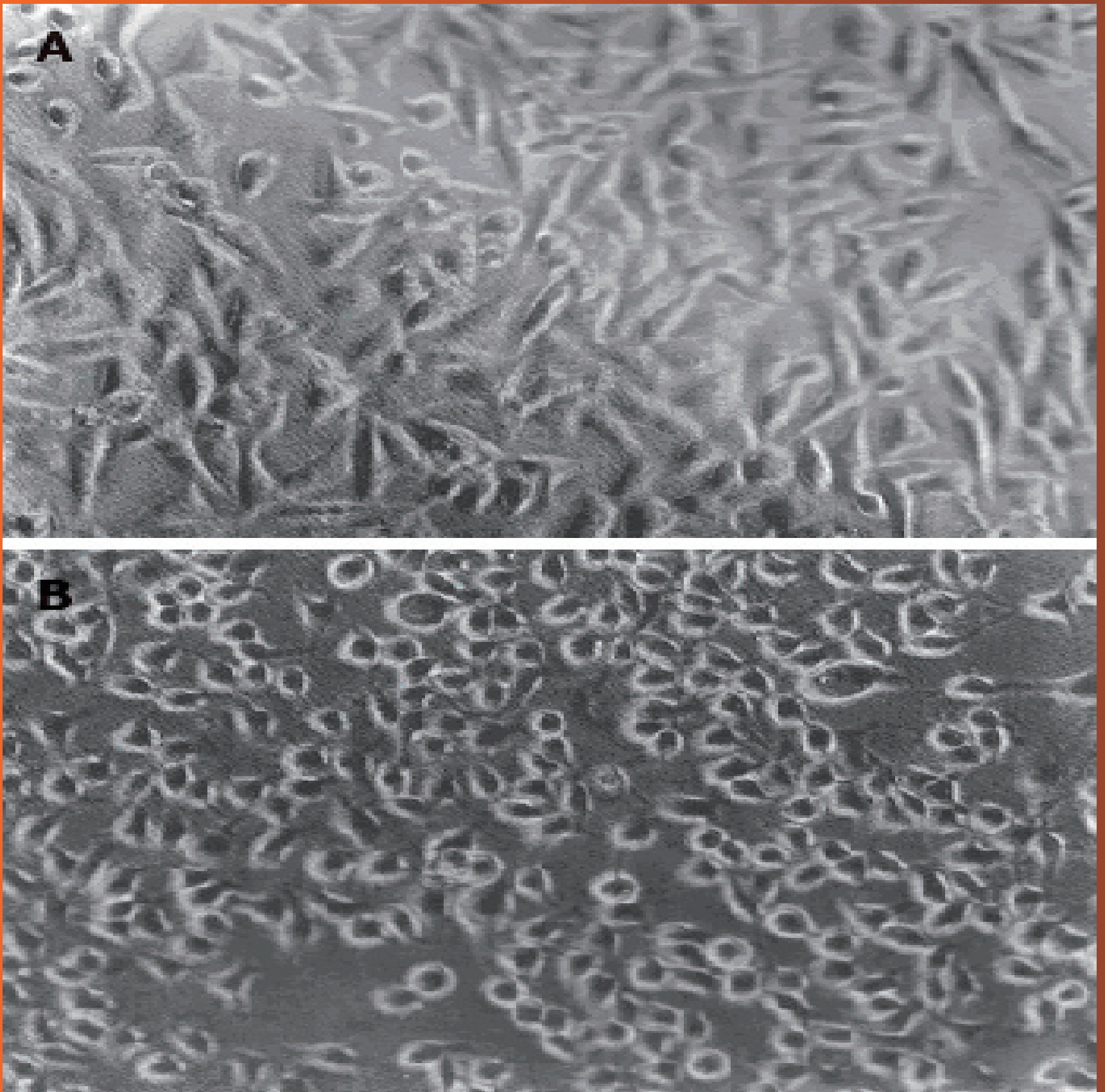


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Gastroenterology in the next century: Megatrends in science and practice

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I realize that my presentation may have a somewhat ponderous title, implying that I might possess a crystal ball able to foretell the future. I don't. But because of my over 40 years of experience in gastroenterology and hepatology, I have been invited to present some speculations about how and in which direction the field may move in the coming century.

Looking back half a century to the end of WWII and China's liberation, it is astounding how primitive gastroenterology had been at that time. Modern science hardly had touched it and most of the diagnostic and therapeutic dogmas were still those of the 19th century. But over the past 50 years, as modern biomedical science and technology were taking off, gastroenterology and hepatology have profoundly changed. We have witnessed a huge increase in insight into the causes and mechanisms of disease and our diagnostic and therapeutic capabilities have enormously expanded and improved. For example, think of the discovery of the viruses causing infectious hepatitis, of transplantation of the liver, pancreas and small bowel, or the introduction of fiberoptic endoscopy. And to top it all, recall the recent revolution in peptic ulcer disease which unceremoniously toppled old dogmas about gastric acid and made it instead a readily curable infectious disease.

I believe with confidence that this dynamic evolution will continue and probably accelerate in the coming century. And there is no question that it will bring much novel and unanticipated information about currently obscure diseases. And it will greatly

refine diagnostic procedures and expand therapeutic choices. What seems more difficult to predict, though, are the directions which this evolution may take, and how we are going to make use of these new opportunities and will pay for them.

The Human Genome Project undoubtedly is an international undertaking that will have an enormous and irreversible impact on the future of gastroenterology and hepatology. Once its ultimate goal will have been reached, presumably early in the next century, the entire human genome will have been sequenced and mapped and it will be possible and perhaps become routine to screen an individual's entire genome from a simple blood sample. Genetic mutations which result in hereditary diseases of the gastrointestinal tract or the liver will readily be identified. Individuals or families at risk for a hereditary disease may be screened for the genetic defect. And eventually, such screening may become available even for prenatal use.

Sequencing of the full human genome will be useful in many other circumstances. Many genetic diseases are polygenic, *i.e.* the phenotypic expression of a primary gene defect is modified by one or several additional as yet unidentified genes. This probably accounts for the wide spectrum of clinical expression that is seen in many primary genetic defects. For example, homozygous Wilson disease, copper storage disease, may clinically present as progressive cirrhosis, as a severe disease of the central nervous system, or as acute hemolytic anemia. This phenotypic variability most likely reflects the polygenic nature of the disease, a hypothesis which will be resolved by the successful sequencing of the human genome.

Another benefit of the genome project will be identification of the genetic factors which determine individual susceptibility to environmental assaults, such as viral, bacterial or fungal infections or exposure to toxins or poisons. Clearly, different people respond to such noxious assaults differently. For example, some experts believe that inflammatory bowel disease, such as ulcerative colitis or Crohn's disease, may be the result of a genetically determined aberration of the immune response to the trillions of microorganisms that live in the intestinal lumen. Of course, no such genetic defect has ever been found but sequencing of the genome may change this.

Another example of a differentiated response to a toxin is observed in chronic alcoholism. Surprisingly, only about 25% of severe chronic alcoholics develop cirrhosis of the liver. Why is it that the majority is escaping hepatic injury? It clearly is not due to dietary factors or to the preferred alcoholic beverage. Rather, I suspect that this striking difference is caused by genetic factors which determine how the liver is reacting to the metabolic products or reactive oxygen radicals which are produced when alcohol is metabolized. Hopefully, sequencing of the genome in the next century will help to provide plausible answers.

It is likely that the function of most of the genes identified by sequencing of the human genome initially will be unknown and will have to be determined stepwise, one by one. This will

be an enormous task which may well take several decades of painstaking investigation. But once this has been accomplished, gastroenterologists of the future will look at intestinal and liver diseases from a vastly different perspective, and they will use treatments which are far beyond today's imagination.

The Human Genome Project also is crucial for the future of gene therapy of inherited diseases. This is because it will allow identification of the nature of the genetic error in a mutated gene *e.g.* transposition of a base pair, missense mutations, or deletion of several nucleotide sequences. This information is crucial for construction of the new gene to be transposed.

As you are aware, gene therapy *in vivo* has been used successfully in animal models and in a few highly selected genetic defects in humans. There still are problems which need to be addressed but I am confident that they will be resolved in the not too distant future. One of these problems concerns the vehicle or vectors which are used to transport the replacing gene to the targeted cells or organ. At present, this generally is accomplished by packaging it into adeno- or retroviruses or more recently into adeno-associated viroids. But these RNA viruses often cause immune or toxic reactions which limit their usefulness as vectors. Most recently (Nature Medicine, March 1998), Kren *et al* have proposed a very exciting and highly imaginative new approach, using a chimeric RNA/DNA oligonucleotide embedded in a short stretch of DNA. This is coated with a polycation containing a ligand that permits targeting of specific cells. And it is the cells' own DNA mismatch repair mechanism which is used for integration of the new oligonucleotide into the DNA. This and other new approaches to gene therapy, particularly for hereditary diseases that are expressed in the liver, are holding immense promise and undoubtedly will play a commanding role in the new century.

A second problem with current gene therapy is that the somatic cells selected for gene repairs have a limited natural life span and then undergo apoptosis. A repaired gene therefore can be expressed no longer than the life span of its cell, which may range from a few days for intestinal mucosa cells to several hundred days for hepatocytes. To overcome this time limitation, one would need to repair the genetic defect in embryonic germ cells which at present is neither possible nor ethically justifiable. A more appealing approach might be to target gene therapy to an organ's stem cell compartment. Stem cells, in addition to producing daughter cells, are replicating themselves. Therefore new genetic information transposed into stem cells' genome would be immortalized and thereby indefinitely transferred to daughter cells. I believe that in the coming century, such technology may become available which would be a breakthrough in gene therapy, particularly for hereditary defects expressed in the liver. At present, of course, this can be achieved only by orthotopic liver transplantation which has been used for permanent cure of Crigler-Najjar disease, OTC deficiency and hereditary analbuminemia, to name the most prominent.

Another, new and very promising use of gene therapy is in the treatment of primary cancer or malignant metastases of the liver. The majority of malignant tumors exhibits mutations in genes expressing so-called cancer repressor proteins, such as *p53*, *p16* and others, which act primarily by controlling the cell's mitotic cycle. When these genes are mutated or lost, the result is unregulated cell replication and tumor growth. In animal models, gene therapy targeted specifically to malignant cells was able to reconstitute functioning *p53*, *p16* genes, which led to significant tumor shrinkage and prolonged survival. Although these are preliminary results in animals and the technique needs refinement, I believe that it has enormous promise and eventually may well replace surgery, radiation or chemotherapy.

I have discussed the Human Genome Project and gene therapy in some detail because they are likely to revolutionize the practice of gastroenterology and hepatology. But there are countless other areas where modern molecular biology will make a big difference. For example, there are many obscure disease processes for whose exploration we simply did not have the necessary tools. Here, molecular biology and virology will profoundly expand and improve the future gastroenterologist's choice of diagnostic and therapeutic options. Because time is limited, I will mention only one: chronic viral

hepatitis, notably hepatitis B and C, which world-wide are causing immense morbidity and mortality. Despite remarkable advances, we still do not understand how these viruses survive and cause liver injury nor do we have effective, reliable and safe therapies to arrest progression, let alone to achieve a permanent cure. To many of us, who are old enough to remember the fiasco with steroid treatment of chronic viral hepatitis, the current hyperbole about interferon treatment is astonishing, if not lamentable. I hope and anticipate that in the new century, chronic viral hepatitis at long last will find a definitive therapy and eventually effective prevention.

And finally, the rapid evolution of molecular biology has created a new discipline, molecular diagnostics, which will offer an ever-increasing number of tests of previously unthinkable sophistication and sensitivity. For example, molecular techniques already are used to quantitate viral loads in viral hepatitis. But a most promising application will be in the search for new infectious agents which to date have escaped detection by available staining or immunologic methods. As you are aware, several gastrointestinal diseases, previously of unknown etiology, have recently been found to be caused by newly discovered microorganisms. These include, of course, peptic ulcer, but also Whipple's disease, bacillary angiomatosis and most recently, nanobacteria which cause connective tissue calcification in scleroderma, sclerosing cholangitis and in the CREST syndrome associated with primary biliary cirrhosis (PNAS, July 1998). But there are several other gastrointestinal diseases of unknown etiology whose clinical and pathological features seem consistent with, if not suggestive of, an infective origin. These include Crohn's disease, ulcerative colitis, granulomatous hepatitis and sarcoidosis, primary biliary cirrhosis and sclerosing cholangitis. Although many experts have postulated an immunologic origin of these diseases, no convincing evidence has yet been reported. Now that highly sensitive molecular RNA and DNA probes have become available to hunt for elusive microorganisms, I am confident that the search for pathogens in these diseases will be renewed. And I would not be surprised if one or more would be discovered to have an infectious etiology.

Predicting the future of gastroenterology would be incomplete without briefly considering what new diagnostic and therapeutic instruments and machinery may become available in the next century. Here, progress, driven by intense market competition, is so rapid that precise predictions are quite impossible. Nonetheless, some trends seem to become detectable. Radiology is likely to progress by leaps and bounds, particularly spiral computerized tomography and three-dimensional imaging. They increasingly will replace invasive diagnostic procedures, including fiberoptic endoscopy; the only exception will be the novel fiberoptic, laser-induced fluorescence spectroscopy, which has great diagnostic potential. On the other hand, Magnetic Resonance Imaging, with its very expensive equipment, appears to be taking a back seat. And in gastrointestinal surgery, a large proportion of invasive procedures will be performed by laparoscopy, which often makes hospitalization unnecessary and thereby reduces costs.

And this brings me to a true mega factor which in a major way will shape and restrain the practice of gastroenterology in the next century. This is the economics of health care. All over the world, per capita costs of medical care are rising steeply, far outpacing the rate of inflation. To a considerable extent, this is due to the accelerated appearance on the market of new or advanced but always more expensive machines, procedures and drugs which seem necessary to keep up with contemporary medicine. In the United States, this continuing price increase has driven health care costs to a level, equaling 15% of gross domestic product, and other developed countries are not far below. Although in the developing world, health care costs generally are lower, the cost increase in proportion is similar. It seems evident that if this trend should continue, health care eventually will consume a major part of the GDP. But I am afraid that as long as medical care continues to be unregulated or is remaining a market commodity, it will be very difficult, if not impossible to bring quality of medical care and its costs into some sort of reasonable balance. Consider, for example, who would be qualified and publicly acceptable as decision makers? Would it fall to third party payers, that is insurance companies or health

maintenance organizations? Or to employers who are funding the costs of health care? Or to the medical care establishment, that is to physicians and hospitals? Or perhaps to the government? However this paramount issue will be resolved, it will have an enormous impact on the future practice of gastroenterology and hepatology, both in the developed and in the developing world. Developing countries are rapidly coming on mainstream in health care as they are striving to catch up with modern Western medicine. But we should care that their evolving markets are not being deluged by the aggressive pharmaceutical and medical equipment industry of the developed world.

Ladies and Gentlemen, in concluding, I believe that this brief glimpse into the science and practice of gastroenterology in the

next century offers us a mixed perspective, one of an ever widening disparity between rising opportunities on the one hand, and restrained resources on the other. I am afraid that unless this serious dilemma will be resolved early in the next century, the practice of gastroenterology and the quality of health care world wide will suffer. We need to learn how to cut expenses by volutarily reducing our dependence on technical procedures and expensive equipment, and by avoiding use of only marginally effective medications and surgical interventions. And last but not least, in hopelessly ill patients, we should forgo trying to prolong dying by every means at our disposal. These, I am afraid, will be painful adjustments for the medical establishment, but they must be faced in the coming century.

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Advances in clinical research of hepatocellular carcinoma in China

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Based on the survey in 1990/1992, hepatocellular carcinoma (HCC) has become the second cancer killer in China, the mortality rate was 20.37/100000^[1]. The etiological background of HCC in China includes: Viral hepatitis-around 90% of HCC in China had evidence of hepatitis B virus (HBV) infection, whereas hepatitis C virus infection was found in only 10%-30% of HCC patients. HGV-RNA was less important as compared to HBV/HCV. The second factor was aflatoxin B1 (AFB1), particularly in areas with high temperature-humidity index. In the rural areas, contamination of drinking water was claimed correlates with high HCC mortality, and microcystin was found to be promoter of hepatocarcinogenesis. The others include alcohol, smoking and genetic factors. Using trees hrew experiment, synergetic effect was found between HBV and AFB1, the incidence of HCC in HBV + AFB1 group was 52.9%, whereas it was only 12.5% in AFB1 group, 11.1% in HBV group, and 0% in the control^[2]. For primary prevention, "control of water, control of crops, and prevention of hepatitis" has been advocated, and being proved to be effective since the 1970s^[3]. It was reported, during the period of 1993/1994, HB vaccination has been given in 96.9% of new born babies in the cities, and 50.8% in the rural areas. It is predicted that a decline of HCC incidence will probably happen in decades later.

In clinical aspect, lobectomy for large HCC in the 1950s has benefited to 5%-10% of HCC patients. Liver transplantation appeared in the 1960s. In the 1970s, as a result of alpha fetoprotein (AFP) serosurvey, the study of small HCC has benefited to the second part of 5%-10% of HCC patients. Diagnostic level of HCC has been greatly improved due to the rapid progress of medical imaging. The advances in regional cancer therapies and

multimodality combination treatment have resulted in cytoreduction and sequential resection for initially unresectable HCC, which will benefit to the third part of 5%-10% of HCC patients. In the 1990s, the rapid progress of molecular biology will be certainly of implication in the diagnosis and treatment of HCC, and the study of recurrence and metastasis have become an attractive field of study. Unfortunately, the prognosis of HCC remains disappointed. The relative 5-year survival rates reported in the United States during 1974/1976-1980/1982 and 1986/1993 were 4%, 4% and 6% in white, and being 1%, 2% and 4% in black^[4]. The relative 5-year survival rates in a high risk area of China-Qidong county in the period of 1972/1981 and 1982/1991 were only 2.2% and 2.3% respectively^[5].

DIAGNOSIS OF HCC

No remarkable progress was made in the field of tumor marker for HCC. A report said that detection of fragment of fibronectin in plasma was helpful for diagnosis of HCC, the value in HCC patients was 28.91 g/mL ± 1.96 g/mL, being 9.60 g/mL ± 2.42 g/mL for chronic liver disease, and 4.32 g/mL ± 3.10 g/mL in normal control^[6]. Spiral CT was claimed of value for diagnosis, the sensitivity was 89% in the arterial phase, 72% in portal phase and being 91% for double phase^[7].

LONG-TERM SURVIVORS RELATED TREATMENT

By the end of 1992, at the Liver Cancer Institute of Shanghai Medical University (author's institution), 320 HCC patients have survived more than 5 years, 100 of them survived more than 10 years. Most of the long-term survivors came from small HCC resection, the second source being large HCC resection, and cytoreduction and sequential resection ranked third, palliative surgery other than resection ranked fourth. At the author's institution, treatment modalities that resulted in prolonging survival included: (1) Small HCC resection, the 5-year survival was 63.4% in 806 cases. (2) Large HCC resection, the 5-year survival was 39.6% in 1061 cases. (3) Cytoreduction and sequential resection for initially unresectable HCC, the 5-year survival was 64.7% in 93 cases who had tumor cytoreduction by hepatic artery ligation and cannulation; in another 70 cases, sequential resection was done after cytoreduction by transcatheter arterial chemoembolization (TACE), the 5-year survival was 56.0%. (4) Reresection for recurrence, the 5-year survival of 155 patients was 50.9% calculated from the first resection. (5) Palliative surgery other than resection, the 5-year survival of 784 cases (including some patients who had sequential resection) was 21.6%. Cheng *et al*^[8] reported that the 5-year survival of 240 patients treated by TACE was 18.9% (including some patients who had sequential resection. Other treatment that resulted in long-term survivor included radiotherapy combined with Chinese traditional medicine, etc. In short, surgery played the most important role, however, the role of regional cancer therapies seems increasing

SURGICAL TREATMENT

The advances of surgical treatment for HCC in China might include: Early resection, first stage resection for HCC in difficult location, re-resection, cytoreduction and sequential resection for unresectable HCC, and palliative surgery other than resection^[9]. The 5-year survival of 2051 HCC resections was 36.1% reported by Wu *et al*^[10], and being 50.6% at the author's institution ($n = 1866$).

Small HCC resection: The encouraging result of small HCC resection was mainly a result of screening in high risk population and yearly checkup using AFP and ultrasonography. At the author's institution, a prospective controlled trial of screening every 6 months indicated that the percentage of subclinical HCC, resectability rate, and 2-year survival rate were 76.3%, 70.8%, and 77.5% respectively, much higher than that in the control group (0%)^[11]. However, the retrospective analysis in Qidong County demonstrated that screening group was only slightly superior to that of nonscreening group, the 5-year survival was 4.0% (being 8.3% for subclinical HCC) versus 1.6%^[12]. In the recent years, the 5-year survival of small HCC resection reported in China were around 50%: being 52% ($n = 50$) reported by Feng *et al*^[13], 79.8% reported by Wu *et al*^[10], and 63.4% at the author's institution ($n = 806$).

Large HCC resection: The 5-year survival rates reported in the recent literature were: 32.9% reported by Du *et al* ($n = 407$, including small HCC)^[14], 36.1% reported by Wu *et al* ($n = 2051$, including small HCC)^[10], and 39.6% at the author's institution ($n = 1061$). Aggressive surgical approach was also reported for the management of tumor emboli in the main trunk of portal vein^[15]. In the technical aspect of HCC resection, unilateral inflow occlusion has been employed more frequently^[16,17].

Re-resection for recurrence: As reported, the 5-year survival rates calculated from the first resection were 41.5% ($n = 49$, Du *et al*)^[14], 53.2% ($n = 95$, Wu *et al*)^[10], and 50.9% ($n = 155$, author's institute).

Cytoreduction and sequential resection for unresectable HCC: At the author's institution, during 1958/1994, 663 patients with HCC were verified to be unresectable, of them, 72 patients received sequential resection when tumor shrank after treatment; the median tumor diameter reduced from 10 cm (maximum 24 cm) to 5 cm at the sequential resection; the pre-resection treatment including hepatic artery ligation (HAL) plus cannulation (HAI) (38.9%), HAL + HAI + radioimmunotherapy/regional hyperfractionated radiotherapy (58.3%), single treatment only accounted for 2.8%; the median duration between the first and the second resection was 5 months (1-16 months); operative mortality of sequential resection was 1.4%^[18,19]. The 5-year survival rates of sequential resection were 64.7% at the author's institution ($n = 93$), 61.5% reported by Wu *et al* ($n = 73$)^[10], and 25% in Du *et al*'s series ($n = 20$)^[14]. Besides, cytoreduction by TACE and followed by resection was also reported: the 5-year survival was 56% ($n = 59$ at the author's institution)^[20], 39.2% ($n = 33$, Wang *et al*)^[21], 60.5% ($n = 11$, after operative hepatic artery cannulation HACE/TAE, Peng *et al*)^[22], and 62.3% ($n = 13$, after HACE/TAC-E, Yuan *et al*)^[23].

Palliative surgery other than resection: Palliative surgery for HCC includes hepatic artery ligation (HAL), hepatic artery cannulation (HAI), cryotherapy, microwave, intralesional ethanol injection during operation, etc. At the author's institution, the 5-year survival of 235 patient with HCC treated by cryotherapy was 39.8%, and being 55.4% for small HCC ($n = 80$); further analysis revealed that it was 26.9% in single cryotherapy subgroup ($n = 78$), 39.6% for cryotherapy+HAL/HAI ($n = 58$), 46.0% for cryotherapy of residual cancer after resection ($n = 27$), and 60.4% for resection after cryotherapy ($n = 72$)^[24]. Experimental study demonstrated that high intensive focussed ultrasound (HIFU) was one of the hopeful approach for regional therapy of HCC, and Lipiodol could enhance the response of HIFU^[25,26].

NONSURGICAL TREATMENT

Regional cancer therapy is a recent trend for the treatment of HCC, which includes surgical approach as mentioned above, and nonsurgical approach. Interventional radiology and percutaneous

ultrasound guided intervention are two major parts of nonsurgical approach. Recently, TACE has surpassed radiotherapy to be the first choice of treatment for unresectable HCC. The 5-year survival rate reported by Cheng *et al*^[8] was 18.9% ($n = 240$, including patients with sequential resection); another series was 7.5% ($n = 621$), reported by Liu *et al*^[27], and patients with single HCC and without tumor emboli in the portal vein had better prognosis. The commonly used internal radiotherapy was 1311 labeled lipiodol. Radioimmunotherapy is currently under clinical trial, effective tumor shrinkage and followed by sequential resection had been reported using 1311-antiferritin/1311-anti human HCC mAb^[28,29]. However, human anti-murine antibody appeared in one third of the patients even administered intra hepatic arterially^[30]. At the author's institution, chimeric human-mouse antibody has been reconstructed, and radioimmunoimaging obtained in nude mice model^[31,32]. In the field of biotherapy, response observed in author's institution when LAK/IL-2 plus TAE were used^[33]. For drug therapy, Zheng *et al*^[34] reported that tamoxifen is a treatment choice for HCC patients with expression of estrogen receptor^[34].

PREVENTION AND TREATMENT OF RECURRENCE AND METASTASIS

At the author's institution, the previous report indicated that the 5-year recurrent rate after curative resection was 61.5%, and being 43.5% for small HCC; using analysis of HBV-DNA integration and p53 genotype, we also demonstrated that there are both unicentric origin and multicentric origin for recurrent HCC^[35]. In this paper, only invasiveness related recurrence will be discussed.

Prediction of recurrence: Predictive markers include serum marker and examination of surgical specimens, which cover molecular and cellular levels. Proliferating cell nucleus antigen (PCNA) and overexpression of p53 in immunohistochemistry indicate poor prognosis^[36]. At the author's institution, poor prognosis has been observed in patients who had higher expression of matrix metalloproteinase-2 (MMP-2) in HCC than that in the surrounding liver^[37].

Prevention of recurrence: Peng *et al*^[38] reported that preoperative TACE was only good for HCC > 8 cm but not for HCC < 8 cm. Zhou *et al*^[39] claimed that postoperative immunochemotherapy was helpful to reduce recurrent rate. Han *et al*^[40] reported that postoperative intraarterial chemotherapy decreased 5-year recurrent rate, being 72.0% versus 80.7% when compared to the control, and was only 67.8% in double cannulation group. At the author's institution, 68 patients with curative resection verified by postoperative lipiodol-CT received TACE and interferon therapy, the 3-year recurrent rate was lower than that reported previously, being 14.7% vs 32.5%; a another group comprised 105 patients with curative resection and treated with transhepatic arterial/portal vein chemotherapy, the 3-year recurrent rate was also lower than that reported previously, being 18% vs 32.5%.

Experimental model of metastasis: At the author's institution, we established a metastatic model of human HCC in nude mice (LCI-D20) after orthotopic implantation of intact HCC tissue from 30 patients' surgical specimens, the metastatic rates to lung, liver and lymph node were extremely high, and 90% of cells were a neuploid, with expression of invasive related genes, the biological characteristics remained unchanged after 50 passages^[41,42]; recently, a high metastatic potential HCC cell line-MHCC97 was also established, and lung metastasis appeared after inoculation into liver of nude mice.

Molecular mechanism of HCC metastasis: At the author's institution, the followings were found to be positively related to HCC invasiveness: p16 (CDKN2) mutation, p53 mutation, p21 (ras), mdm-2, c-erbB-2, TGF EGFR, VEGF, MMP-2, ICAM-1, etc; whereas the followings were negatively related to invasiveness: nm 23-H1, Kai-1, TIMP-2, E-cadherin, etc. However, the difference between expression in small HCC and large HCC was not significant, indicating that even small HCC still facing the problem of biological characteristics^[43-54].

Experimental intervention of metastasis: Experimental

interventions have been done in metastatic model of human HCC in nude mice (LCI-D20), including: antisense H-ras, anti-HBx/anti CD3 bispecific antibody, BB94-inhibitor of MMP, a ntiangiogenic TNP-470, Suramin, CAI, and antisense VEGsF, and inhibition of tumor growth as well as inhibition of lung metastasis were observed^[55-60].

PROSPECTS IN THE 21ST CENTURY

The followings are important issues to be studied: the "cost effectiveness" of screening, early diagnosis of AFP nonproducing HCC, the better combination mode of surgery and other therapies, the problem of inadequacy of regional cancer therapies for HCC, the balance of inadequate-treatment and over-treatment, the high recurrent rate after curative resection, the multicentric origin of recurrence, the invasion to blood vessel and distant spreading, the coexisted Child C cirrhosis, etc. It is expected that molecular biology will certainly play an important role, however, it also take time to translate into clinical application. Therefore, prospective control trial using clinically available approaches, particularly multimodality combination treatment, remains important to improve prognosis of HCC.

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Present status of biliary surgery in China

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Progresses of biliary surgery in China in recent years were focused on the epidemiology of biliary stone diseases, the development of laparoscopic surgery, diagnosis and treatment of biliary diseases, and bile duct cancer.

CHOLELITHIASIS

In the 1950s, one of the characteristics of biliary tract stone in China was the frequent occurrence of primary bile duct stone which accounted for 50% of the total stone cases. The relative incidence of intrahepatic stones was about 38%, as was found postmortemly. The first national surgery of clinical epidemiology of cholelithiasis in 1983-1985, revealed that the relative incidence of primary bile duct stones lowered to 36.2%, coinciding the increasing incidence of gallbladder stone since the 1970s. Ten years later, tendency of changing pattern of biliary cholelithiasis became even more conspicuous as the relative incidence of gallbladder rose from 69.3% to 78.9% in 1992, while that of primary duct stone further lowered from 30.7% to 21.1%. Furthermore, in some metropolitan cities in China, such as Beijing and Shanghai and in Northern China, the relative incidence of intrahepatic stone fell to 4.5%, 4.8% and 4.1%, respectively.

However, intrahepatic lithiasis is not a vanishing disease in China. It is still prevalent in most of the inland provinces of China, i.e. in Kuangxi Province the relative incidence of gallbladder stone increased from 12.7% to 19.8% within 10 years, while that of primary bile duct stone dropped from 55.2% to 41.8%, intrahepatic lithiasis is still the challenging problem of daily practice of surgery.

Formerly, we were accustomed to the late manifestations of advanced intrahepatic lithiasis such as biliary obstruction, infection and widespread liver parenchymal damage. But, at the present, owing to improved nutritional status of the people, the improved health care and the early use of antibiotics, especially when early diagnosis of intrahepatic lithiasis is no more difficult with the modern modalities of imaging diagnostic facilities, more and more early cases of intrahepatic stones were recognised at their early stage. Intrahepatic stone formation at its early phase was commonly a localized disease, most often found in the hepatic segments VI, VII and II, and the other part of the liver and the extrahepatic bile duct was normal. Therefore, surgery of intrahepatic stone at its early phase may offer a cure instead of only symptomatic relief.

Hepatic lobectomy has been proved to be the most effective approach for treatment of intrahepatic lithiasis, which has been the routine procedure in cases of left-sided disease. Hepatic lobectomy was reported as the chief operation in 11%-31%, averaging 18%, in the recent literatures of China. But in some of the hepatobiliary surgical centers, lobectomy was used in about 50% of the cases operated upon. However, as to the kind of hepatic resections, most of them were confined to left-sided hepatectomy, especially the left lateral lobe or segment of the liver. Resection of the right lobe or segment of the liver was unusual, at most to about 10% of the total resections. This may be the reason responsible for the unsatisfactory result in the treatment of right-sided intrahepatic stones. Recently, we advocated the adoption of "systemic regular segmentectomy" in the treatment of intrahepatic stones in which regular segmentectomy may be performed on the right liver as well as on the left side or on both sides.

Cases of hepatic bile duct carcinoma associated with intrahepatic lithiasis was reported to be increasing over the recent years. The incidence of hepatic duct carcinoma as a complication of intrahepatic lithiasis ranged from 0.36% to above 10%, the average figure of 6 series recently reported in Chinese literature was 2.4%. Our records was that bile duct cancer occurred in 1.5% of all the operations for intrahepatic stones, in some of the cases, the intrahepatic ducts were free from stones, but, however, bile stasis and chronic infection were found. This fact also supports the concept that intrahepatic stones needs to be treated early and radically.

INJURY AND STRICTURE OF THE EXTRAHEPATIC BILEDUCT

Since the first total cholecystectomy performed in 1882, open cholecystectomy has become one of the most frequently adopted operations and was considered as the "gold standard" of surgical treatment of gallstones. In Roslyn (1993) report, the one-year overall mortality rate of 42 474 open cholecystectomy for stone was 0.17% in North America, with a bile duct injury rate of 0.2%. In a nationwide survey conducted by the Chinese Association of Surgery the operative mortality rate of open cholecystectomy for gallstone was 0.16%.

Laparoscopic cholecystectomy carried a somewhat higher bile duct injury rate than that of conventional cholecystectomy. Laparoscopic cholecystectomy was first introduced to China in 1991. In a collective review of Chinese literature from 1991-1995, the bile duct injury rate was 0.32% and the biliary complications rate was 0.6% in 39238 cases of laparoscopic cholecystectomies. In fact, the real incidence of bile duct injury may be higher than that reported.

At present, in the era of laparoscopic cholecystectomy, management of bile duct injuries and the late biliary strictures deserved special attention because of the high level injury, the thermo-coagulative nature of injury, and the extensive tissue injury often complicated with vascular damage were the prominent features peculiar to laparoscopic bile duct injuries. Such complicated injuries should be handled by an experienced biliary surgeon at the first setting.

SURGERY OF BILIARY TRACT CANCER

In recent years, cases of biliary carcinoma appeared to be increased. A nationwide survey organized by the Chinese Association of Surgery in 1989 showed that 75.2% were bile duct cancer in 1098 cases of extrahepatic biliary cancer operations, while 24.8% were gallbladder cancer. In a recently reported series from Xi'an Medical

University Hospital in China, carcinoma of gallbladder occurred in 72.4%, and bile duct carcinoma in 27.6%. This reflected the variations of disease prevalence in different parts of China.

Carcinoma of hilar bile duct is the most frequent site of extrahepatic bile duct cancer in China. The resectability rate of hilar bile duct cancer was about 10% generally in the past, but has been increased to about 60% since 1990 with a low operative mortality rate of below 5%. This was due to the improvement of surgical technique as well as the employment of modern imaging modalities for early diagnosis. The result of surgical treatment of hilar bile duct cancer is still far from satisfactory. A series of 66 cases of hilar bile duct cancer reported from the General Hospital of PLA, the cumulative 5-year survival rate after resection was 13.2%.

Primary carcinoma of the gallbladder is a more common malignancy of the biliary tract in the Northern part of China. In China, carcinoma of gallbladder accounted for 1.1%-4.0% of gallbladder operations, with a median of 2.0%. In the 2300 surgical cases of gallbladder cancer, the peak age incidence was 57 years, with a female to male ratio of 2:1, and 60% of the cases were complicated with gallbladder stones. Recently a few cases of extended resection including hepato-pancreaticoduodenectomy were reported, but this can hardly change the poor outlook of the disease as a whole.

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Is there a pathologic basis for gastrointestinal dysmotility?

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INTRODUCTION^[1-10]

Based on their high prevalence in clinical practice, there has been an understandable tendency, in the area of gastrointestinal motility, to focus on "functional" disorders. Thus, considerable time and energy has been expended on the performance, analysis and interpretation of motility studies in such disorders as non-cardiac chest pain, non-ulcer dyspepsia (NUD), irritable bowel syndrome (IBS) and idiopathic constipation. I believe it is fair to say that the role of motility in these disorders remains debated and controversial. Progress in this area has been limited by the lack of truly objective criteria for the definition of these disorders—none is based on a clearly defined biochemical or pathological abnormality. The utilization of these disorders as templates for the evaluation of motility tests is clearly, therefore, fraught with problems.

If a definition for a disorder is not uniform, then different study population may not be comparable. Given the non-specificity of many of the symptoms experienced by these patients, it is also likely that each category, whether it be IBS or NUD, includes a heterogeneous collection of patients—a factor that may exert a significant influence on the likelihood of finding a motility "abnormality" in a particular study group. Studies in this area are also hampered by the apparent ubiquity of epi-phenomenology. Thus, it is often difficult to unravel the confounding effects of stress, anxiety, depression, patient expectations and various therapeutic interventions, and to truly decide what motor abnormalities are primary or secondary. Therapeutic trials in disorders such as non-ulcer dyspepsia or the irritable bowel syndrome have led to the

greatest frustration. It should come as no surprise that trials of therapy in a disorder whose definition is difficult and which may encompass entities of varying pathophysiology often lead to inconclusive and disappointing results. When such studies are performed in major referral centers, the influence of selection bias and, in particular, of "learned illness behavior" must be borne in mind—the patient studied in these centers may be very different from those seen in the community. The motility literature is dominated, therefore, by conflicting data on the role of dysmotility, on the value of various types of motility studies and the efficacy of motility-altering drugs in functional disorders; syndromes which share a lack of a clearly defined basic pathology. The goal of this presentation is to remind the audience of those motility disorders which have a pathologic basis, whose pathophysiology is understood either in part or in whole, and which may serve as better templates for the evaluation of motility and its therapy.

ENTERIC NEUROPATHOLOGY^[11-27]

Before describing those "organic disorders" associated with dysmotility, it seems only reasonable to discuss, in brief, the techniques of enteric neuropathology. It must be admitted, from the outset, that this is very much a minority sport. Several technical problems have limited our ability to examine pathological tissue from the muscle or nervous system of the gut. First and foremost, any complete evaluation of intestinal muscle or nerve must be performed on a full thickness specimen of the gut wall. Up until recently, this has required open laparotomy and full thickness biopsy or examination of tissue removed during the course of a gastrointestinal surgical procedure. More recently, some centers have developed the technique of laparoscopic intestinal biopsy, and validated its utility in the diagnosis of intestinal myopathy and neuropathy. This procedure has usually been performed in the context of the laparoscopic placement of intestinal feeding or decompression tubes in patients with severe dysmotility syndromes. Some have raised concerns regarding the safety of this procedure, cautioning of the possible development of post operative adhesions and related obstruction. A second major hurdle relates to the processing and interpretation of the biopsy material. While the morphology of the intestinal muscle layers can be evaluated using conventional hematoxylin-and-eosin-stained sections, this technique is inadequate for the study of enteric neurons. Large amounts of fatty constituents of neurons are lost during dehydration, clearing, and paraffin infiltration of tissue for hematoxylin-eosin histology, leading to artifactual vacuolization and other defects, and axonal and dendritic processes cannot be seen. Traditional transverse sections provide a poor demonstration of the myenteric and submucosal plexuses—these are best visualized when seen in a flat, en face view. Specimens for the evaluation of enteric neurons need, therefore, to be specially prepared and mounted. Staining of these sections is particularly important and potentially problematic. The standard technique in use is the silver method. The gut is fixed

for a week or two in buffered formalin, then impregnated with a strong silver nitrate solution, the excess silver washed out with formalin and the bound silver developed with strong ammoniacal silver nitrate or silver diamine. This is not an easy technique—if successful, the entire plexus is stained brown against a lighter muscle background. It is evident from the above that enteric neuropathology is a highly specialized and technically demanding technique. Not surprisingly, few centers can provide this level of expertise, and, in particular, are sufficiently experienced to interpret these sections. This remains a further limitation to progress in this area. There is a great need for an expansion of availability of these enteric neuropathological services and for standardization of their interpretation. Until this is achieved, enteric neuronal pathology will remain beyond the reach of most physicians and their patients. Though not included as a standard component of diagnostic enteric neuropathology, considerable information has recently been provided by immunohisto-chemical studies of the enteric nervous system. Using specific antibodies, deficiencies of various neurotransmitter substances often described in a number of clinical disorders. This again, however, is a technically exacting technique.

Parallels between the enteric and central nervous systems are increasingly appreciated—the description of a variety of pathological findings in the autonomic and enteric nervous systems in Parkinson's disease has provided a clinically relevant example of such parallelism.

WHAT CAN WE LEARN FROM “ORGANIC” DYSMOTILITY SYNDROMES?

It should be no surprise, based on the above, that detailed descriptions of enteric myopathies or neuropathies remain limited. More commonly, these organic disorders are defined on the basis of the occurrence of a dysmotility syndrome in a patient with a clearly-defined disease process. Typical examples of the latter would include post-operative ileus, Ogilvie's syndrome and the various manifestations of diabetic gastroenteropathy. Important lessons regarding the pathophysiology of dysmotility can also be gleaned from iatrogenic motility disorders (whether induced by medications, radiation therapy, or surgical intervention) and various models of experimentally-induced dysmotility.

Lessons from the Classics (and the Tropics)^[28-52]

Perhaps the most detailed information on the basic pathophysiology of motor disorders has been gleaned from three rather rare disorders, namely, achalasia, infantile hypertrophic pyloric stenosis and Hirschsprung's disease. Each of these disorders has been characterized by neuronal loss within the affected segment, and when examined in further detail by the specific dropout of VIP- and NO-containing neurons. Loss of nitrergic neurons appears to be highly characteristic of the aganglionic segment in both achalasia and Hirschsprung's disease. It is important to remember that very similar changes have been described in a much more common disorder, on a worldwide basis, namely Chagas' disease. We have much to learn from this disorder which affects many millions, especially in South America.

Further abnormalities, of particular interest to the physiologist and pathophysiologist, have been demonstrated in pyloric stenosis. These findings relate to a group of highly specialized cells known as the interstitial cells of Cajal. These cells, which appear to be of fundamental importance in motility through their ability to generate the basic electrical rhythm of the intestine, have been the subject of considerable interest in recent years. A “knockout” animal model has been developed whereby interstitial cell development can be arrested—this leads to the loss of electrical rhythmicity throughout the intestine, but does not necessarily impair the generation of contractions or the peristaltic reflex. Now, two groups have reported a deficiency of interstitial cells in the hypertrophied segment in pyloric stenosis.

Studies in Hirschsprung's disease have provided additional insights. It is evident for example, that there is some overlap between Hirschsprung's disease and that group of disorders referred

to as intestinal neuronal dysplasia. Though the hallmark of the latter disorder is hyperganglionosis rather than aganglionosis, affected individuals have severe dysmotility symptoms usually manifested by intractable constipation. It is also clear that in some patients with “Hirschsprung's disease” the aganglionosis may extend to involve the entire colon or, indeed, the small intestine. Similar overlap has been suggested between achalasia and the pseudo-obstruction syndromes.

The description of these various subtle morphological and immunohistochemical abnormalities in these three disorders does not, of course, necessarily imply that these are the primary defects. It has been suggested, for example, that the neuronal injury in both achalasia and Chagas' disease is based on an immune mechanism and specific autoantibodies have been described. Others have described autonomic dysfunction in achalasia and others still have suggested a viral trigger. Given the, albeit anecdotal, association between various “dysmotility” disorders and prior infective episodes, these observations are of considerable interest, and may yet provide important clues to the etiology of a wide variety of common disorders. Both achalasia and Hirschsprung's disease may also occur in the context of genetically-based disorders with multi organ involvement. Of special interest is the recent description of genetic markers for Hirschsprung's disease. Mapping studies in both man and animal models have suggested that specific genes may be involved: mutations in the RET protooncogene and the endothelin-B receptor gene have been described in an autosomal dominant (with incomplete penetrance) and recessive type of Hirschsprung's disease, respectively. Mutations of the RET protooncogene have also been described in MEN 2A, MEN 2B and sporadic medullary and papillary thyroid carcinoma. These genetic abnormalities are thought to result in impaired neural crest migration, colonization or differentiation. Hirschsprung's disease is now regarded as an example of a neurocristopathy—disorders of the neuronal crest: from the above genetic studies, a basis for the overlap of Hirschsprung's disease with other dysmotility syndromes is revealed.

It is clear, therefore, that highly specialized, sophisticated and focused studies on these, albeit rare but well-defined disorders, are of great importance and hold considerable promise towards an understanding of dysmotility syndromes in general. In these disorders, where the clinical definition is agreed, manometric criteria are well-defined and pathologic diagnosis is possible, it may well prove possible to define, at the most basic level, relationships between molecular abnormality, physiologic dysfunction, and clinical presentation.

Sizing up the Syndromes^[53-106]

At the next level, from a pathologic point of view, are those organic disorders of motility which do not possess a uniform pathology but are defined clinically on the basis of a uniform abnormality of function. These include:

- Diffuse esophageal spasm
- Gastroparesis
- Intestinal pseudo-obstruction
- acute (ileus)
- chronic
- colonic (Ogilvie's syndrome)
- Megacolon

Each of these syndromes includes a wide variety of disorders of varied etiology—what they share is a common abnormality of motor function which can be reproducibly demonstrated by studies of gut anatomy or function (including manometry). For some, such as the many motor manifestations of scleroderma or amyloidosis, a pathologic basis is evident; for others, such as those with post-operative ileus, it is assumed, and for others still the functional abnormality such as gastroparesis remains unexplained. It is in this latter category that we begin to move into the territory of functional disease and so to consider the possible contribution of motor dysfunction to otherwise unexplained symptomatology. For the moment, however, we will focus on those individuals with one of the above syndromes whose symptoms appear to have an organic basis.

Diffuse esophageal spasm (DES) is a rare disorder of esophageal

motor function whose etiology remains undefined. Many patients with "spasm" and more non-specific motor disorders have underlying reflux—an important pathologic basis for many instances of non-obstructive dysphagia. A recent report provided some fascinating insights into the pathophysiology of spasm by demonstrating the induction of DES by recombinant human hemoglobin, a potent inactivator of nitric oxide!

Because of the relative accessibility of gastric emptying studies, gastroparesis is probably the most frequently defined abnormality of motor "function". Gastroparesis, in of itself, is a nonspecific finding and may not imply a primary disorder of gastric motor function. Several organic dysmotilities, such as diabetic gastroenteropathy, include gastroparesis as a prominent feature. Studies in this and other organic gastropareses have served to emphasize the complexity of gastric motor function and have emphasized the importance of regional differences in gastric motility as well as the role of visceral afferents, central input and "long" reflexes in the regulation of gastric contractility. It is becoming evident that gastroparesis may be inadequate to describe gastric motor dysfunction in many circumstances; in diabetes, for example, emptying may be accelerated or delayed; following vagotomy disturbed gastric compartmentation may be more prevalent than altered emptying. The inadequacy, up until recently, of our methodologies for the evaluation of any gastric motor function other than emptying may go some way towards explaining our inability to explain many symptoms suggestive of foregut distress.

The term *chronic intestinal pseudo-obstruction* refers to a diverse and heterogeneous group of disorders with somewhat similar clinical features regardless of etiology. Patients typically present with repeated episodes of nausea, vomiting and abdominal pain and distention. On clinical grounds, they are often suspected initially of having a mechanical obstruction. Many patients are subjected to more than one diagnostic laparotomy before the correct diagnosis is even considered. Stasis may lead to bacterial colonization, with the subsequent development of diarrhea, steatorrhea, weight loss, and nutritional problems. In some individuals, constipation may be prominent, and in acute episodes, abdominal distension may be striking. This syndrome may be the intestinal manifestation of a systemic disorder (a secondary pseudo-obstruction) or may reflect a primary disorder of the intestinal musculature or its neural apparatus (primary chronic idiopathic intestinal pseudo-obstruction, or CIIP). Whether the disorder is primary or secondary, other parts of the GI tract may be involved, as well as extra-intestinal organs, in particular the urinary tract.

The pseudo-obstruction syndromes provide several insights into our understanding of gastrointestinal dysmotility. Some disorders are based on a primary pathologic abnormality of intestinal muscle and/or nerve. Of the many causes of pseudo-obstruction, scleroderma and the other mixed connective tissue diseases are by far the most common. In its earlier stages, sclerodermatous involvement of the small intestine results in motility changes indicative of a neuropathic process, and recent studies suggest an autoimmune-mediated injury to intestinal nerves. In the later, much more familiar stages, the predominant features are those of a diffuse myopathic disorder; biopsies demonstrate the widespread replacement of the circular muscular layer, in particular, by fibrosis. Manometric studies demonstrate marked hypoactivity, and radiologic studies dilatation of the intestine with megaduodenum and megacolon being particularly prominent. In its advanced stage, scleroderma serves as an excellent model of an intestinal myopathy.

The range of neuropathic disorders that may result in the pseudo-obstruction syndrome provide considerable insights into the various levels at which intestinal motility is controlled, and may, therefore, be potentially disrupted. These disorders include those well-described, though very rare, disorders where the pathology lies within the enteric nervous system itself; so-called visceral neuropathies. Disorders of the autonomic nervous system (e.g., diabetes mellitus, familial dysautonomia, ganglioneuromatosis and paraneoplastic neuropathy), disorders of the spinal cord and central nervous system (e.g., brain stem and spinal cord space-occupying lesions) and a variety of hormonal disorders (hypothyroidism, hypoparathyroidism) may also result in CIIP. Through actions at

various levels, a variety of external agents may also cause a pseudo-obstruction syndrome. Important and common examples include radiation enteropathy and the effects of such drugs as opiates, anticholinergics and antineoplastics (e.g. vincristine).

Acute *gastroparesis*, *ileus* and *Ogilvie's syndrome* represent the various manifestations of acute intestinal pseudo-obstruction. Gastroparesis is, perhaps, the least common of these disorders, but is often overlooked, as gastric distention may not be clinically evident, especially in the sedated or anesthetized subject. It is important to remember that acute gastric dilatation has also been reported following blunt abdominal trauma, and has been commonly described among transplant patients, being reported in 24% of heart/lung transplant recipients, for example.

Ileus has come to be regarded as a physiologic response to surgery, and abdominal surgery, in particular—its duration being well related to the extent of the intra-abdominal procedure. The pathogenesis of post-operative ileus, has been extensively investigated. Such investigations have again highlighted the complexity of the control of motor activity. Clinical and experimental studies have, for example, revealed evidence for a role for the central nervous system (through corticotrophin-releasing factor), autonomic neurons (and especially sympathetic hyperactivity), enteric neurons (through the release of inhibitory neurotransmitters in the gut wall), and most recently for afferent neurons. With regard to the latter, a role for both splanchnic, capsaicin-sensitive afferents and CGRP have been proposed. The primacy of any or all of these mechanisms has not been established. It should come as no surprise, therefore, that therapeutic maneuvers based on a single mechanism have proved disappointing.

Ileus is being increasingly recognized in non-surgical conditions and has been reported in a variety of acute neurological conditions, including spinal trauma and acute neuropathies (such as the Guillain-Barre syndrome and porphyria). Ileus is also a feature of ischemic disorders of the intestine, and is a cardinal manifestation of mesenteric ischemia. Ileus is being increasingly recognized as a manifestation of severe inflammatory disorders of the gastrointestinal tract, especially in the context of transmural inflammation. A classical example here is severe graft-versus-host disease—in this condition, the development of ileus is most ominous. Ileus may also be seen in relation to apparently remote events such as retroperitoneal hemorrhage, infection or tumor, disorders of the thoracolumbar cord (such as fractures or tumors), and as a non-metastatic manifestation of a variety of tumors.

Though also seen in the post-operative state, *Ogilvie's syndrome* is more commonly seen, nowadays, in the non-surgical patient. It is particularly associated with disease, trauma or surgical procedures in the retroperitoneum, hips, pelvis and lumbosacral spine. Colonic ileus has also been described in association with gynecological surgery, pregnancy, open heart surgery, and cesarean section. As with other forms of ileus, Ogilvie's syndrome has also been described in the severely ill patient, for example, those with severe burns or overwhelming infections. Many factors may contribute to the evolution of both ileus and Ogilvie's syndrome, including electrolyte abnormalities, analgesics and anticholinergic medications.

All of this information indicates that for ileus of any form, where no obvious cause is evident, possible associated lesions, such as pneumonia, spontaneous bacterial peritonitis and intra-abdominal abscess as well as disease of the retroperitoneum, lumbosacral spine, hips and pelvis should be sought.

New Horizons—Infections and Immunity^[107-128]

Of considerable clinical importance, several recent studies have suggested an important role for various infections in the pathophysiology of dysmotility syndromes. While both acute and chronic syndromes have been described in association with a variety of infective agents, acute disorders, such as gastroparesis, ileus and megacolon have been best described. Clinicians have recognized for some time that many acute illnesses, including acute viral infections, may be associated with the development of symptoms suggestive of gastric motor dysfunction, and a post-infective irritable bowel syndrome is well recognized, although poorly defined.

In some instances, viral infections of the gastric mucosa have

been directly linked with disturbed emptying. Important examples here include those instances of cytomegalovirus and herpes simplex virus gastritis, which may occur in immunocompromised patients. The author has seen a number of liver transplant patients with a profound gastroparesis syndrome in whom cytomegalovirus has been identified in gastric mucosal biopsy specimens, and who have responded dramatically to gancyclovir therapy alone. CMV has been isolated from intestinal ganglion cells and has also been shown to result in a severe ileus and meconium-like syndrome in neonates and a chronic intestinal pseudo-obstruction syndrome in heart/lung transplant patients. Reports of ileus and Ogilvie's syndrome in relation to disseminated herpes zoster virus infection have also been described. Again, in immunocompromised patients, HZV has been shown to result in infarction of the celiac sympathetic ganglia. Following oral inoculation, herpes simplex virus type 1 has been shown, in immunodeficient mice, to lead to prolonged sustained replication of the virus in the enteric nervous system of the esophagus and stomach as well as in the nodose ganglion. In this particular model, this virus, when administered orally, can result, therefore, in long-term latent infection, with replication confined to the enteric and autonomic nervous systems. This is a particularly intriguing finding, and provides a pathologic basis for a possible role for an initial viral infection in a prolonged motor disorder. The previously mentioned association of viral infections with achalasia is another example of a possible role for a viral initiation. A number of case studies have reported gastrointestinal motor dysfunction in non-immunocompromised patients in relation to other viral infections. Although the evidence for such an association are somewhat inconclusive and a direct cause and effect relationship remains to be established, the suggestion that common viruses, such as members of the herpes simplex virus family, might evoke, in susceptible individuals, dysmotility (through effects on the central nervous system, autonomic supply or the motor apparatus of the gut) is extremely intriguing and deserving of further study. Dysmotility has also been reported in relation to salmonella and strongyloidosis infections, Legionnaire's disease and spontaneous bacterial peritonitis.

Again, at an experimental level, considerable evidence has been advanced to support a role for inflammatory mediators, released from immune cells in the gut wall, in the regulation of smooth muscle and enteric nervous function. It has been suggested, for example, that such interactions might explain motor abnormalities reported in patients with inflammatory bowel disease as well as in infective and parasitic diarrheas.

CONCLUSION

I would suggest that there is ample evidence for a pathologic basis for many dysmotility syndromes. In some, albeit rare, instances, characteristic pathological abnormalities have been defined and we are well on our way to an understanding of pathophysiology. In many other disorders, enteric, neural or muscle pathology is either undefined or has not been examined, yet there is considerable evidence to invoke an organic basis for dysmotility. These disorders have shown us that a wide variety of disorders may affect intestinal muscle and nerve, and may also influence motor function through actions in the autonomic nervous system, spinal cord and central nervous system. Circulating hormones and motor-active peptides also have a role. An important role for infective agents, and viruses in particular, is being increasingly advanced, and mechanisms whereby they may exert their effects are being increasingly understood. In this way, well-defined motility syndromes, such as gastroparesis, ileus, Ogilvie's syndrome, chronic intestinal pseudo-obstruction and megacolon are being increasingly investigated and, in many instances, their etiology understood. Advances in basic investigational tools, as well as increasing access to intestinal tissue, may well provide a "pathologic" basis for at least some of the patients now included under the umbrella of functional disorders, such as non-ulcer dyspepsia and the irritable bowel syndrome.

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Gene therapy and liver diseases

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INTRODUCTION

We have shown previously that cell-surface receptors have been used as natural internalization sites for targeting genes to hepatocytes^[1]. This targeting is based on the fact that parenchymal liver cells are the only cells that have large numbers of high affinity receptors that can recognize galactose-terminal(asialo-)glycoproteins. Binding of these glycoproteins by the receptor leads to invagination of the plasma membrane and internalization of the ligand- receptor complex in membrane-bound vesicles.

METHODS AND RESULTS

A carrier system was developed consisting of two components: (1) an asialoglycoprotein ligand covalently bound to (2) a polymer containing multiple positive charges, a polycation. The asialoglycoprotein component provided the recognition signal for hepatocyte targeting, while the positively charged polycation served to bind DNA in a strong, non-damaging electrostatic manner to form a soluble protein-DNA complex^[2].

To determine whether normal genes could be targeted *in vivo* to correct metabolic dysfunction in genetically defective animals, the WHHL rabbit model for familial hypercholesterolemia was used. A plasmid carrying a full-length cDNA for the human low density lipoprotein (LDL) receptor was constructed using regulatory

elements from the mouse albumin gene inserted upstream to drive the LDL receptor gene. The plasmid was complexed with the carrier and injected intravenously into rabbits. Cellular DNA extracted and analyzed for the presence of human LDL receptor sequences demonstrated approximately 1000 copies of plasmid per cell, 10 min after injection. These levels declined progressively, and by 48 h plasmid DNA was less than 0.1 copies/cell. The transcriptional activity of the recombinant gene was analyzed by RNase protection assay for the presence of human LDL receptor transcripts. Exogenous LDL receptor mRNA was detected at 4 h, reached a peak at 24 h and decreased to undetectable levels by 72 h after transfection. Maximal levels of LDL receptor mRNA were found at 24 h and estimated to be 2%-4% of normal endogenous levels. In order to determine the metabolic effects of hepatocyte-directed gene transfer *in vivo*, WHHL rabbits injected with complexed LDL receptor gene or CAT gene were analyzed for changes in total serum cholesterol. Administration of the LDL receptor gene complex resulted in a rapid. But transient decline in serum cholesterol that lasted 6 d. The drop in cholesterol levels was maximal at 2 d post-injection and was 25% to 30% of pretreatment values^[3].

Based on the known requirement of migration of endosomal vesicles on microtubules, a microtubule-disrupting drug, colchicine, was administered to try to block lysosomal degradation of targeted DNA. The gene for normal glucuronyl transferase in a targetable complex was injected intravenously following a single colchicine injection into Gunn rats which possess defective glucuronyl transferase enzyme. This resulted in substantial decreases in serum bilirubin and production of bilirubin conjugates in bile that lasted at least 60 d^[4].

It was recognized that the carrier system could potentially target single-stranded DNA in the form of antisense oligomers. Because of the remarkable specificity of the action of antisense DNA in the inhibition of the synthesis of specific proteins based on hybridization of antisense to target mRNA, it was hypothesized that receptor-mediated delivery of antisense DNA specific for hepatitis B viral (HBV) mRNA sequences could inhibit viral gene expression in target cells. A 21-mer oligo DNA sequence complementary to the polyadenylation signal for human hepatitis B virus (HBV) was complexed to a soluble DNA-carrier system. A cell line, HepG2 (2.2.15) that possesses asialoglycoprotein receptors^[5] and which is permanently transfected with hepatitis B virus (ayw subtype) was exposed to complexed antisense DNA or controls. In the presence of complexed antisense DNA, the concentration of hepatitis B surface antigen in medium was decreased by 80% by day 1, and by greater than 95% through the 6th day compared to untreated cells. There was no significant increase in surface antigen concentration in the presence of complexed antisense DNA after the first day of exposure. This inhibition was blocked by competition with an excess of free asialoglycoprotein. Protein secretion from cells was not affected and could not account for the decrease in HBV surface antigen concentration in the medium after exposure to antisense DNA. Also, total protein synthesis remained unchanged by exposure to complexed antisense sequences under identical conditions.

Finally, HBV DNA in the medium and cell layers after 24 h exposure to complexed antisense sequences was 80% lower than in controls. Exposure of cells to a random 21-mer oligo DNA sequence under identical conditions failed to alter HB V surface antigen concentration or HBV DNA in medium or cells^[6].

Bartholomew *et al.*^[7] showed that targeted delivery of an antisense sequence against the poly A signal and 5'-upstream region of Woodchuck Hepatitis Virus (WHV) using a complex with an ASGP-based conjugate in a woodchuck hepatitis model, significantly decreased the virus particles in bloodstream by 5 to 10 fold, and this decrease was maintained over two weeks.

The DNA delivery system was tested to determine whether antisense oligonucleotides against the 5'-NTR of HCV genome could be targeted to inhibit HCV gene expression. The strategy was based on the fact that the 5'-Non-Translated Region (NTR) of Hepatitis C Virus (HCV) contains important elements that control HCV translation. Antisense oligonucleotides directed against a sequence in the internal ribosomal binding site of the NTR (Anti-III), and a portion of the NTR (Anti-IV) overlapping the core protein translational start site of HCV were prepared. In transient transfections of a plasmid containing a luciferase gene immediately downstream from an HCV NTR insert, oligonucleotides Anti-III and Anti-IV in the form of asialoglycoprotein-polylysine complexes were administered to Huh7 cells, and luciferase activity generated by CMV HCVluc measured. Anti-III inhibited luciferase activity by 75%, and 99% at 0.01 $\mu\text{mol/L}$, and 0.1 $\mu\text{mol/L}$, respectively. Similarly, Anti-IV inhibited luciferase activity 88%, and 99% at 0.01 $\mu\text{mol/L}$ and 0.1 $\mu\text{mol/L}$, respectively. In cell lines stably transfected with CMV HCVluc plasmid, complexed Anti-III inhibited luciferase activity in Huh7 cells by 20% at 10 $\mu\text{mol/L}$ and 85% at 60 $\mu\text{mol/L}$, and was compatible by an excess asialoglycoprotein^[8].

CONCLUSION

A DNA carrier system can target polynucleotides to hepatocytes to provide new gene expression or to inhibit endogenous gene expression in a cell-specific manner.

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Current concepts of the pathogenesis of inflammatory bowel disease

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Over the past decade, the focus of the etiopathogenesis of chronic inflammatory bowel disease (IBD) has turned toward defining a deficit in immune regulation. The problem inherent in presenting IBD as the result of a disordered immune system is the lack of knowledge of what is primary to disease itself and what is secondary to disease effects. Whether the immune system plays an initiating or a perpetuating role in the pathogenesis of IBD, it is the local immune response that causes the tissue damage and is responsible for the clinical presentation in IBD.

Presently, the utility of stratification of CD and UC into pathogenetically homogenous groups remains a question. Thus, CD and UC may be a heterogenous set of diseases with similar, yet distinctive, clinical phenotypes, and each subgroup may have different clinical courses and require different treatment approaches. The basis for this heterogeneity is at the primary genetic level, but the expression of genetic susceptibility requires environmental triggers. Despite extensive research, a common etiological agent has not yet been defined. Consequently, the primary events, which initiate the inflammatory response, remain unknown and treatment is empirical.

Clinical, epidemiological and experimental animal model studies strongly suggest an important genetic influence in the development of IBD. Approximately 10%-20% of patients with CD or UC have affected family members, with the highest risk among first-

degree relatives. Several studies have demonstrated a greater than expected concordance for site and clinical type within multiple affected relatives.

These results suggest the presence of genetically defined subsets of CD and allow classification of CD according to anatomical location, extent (localized or diffuse) and behaviour of disease (stenotic vs aggressive fistulizing disease), and operative history.

Genetic studies have recently identified alleles of genes that are associated with CD and UC. The Table shows recently described IBD susceptibility loci of interest, which involve chromosome 3, 6, 7, 12 and 16.

A number of genetically determined immune system characteristics, including HLA haplotype and IL-1ra, tumor necrosis factor, adhesion molecules, and complement subunit polymorphisms, have been associated with IBD. By using random microsatellite markers, it has recently been demonstrated that a specific area on chromosome 16 also possesses a gene or genes related to CD. Similarly, among patients with UC, several genes have increased associations and the allelic associations of each of these genes seem to vary depending on the ethnic background.

In recent years much has been learned from genetically engineered knock-out and transgenic rodents, in whom modulation of a single gene induces spontaneous colitis or increased susceptibility to experimental colitis.

The current concepts of the pathogenesis of IBD assume that Crohn's disease and ulcerative colitis are idiopathic disorders, which are immunologically mediated and caused by an unrestrained activation of the inflammatory response. This may be due to a defective immunosuppression. Patients with IBD also have abnormalities in epithelial antigen presentation. The inflammation may be driven by ubiquitous antigens, including normal resident luminal bacteria, bacterial products and toxins.

Three theories of IBD etiology are currently under consideration: (1) reaction to a persistent intestinal infection, (2) existence of a defective mucosal barrier to luminal antigens, and (3) a dysregulated host immune response to ubiquitous antigens. IBD may develop as an appropriate reaction to a persistent specific infection of the intestine. In CD infectious agents under current consideration include *Mycobacterium paratuberculosis*, paramyxovirus—more specifically measles or the association of measles and mumps or vaccination with MMR within the first year of life, and *Listeria monocytogenes*.

Most work has concentrated on the role of mycobacterial infection, but the absence of acid-fast bacilli and the fact that the granulomas in CD are non-caseating, have dampened enthusiasm. In serological and immunohistochemical studies on CD sera, the results are overlapping and less than 65% positive signals are reported using sensitive polymerase chain reaction (PCR) to detect *Mycobacterium paratuberculosis*.

Several investigators have suggested a possible etiological role for small cytopathic RNA virus. One group reported measles-like particles in cells adhering to the vascular endothelium in CD—and later, that the presence of primary antibodies identified their target antigens. Others have found no evidence of target RNA with PCR-

technique, and the hypothesis that measles vaccination is a risk factor has not been confirmed.

In UC, some evidence supports an etiological role in abnormal *Escherichia coli*. Abnormal bacterial metabolites and products may also contribute to the etiology of UC. Hydrogen sulfide, which is a product of anaerobic colonic bacteria, is found in increased concentrations in the colonic lumen of patients with UC. This agent selectively inhibits butyrate metabolism in colonic epithelial cells.

A defective mucosal barrier between the intestinal lumen and the circulation may allow unrestrained uptake of antigens and pro-inflammatory molecules.

Enhanced mucosal permeability has been observed in relatives of CD patients, with evidence of excessive response to NSAIDs in some asymptomatic family members. Specific abnormalities in mucosal barrier function have been found in patients with UC. These include reduction in colonic mucin species IV and alterations in mucin structure and lectin binding. Spontaneous colitis is observed in chimeric mice with defective epithelial tight junctions. Furthermore, reduced mucosal defence has been demonstrated in mice deficient of intestinal trefoil factor and excessive inflammation has been described in mice deficient of growth factors.

Finally, IBD may be the result of an abnormal host response to ubiquitous antigens.

In CD, the response may be elicited by luminal constituents, whereas in UC, an autoimmune response may be the causative factor. A disordered regulation of the mucosal and systemic immune system results in activation of a self-perpetuating inflammatory cascade.

The assumption that CD and UC are autoimmune diseases has very little immunological documentation. Most likely, anti-epithelial cell responses observed in UC are nonpathogenic, secondary responses. Anti-neutrophil cytoplasmic antibodies with perinuclear nuclear staining (pANCA), which are produced within the mucosa and present in 60%-70% of UC patients and 10%-15% of CD patients, may, however, be subclinical markers of disease phenotype. The population of UC patients producing pANCA has a stronger association with the MHC class II allele than the UC population as a whole. A second autoantibody, anti-Saccharomyces cerevisiae antibody (ASCA), has been observed in 50%-60% of CD patients, but only 10%-15% of patients with UC. The combination of genotyping with stratification by subclinical markers has provided the existing evidence of disease heterogeneity.

The most important pro-inflammatory and anti-inflammatory mediators may be involved in the pathogenesis of IBD. An imbalance between stimulating and inhibiting factors can start the process. For example, mice lacking T-cell receptors develop spontaneous colitis, whereas mice that do not produce the anti-inflammatory mediators, TGF β or IL-10, develop chronic intestinal inflammation.

An important immunoregulatory balance is the one between IL-1 and IL-1ra, an anti-cytokine that inhibits the activity of IL-1 by binding to IL-1 receptors without causing agonist activity. In IBD, the ratio of IL-1ra to IL-1 in mucosal biopsies is significantly decreased compared to the healthy controls—and the defective production of IL-1ra is genetically determined.

However, genetic susceptibility is modulated by environmental factors, because the incidence of IBD is altered when populations move to new locations, and colitis fails to develop in genetically susceptible rodents raised in a sterile environment. UC is negatively correlated to smoking, while CD is positively correlated to smoking. Other less well-documented influences, such as oral contraceptives, refined sugars, lack of dietary fibers, perinatal infections, domestic hygiene, and nonsteroidals (NSAIDs), have been implicated to explain the rising incidence of CD in the industrialized countries compared with third world environments.

The pathogenesis of IBD progresses through a series of steps. The initiating events are separate from the perpetuating events, so, in theory, intervention can be undertaken at either stage. The immunoregulatory abnormalities characteristic of IBD will amplify the inflammatory reaction, leading to tissue damage and finally the well-known clinical symptoms. Either an infectious or a non-infectious agent may start the process. Any agent capable of breaking the mucosal barrier or stimulating an inflammatory response can start the process in susceptible patients. Luminal microbial agents break through the mucosa, where they activate inflammatory cells, with

in turn release cytokines, arachidonic acid metabolites, platelet activating factor (PAF), reactive oxygen metabolites (ROMs), and nitric oxide, thus perpetuating the inflammatory response. The importance of luminal resident bacteria, such as *bacteroides species*, is illustrated by the lack of colonic and joint inflammation in germ-free transgenic rats (HLA-B27).

There is some evidence of dysregulation of pro and anti-inflammatory regulatory cytokines and T-helper lymphocyte subsets in chronic intestinal inflammation. The key aggressive regulatory cytokines appears to be IL-1, TNF α , IL-12, and interferon γ (INF γ), whereas the most important immunosuppressive regulatory molecules are TGF β , IL-4, and IL-10.

Other immunoregulatory abnormalities in IBD are related to the activities of the T_{H1} and T_{H2} subsets of T_H lymphocytes. T_{H1} cells mediate cellular immune responses and macrophage activation (lymphokine and complement production, and antibody-mediated cytotoxicity), whereas T_{H2} cells mediate hypersensitivity responses and down-regulate macrophages (B-cell and mast cell activation, IgG1 and IgE production, and eosinophilia). In experimental colitis, blockade of INF γ prevents inflammation, suggesting that T lymphocytes play an essential role in chronic colitis.

Patients with CD seem to have selectively activated T_{H1} lymphocytes, whereas those with UC have selectively activated T_{H2} lymphocytes, suggesting that the two disorders have different, genetically determined pathogenic pathways. Of clinical interest is the aggressive fistulizing and stenotic forms of CD seem to have different T_{H1} and T_{H2} lymphokine profiles.

The activation of macrophages and T lymphocytes results in outpouring of cytokines, which in turn amplify the inflammatory response by recruiting other inflammatory cells. Expression of adhesion molecules is increased, which allows adherence of neutrophils, monocytes, and lymphocytes to blood vessels and their migration through the vessel wall and interstitial matrix. The inflammatory response is further augmented as an increasing number of effector cells, epithelial cells, and mesenchymal cells are stimulated.

As cells are activated, they release soluble mediators of inflammation that induce tissue injury. Activated neutrophils and macrophages release for example TXs, LTs, and PAF—and in response to bacterial products, such as FMLP, lipopolysaccharides, and peptidoglycan-polysaccharide—reactive oxygen metabolites, which oxidize essential sulfhydryls, degrade proteins, carbohydrates, hyaluronic acid, and mucin, inactivate NADPH and NADH, peroxidize membrane lipids, and promote DNA breaks.

The clinical manifestations of IBD—diarrhea, bleeding, pain, and weight loss—are the end result of the pathogenic process described here.

In conclusion, CD and UC are two forms of intestinal inflammation with possible common genetic predisposition—and may be part of a spectrum, rather than two distinct diseases. Induction may be non-specific. Genetic susceptibility and uptake of bacterial products perpetuate inflammation. Genetic and environmental factors are critical, but neither alone is sufficient. Progression and resolution of CD and UC are dependent on the balance of pro- and anti-inflammatory mediators. Homeostasis or chronic inflammation depends on the balance between inflammatory luminal constituents and protective mucosal factors. Specific therapy directed at an immunoregulatory defect or an inciting agent could alter the disease course.

Current therapies, such as glucocorticoids and 5-aminosalicylic acid (5-ASA), inhibit raised concentrations of interdependent, soluble mediators of inflammation, which may amplify one another or have parallel effects. It remains, however, to be defined whether targeting multi-inflammatory actions or a single key pivotal process is the better therapeutic strategy. The type of new drugs being developed include (1) conventional pharmaceuticals, (2) receptor antagonists-agonists, (3) enzyme inhibitors, (4) bio-engineered compounds (monoclonal antibodies, chimeric-targeted toxins, receptor ligands-soluble receptors), and (5) gene therapy.

Future medical options for treatment of IBD should aim at removing perpetuating antigens, blocking entry of inflammatory cells, enhancing endogenous suppressive molecules or correcting genetic defects.

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Genetic disorders of bilirubin metabolism

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Bilirubin (BR) is a yellow pigment formed by enzymatic cleavage of haem (ferroprotoporphyrin) of haemoglobin and other haem-containing proteins. Its chemical structure is an open-chain tetrapyrrole exhibiting extensive internal hydrogen bonding which engenders a highly involuted conformation rendering the pigment totally insoluble in water. In the plasma, BR is firmly bound to albumin which carries it to the liver and transfers it to hepatocytes. In the liver cells' endoplasmic reticulum, BR is esterified with one or two molecules of glucuronic acid, a reaction catalyzed by the microsomal enzyme BR UDP-glucuronosyl transferase. This so-called conjugation breaks the pigment's internal hydrogen bonding which renders the glucuronide-conjugated BR watersoluble and excretable in bile (and urine).

Bilirubin in plasma is easily quantitated colorimetrically using van den Bergh's diazo reagent which reacts directly with conjugated pigment because both are water-soluble (direct diazo reaction). On the other hand, unconjugated, involuted BR is non-reactive unless ethanol is added to the reaction mixture (indirect diazo reaction). Measuring both pigment types is clinically useful because it permits to distinguish cholestatic jaundice from those forms of hyperbilirubinemia in which conjugation of BR with glucuronic acid is impaired. In healthy individuals, total plasma BR concentration ranges up to 1.2 mg/dL, of which approximately one-third is direct-reacting pigment.

In Gilbert's syndrome, unconjugated indirect-reacting plasma

bilirubin is raised to levels raging from 1.3 to 5 mg/dL. There is no evidence of overt hemolysis and individuals with this clinical anomaly enjoy excellent health and have an uneventful prognosis. Plasma bilirubin concentrations commonly exhibit spontaneous fluctuations, at times falling to levels below the upper limit of normal. Fasting, exercise, stress, intercurrent illness, menstruation or large blood extravasations tend to raise unconjugated pigment levels two to four times above normal, whereas certain drugs, such as phenobarbital, reduce it. Although long in doubt, the pathogenesis of Gilbert's syndrome now has been shown to consist of a number of different genomic mutations which result in reduced expression or in functional defects of the BR-conjugating enzyme UDP-glucuronosyl transferase in the liver. Such genetic anomalies have been detected in various ethnically different population groups with surprising frequency, far in excess of the incidence of clinically recognizable Gilbert's syndrome which generally ranges from five to twelve percent. In individuals exhibiting normal plasma BR concentration despite the presence of a genetic mutation in the hepatic BR UDP-glucuronosyl transferase gene, deliberate fasting or stress frequently raises the plasma bile pigment level transiently above normal. Crigler-Najjar disease type I and II are rare forms of severe unconjugated hyperbilirubinemia caused by inherited defects of hepatic BR UDP-glucuronosyl transferase. In type I, no BR conjugating activity is detectable in the liver nor is BR glucuronide present in bile. Plasma unconjugated BR levels commonly range from 25 to 40 mg/dL, and patients uniformly die from BR encephalopathy in childhood or adolescence. Liver transplantation, performed before the appearance of neurological lesions, is the treatment of choice. Several different structural mutations of the gene encoding BR UDP-glucuronosyl transferase have been reported, for which afflicted patients are homozygous. Blood-related family members with "Gilbert's syndrome" have been shown to be heterozygous for one of these mutations. Type II is a less severe form of the disease, with unconjugated hyperbilirubinemia intermediate between type I and Gilbert's syndrome. Residual BR UDP-glucuronosyl transferase activity is present in the liver, and bile contains some conjugated BR, most of it being BR monoglucuronide. BR encephalopathy is rare in Type II disease and induction of hepatic BR UDP-glucuronosyl transferase with drugs, such as phenobarbital, substantially reduces the plasma BR level. Structural mutations of the gene encoding the BR conjugating enzyme have been described, but the mode of inheritance remains unclear. Type II patients do not require treatment and their long-term prognosis is good. Low doses of phenobarbital or comparable enzyme inducers may be used for cosmetic reasons.

In Dubin-Johnson and Rotor's syndromes, the genetic defects cause impaired hepatic excretion of BR glucuronides, resulting in their accumulation in plasma and excretion in urine. Levels of plasma BR usually range from 2 to 6 mg/dL but are fluctuating and occasionally may rise to 20 mg/dL; at least half of the bile pigment is BR glucuronide. Patients with these benign conditions usually are asymptomatic, and except for mild icterus and bilirubinuria, abnormal physical findings are lacking and conventional liver

function tests yield normal results. Pruritus is absent as plasma bile acid concentrations are normal. The mode of inheritance in both conditions is autosomal recessive but the molecular mechanisms of the hepatic excretory defects are unknown.

In Dubin-Johnson syndrome, hepatic transport of organic anions, such as BR, sulfobromophthalein (BSP) and indocyanine green is severely impaired. After intravenous bolus injection, their initial plasma disappearance rate is normal, but after a delay, conjugated BR and BSP are reappearing in the circulation, reflecting hepatic regurgitation. The liver exhibits normal histology except for a unique black color caused by dark melanin-like pigment stored in the hepatocytes' lysosomes. Urinary excretion of coproporphyrin is quantitatively normal but as compared to controls, the ratio of coproporphyrin isomers I and III is reversed which is characteristic for Dubin-Johnson syndrome and allows identification of heterozygous carriers of the trait. The mechanism underlying this

unique pattern of coproporphyrin excretion is unknown.

Rotor's syndrome resembles Dubin-Johnson syndrome in that patients are asymptomatic, abnormal physical findings are lacking except for mild icterus, and with the exception of hyperbilirubinemia, conventional laboratory tests yield normal results. The liver exhibits normal histology without pigmentation. Total urinary coproporphyrin excretion is substantially increased with a modest excess of isomer I, as is seen commonly in other hepatobiliary disorders. Kinetics of the transport of organic anions in the liver differ from those of Dubin-Johnson syndrome in that after bolus injection, their removal from plasma is greatly delayed. However, their overall hepatic transport is only moderately impaired though calculated hepatic storage capacity is very low. In individuals heterozygous for the trait, values for urinary coproporphyrin and hepatic anion transport are intermediate between those of homozygous patients and healthy controls.

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Epidemiology and disease outcome in inflammatory bowel disease: observations from the European Collaborative Study

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INTRODUCTION

Epidemiology is concerned with the study of distribution and determinants of disease in the population. It can be also applied to study the course and prognosis of disease over time.

Ulcerative colitis (UC) and Crohn's disease (CD) are chronic, inflammatory diseases of the gut. They are more prevalent in the urban-industrial societies of America and Europe than in the populations of Africa, China or India. Environmental factors, lifestyle (diet, smoking, oral contraceptives) and genetic susceptibility are being investigated as possible causal factors in disease onset/or as determinants of disease behaviour and disease outcome.

EPIDEMIOLOGY OF IBD IN EUROPE

Over the years it has been suggested that the incidence of IBD is three or more times higher in northern than in southern Europe. The aim of the ECIBD study was to investigate the hypothesis of north-south gradient in a prospective epidemiological survey of disease incidence between 1991-1994. The study group consisted of investigators from 20 centres across Europe ranging from Iceland, Copenhagen and Oslo in the north to Heraklion and Palermo in the south. In the middle were centres from the Iberian peninsula, Britain, France, Germany, Ireland, and the Netherlands,

All participants designated a defined geographic area for the study and used uniform criteria of case definition, a common protocol for recording epidemiological and diagnostic data and obtained a "near" complete ascertainment of incident cases, in the respective defined areas, at the symptomatic stage of disease onset. All centres had high quality endoscopy, high quality radiology, and a well trained pathologist to establish proper diagnosis and separate case from non-case in UC, CD and indeterminate colitis.

It was through this process an inception cohort of 2201 patients were identified, of whom 1379 (63%) had UC, 706 (32%) had CD, and 116 (5%) were indeterminate. The overall incidence per 100 000 of the population was 10.4 for UC and that of CD was 5.6. The age and sex-adjusted rates of UC in the populations of northern Europe was 11.8 and in the south it was 8.7. In CD the age and sex-adjusted rate was 7.0 in the north and 3.9 in the south. Disease distribution, by participating centre, in the north and south of Europe is shown in Figures 1 and 2.

An analysis of the diagnostic methods used, anatomical site, and extent of disease showed little overall difference between centres in the north and south of Europe. Likewise, analysis of the presenting symptoms such as bowel frequency, occurrence of rectal bleeding, weight loss, and abdominal pain suggested no systematic differences in severity of symptoms at presentation between cases in the northern and southern Europe^[1,2].

In conclusion, this study suggested a modest excess of incidence of IBD in northern Europe. The magnitude of the observed excess for both conditions was less than expected on the basis of the previous studies. This may reflect recent increases in the incidence of IBD in southern Europe whereas those in the north may have stabilised. The aetiology of these conditions is unclear and it is therefore difficult to explain the pattern found. That similar north-south gradients in incidence have also been documented in the United States suggests that several factors may be involved, including climate, diet, economic wealth and development, or genetic susceptibility. The collaborative network established under the EC-IBD study provides a framework for conducting such studies in low incidence areas such as China, and to examine putative environmental factors involved in disease causation.

DISEASE OUTCOME IN EC-IBD INCEPTION COHORTS

Follow-up data on disease outcome in 595 (27%) of the original cohort of 2201 patients with IBD was available for review in 1997. 394 (66%) of the patients in follow-up had UC (40% male); and 201 (34%) had CD (52% male). The follow-up data came from 7 of the 20 original centres participating in the EC-IBD study. They obtained a complete follow-up of more than 95% of their patients and the mean follow-up period was 46 mo (nearly four years). The investigators completed a standard follow-up form containing questions on

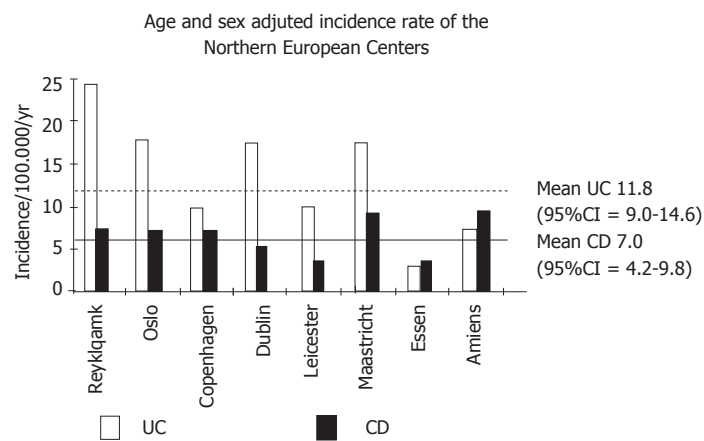


Figure 1 Age and sex adjusted incidence rate of the Northern European Centers.

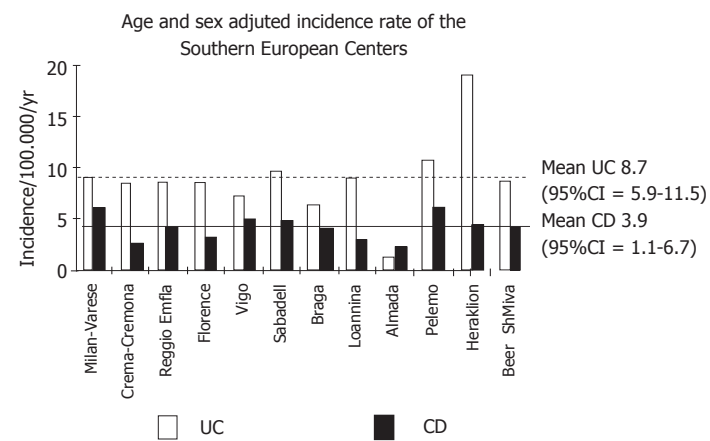


Figure 2 Age and sex adjusted incidence rate of the Southern European Centers.

Table 1 Physician global assessment of disease activity n (%)			
	UC	CD	Total
Symptom free	176 (45)	62 (31)	238 (40)
Improvement	151 (38)	94 (47)	245 (41)
No change	22 (6)	16 (8)	38 (6)
Worse	9 (2)	10 (5)	19 (3)
Unknown	36 (9)	19(9)	55 (9)

vital status, physician’s global assessment of disease activity and treatment. The status of 32% of these patients was checked by personal interview, 31% through telephone, 28% from hospital record and contact with medical specialists, and 9% from other sources.

RESULTS

At 1996-1997 follow-up 9 patients had died, 2 of them with causes related to IBD (toxic colitis and complications of UC). Physician’s assessment of disease activity showed that a large proportion (81%) of the cohort had clear symptomatic improvement and only few (9%) had no change or worsening of symptoms (Table 1).

In UC 68% had drug treatment at the time of follow-up, 96% of these used SA SP or 5-ASA. In CD 73% had treatment, of which 80% used SASP or 5-ASA. The remaining patients in both conditions were treated with corticosteroids or immunosuppressives, with a higher proportion receiving this treatment in CD (Table 2).

Table 2 Treatment		
	UC (%)	CD (%)
5-ASA or SASP	65	67
Corticosteroids	13	26
Immunosuppressives	3	11
None	33	19

CONCLUSION

Assessment of disease outcome in a large inception cohort of patients with IBD showed that the majority had symptomatic improvement over a four year period after diagnosis and mortality from IBD relat ed causes was low. In Europe, with present medical treatment, medium-term outcome of IBD appears favourable^[3].

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Interaction of colon carcinoma cells with rat hepatic sinusoidal cells during early stages of metastasis

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In our country, the majority of colorectal cancer patients develop and die with liver metastasis. Chemotherapy, radiotherapy and resection do not provide effective therapy for this disease. We therefore study the possibilities to enhance the hepatic immune system and the defense against metastasizing colon carcinoma cells. Pit cells, one of the sinusoidal cells in the liver, display spontaneous cytotoxicity of colon carcinoma cells and therefore are considered to be natural killer (NK) cells. Isolated pit cells can be divided into equal subsets with low (LD) or high density (HD). HD-NK cells have several characteristics which are intermediate between blood NK cells and hepatic LD-NK cells, suggesting that blood NK cells marginate in the liver, develop into HD-NK cells and later into LD-NK cells. LD-NK cells possess up to six times higher NK activity against

different tumor cell lines as compared to blood or spleen NK cells, thereby reaching the level of lymphokine-activated killer (LAK) cells. Blood NK cells and hepatic HD-NK cells, but not LD-NK cells, can be activated to higher levels of cytotoxicity by several cytokines and biological response modifiers. This opens the possibility to activate the population of hepatic NK cells. Pit cells in normal liver are probably activated by their cohabitation with Kupffer cells, which are able to secrete a number of cytokines. Moreover, pit cells appear to be dependent on the presence of Kupffer cells, because specific removal of these cells by Cl₂MDP-liposomes, makes the pit cells disappear within 2 wk, suggesting a life span of two wk for pit cells. With regard to the killing mechanism, we have routinely measured about 40% specific ⁵¹Cr-release after coculturing colon carcinoma cells with pit cells, indicating membrane damage or cytolysis. Recently, we also observed the induction of apoptosis in colon carcinoma cells by pit cells, as shown by chromatin condensation, nuclear fragmentation, DNA fragmentation and DNA ladder.

Several *in vivo* studies have reported almost complete efficiency (> 99%) in the killing of tumor cells within two days after a mesenteric injection of tumor cells. We have observed the adherence of pit cells and Kupffer cells to tumor cells shortly (1 h) after injection. At this time interval, large numbers of tumor cells are phagocytosed by Kupffer cells, probably after interaction with pit cells. Few tumor cells (< 1%), however, succeed in escaping from the defense system and develop secondary tumors.

Normal Kupffer cells are unable to kill tumor cells. Recent evidence, however, indicates that cocultures of Kupffer cells and pit cells display greatly enhanced killing of colon carcinoma cells.

Single tumor cells get stuck in the sinusoids when entering the liver, because their size largely exceeds the diameter of a sinusoid. After this, their adhesion molecules might react with the surface molecules of the endothelial cells, enabling them to extravasate and enter the liver parenchyma. We suppose therefore, that the adherence of endothelial cells and tumor cells, might as well be crucial in early stages of hepatic metastasis.

Later stages of growing metastasis are supposed not to involve sinusoidal cells. Instead, other members of the cellular immune system, such as cytotoxic T lymphocytes, tumor-infiltrating lymphocytes, monocytes and monocyte-derived macrophages may then play a defensive role.

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Role of nitric oxide in gastrointestinal tract

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Nitric oxide is a gaseous free radical synthesized *via* L-arginine oxidation by a family of nitric oxide synthases (NOS). Isomeric forms of NOS, representing at least three distinct and regulation. NOS isoforms are either calcium dependent and constitutively expressed in response to receptor stimulation in neurons and endothelial cells or calcium independent, inducible and expressed after exposure to diverse stimuli such as inflammatory cytokines.

NO is labile and its half life is < 15 s. In the presence of oxygen it is rapidly metabolized to nitrate and nitrite. NO reacts with superoxide anion to yield peroxynitrite which is not stable and following protonation produce the toxic hydroxyl radical.

The effects of NO in the gastrointestinal tract will be reviewed in this presentation.

NO AND NONADRENERGIC NONCHOLINERGIC (NANC) INHIBITION

NO is the mediator of NANC neurotransmission in the gut. NO is released from ileocolonic junction and stomach during nerve stimulation and induce smooth muscle relaxation in the LES, stomach, small intestine and internal anal sphincter. Its effects on longitudinal and circular muscles grossly mimic the effect of NANC nerve stimulation. Inhibition of NO synthesis attenuate the relaxing effect of electrical stimulation of NANC nerves in guinea pig colon, canine duodenum, rat gastric fundus and in circular muscle of LES, ileum and colon.

Its mechanism of action in the relaxation of gastrointestinal

smooth muscle is probably mediated by induced levels of CGMP and may be linked to modulation of intracellular calcium concentration. NO mimics the descending relaxation in the colon, proximal dilation of the stomach and the increase in gastric capacity-effects that are prevented by inhibition of NO synthesis. Decrease in neural NO production could direct to diseases in which there is sustained or vigorous non peristaltic contractions, such as in the aganglionic segment of Hirschsprung's disease or the non relaxing LES of achalasia. Increase NO production in the LES could play a role in reflux disease and imbalance of normal excitatory and inhibitory nerve activity as a result of disorders in the enteric NO system could lead to disease states such as a result of disorders in the enteric NO system could lead to disease states such as pseudo-obstruction or constipation.

NO AND GASTROINTESTINAL MUCOSAL PROTECTION

NO is an important vasodilator regulating mucosal blood flow and maintaining mucosal integrity in the gastrointestinal tract. Inhibition of NO synthesis reduces gastric mucosal blood flow and NO contributes to mechanisms that protect the gastric mucosa against ulceration.

Topical application of NO reduces the severity of ethanol induced hemorrhagic gastritis and inhibition of NO generation increase the severity-iodoacetamide induced gastric damage. Recently, NO delivery systems combined to NSAIDs were reported to effectively decrease the extent of NSAIDs induced damage to the gastrointestinal tract. Endogenous formation of NO also maintains the microvascular integrity of the intestinal mucosa following acute endotoxin challenge and endogenous NO may be one of the mediators that help protect against the harmful effects of endotoxic shock.

ROLE OF NO IN THE PATHOGENESIS OF INFLAMMATORY BOWEL DISEASE

In several models of experimental colitis-that induced by acetic acid, trinitro benzene sulfonic acid (TNB) and the sulphhydryl blocker, iodoacetamide-colonic NO generation and NOS activity were found to be several-fold higher than in normal colonic mucosa. Inhibition of NOS activity resulted in significant decrease in the extent of tissue injury in all these models. It is consequently suggested that in experimental colitis the enhanced NO generation by stimulated NOS activity contribute to the pathogenesis of tissue injury.

In inflammatory bowel disease (IBD), both in ulcerative colitis and in Crohn's disease, there is a marked increase in the activity of the inducible isoform and intestinal NOx generation is also significantly increased. Increases in the proportion of citrulline, the coproduct of NOS activity, were found in active ulcerative colitis. Direct measurement of rectal luminal NO detected NO in 4/8 ulcerative colitis patients but in none of the controls.

Immunostaining and *in situ* hybridization with an iNOS riboprobe identified in ulcerative colitis iNOS mRNA and translated protein in surface epithelial and crypt cells. The enhanced NO formation by stimulated iNOS may, therefore, have an important role in the pathogenesis of colonic inflammation in IBD. Moreover, since NO also induces muscle relaxation, it may also contribute to the altered motility in colitis. In TNB colitis the colonic perimeter is enlarged and intracolonic pressure is lower. In ulcerative colitis patients with toxic megacolon, iNOS activity in the muscularis propria is stimulated and immunostaining for iNOS is positive. In contrast, in colitis controls muscular iNOS activity is not detected. Local muscular generation of excessive NO in ulcerative colitis may be responsible for colonic

dilation.

L-NAME, the L = arginine analog that inhibits NOS activity, effectively decreases the extent of colitis in capsaicin pretreated rats. Its protective effect was accompanied by significant decrease in colonic NOS activity and NOx generation. The amelioration of experimental colitis by L-NAME supports the contention that enhanced NO generation promotes mucosal injury in these two models. In a similar way, L-NAME was shown also to ameliorate TNB-induced ileitis in guinea pigs.

Selective inhibition of iNOS, when and if appropriate drugs will be available, may be a novel therapeutic modality to decrease the inflammatory response in IBD patients.

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***Helicobacter pylori* infection: Differences between the East and West, and implications for management**

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INTRODUCTION

Helicobacter pylori is a gastric pathogen strongly implicated in the causation of gastritis, duodenal ulcer, gastric ulcer, gastric cancer and gastric lymphoma. Half the world's population or 2 billion people are infected, making it the commonest chronic infection in man, and an important global health problem. There are several striking differences in the pattern of *H. pylori* infection and gastroduodenal disease between countries of the East and West. These include differences in: (1) *H. pylori* prevalence and characteristics; (2) Disease patterns; and (3) Host differences. These differences do not occur on the basis of geographic boundaries, but are the outcome of genetic and environmental factors in the respective populations. Strategies for the management of *H. pylori* infection in Asia must take these factors into account. This presentation will highlight these differences and their implications for clinical management and health care policies in Asian countries.

***H. pylori* PREVALENCE AND CHARACTERISTICS**

Prevalence

There is a high prevalence of *H. pylori* in the more populous countries of the East, while in comparison the prevalence in

Western developed countries is lower. For example in blood donors or volunteer populations, the mean seroprevalence of *H. pylori* antibodies was 50% in Japan, and 60% in China and Vietnam, compared to 25% in England, and 30% in Denver (United States) and France respectively. *H. pylori* prevalence is lower in South-East Asia, with a mean prevalence of 30% among Chinese in Singapore.

Cytotoxin-associated gene (*cagA*) product

Fifty-sixty percent of *H. pylori* strains in the West are *cagA*-positive (*cagA*+) compared to 80%-90% in the East. Several studies in Western populations demonstrated that infection with a *cagA*+ *H. pylori* strain was associated with an increased risk of developing gastric cancer, but studies in China, Japan and Singapore found no increase in risk.

Metronidazole-resistance

Resistance to metronidazole reduces the success rates of treatment combinations which include imidazole antibiotics. Metronidazole-resistance is generally high in Asia, being 50% in Singapore and Hong Kong, and up to 80%-90% in India. It is a lesser problem in the West, with rates between 7% to 49% in Europe (Giupczynski Y *et al*, 1992).

PATTERNS OF *H. Pylori* RELATED GSTRODUODENAL DISEASE

Gastric cancer is a leading cause of cancer in many countries in the East, with strikingly high incidence rates in Japan and parts of China, whereas it is less frequent in most countries of the West. *H. pylori* has been implicated in its aetiology and Forman estimated that 50%-70% of gastric cancer cases are attributable to *H. pylori*.

Duodenal ulcers are more frequent than gastric ulcer in the West, while the difference is smaller in the East, and in Japan, gastric ulcers are more frequent. Differences in the pattern of gastroduodenal disease may be due to the type of gastritis, pattern of *H. pylori* infection, and other environmental factors (Correa P, 1995).

HOST DIFFERENCES

There may be ethnic differences in gastric acid secretion and HLA typing. For example, it was demonstrated that Chinese duodenal ulcer patients had significantly lower basal acid outputs per kg body weight than American duodenal ulcer patients (Feldman M *et al*, 1998). This may have significance not only in predisposition to the type of disease, but also in treatment, where lower doses of acid-blockade drugs may be effective in Asian patients. The frequency of HLA-B5, HLA-B12, and HLA-BW35 has been shown to be increased in patients with duodenal ulcer in Western populations, while a lower frequency of HLA-DQA1*0102 was found in Japanese *H. pylori*

-positive duodenal ulcer patients compared to *H. pylori*-negative controls (Azuma T *et al*, 1995).

IMPLICATIONS FOR MANAGEMENT OF *H. pylori* INFECTION IN ASIA

Screening for disease

In Japan, which has a very high incidence of gastric cancer, screening for early gastric cancer is practised widely. Consequently the proportion of early cancers detected is high, and survival rates in Japan are the best in the world. In parts of China where the ASR of gastric cancer is also high, a screening policy may also be cost-effective. Outcome studies could help to determine a threshold rate of gastric cancer incidence, above which population screening may be warranted.

Screening for *H. pylori*: the “test and treat” strategy for dyspepsia

Experts have advocated the use of *H. pylori* serology to screen dyspeptic patients prior to endoscopy, the so-called the “test and treat” policy. Studies in the United Kingdom and Europe have shown that such a strategy can reduce the use of scarce endoscopy resources, when applied to selected patients. There are reservations about applying such a policy in some Asian countries. Firstly, a high background prevalence of *H. pylori* reduces its effectiveness as a screening method. Secondly, this strategy is directed primarily at detecting and treating *H. pylori*-related peptic ulcer disease. However the high incidence of gastric cancer in Asian countries may result in misdiagnosis or a delay in diagnosis, with tragic consequences. Thirdly, at least a third of gastric cancers are *H. pylori*-negative, moreover there is data to suggest that a greater proportion of young patients with gastric cancer are *H. pylori*-negative.

The Asia Pacific Consensus Conference recognised these issues, and suggested three possible algorithms for the management of uninvestigated dyspepsia, based on the population prevalence of *H. pylori*, the local gastric cancer incidence rates, and the availability of endoscopy.

Screening for disease using *cagA* antibodies

Because *cagA* antibody status was shown to increase the risk of gastric cancer in several Western studies, there have been suggestions that it may be used as a predictive or screening test. This would be useless in Asian populations because of the very high prevalence of *cagA*-positivity in *H. pylori* isolates in Asia (80%-90%), while studies in Chinese and Japanese populations show no correlation with worse disease outcome.

Treatment regimes

The following factors require consideration before selection of an appropriate treatment regime for use in Asian countries. Firstly, it is helpful to know the local prevalence of metronidazole-resistance in *H. pylori* isolates. Secondly, drug costs are extremely important as often either the patient bears the bill (health insurance being uncommon in many parts of Asia), or in the case of public healthcare only inexpensive drugs may be available, and the health budget in many Asian countries is sorely-strained by competing demands. Thirdly, the Asia Pacific Consensus conference recommends use of treatment combinations with demonstrated efficacy of over 90% on per-protocol analysis or over 80% on intention-to-treat analysis. Ideally this should be established in local trials, since the results of treatment regimes may vary according to prevalent imidazole-resistance, compliance and other factors. Generally a triple therapy combination consisting of a proton-pump inhibitor (PPI) or ranitidine-bismuth-citrate (RBC) AND two antibiotics (with a choice from clarithromycin, amoxycillin or metronidazole) gives good eradication rates. In the interests of costs, bismuth may be substituted for PPI or RBC, but with poorer patient tolerance and poorer compliance. The omission of clarithromycin also results in lower efficacy. If cost is the overriding concern, classical bismuth triple therapy for one week is generally reliable.

In conclusion, there are some striking differences in the pattern of *H. pylori* infection and gastroduodenal disease between populations of the East and West. These factors must be taken into account when formulating strategies for the management of *H. pylori* infection in Asian countries.

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Immunological approaches to the breakdown of hepatitis B viral persistence

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In order to resolve chronic HBV infection, it is pertinent to have a better understanding of the underlying mechanism of viral persistence. Though the exact mechanism that leads to HBV persistence is not yet clear, there is cumulating evidence suggesting that immune tolerance to HBV infection is important. It is generally believed that resolution of acute HBV infection requires adequate B and T cell responses which lead to the production of protective antibodies, as well as broad-based T-cell response against multiple HBV antigenic determinants located on the viral envelope, nucleocapsid and polymerase gene products^[1]. Previously, it was demonstrated that serological clearance of HBsAg could occur after allogeneic bone marrow transplantation. Furthermore, it was shown that clearance of HBsAg in chronic HBV carriers was strongly associated with engraftment of anti-HBs positive marrows after allogeneic BMT^[2]. This suggested that persistence of HBV infection is due to an immunological defect in the chronic HBV carriers. So far, the only form of immunomodulatory therapy approved for use in chronic HBV infection is IFN- α . In a meta-analysis that included 15 randomised controlled studies with a total of 837 adult chronic HBV carriers, IFN- α was found to be effective in terminating viral replication. The overall loss of HBsAg occurred 6% more often in IFN- α treated patients than the natural seroconversion seen in

controls (7.8% compared with 1.8%, $P = 0.001$) and the loss of viral replication occurred approximately 20% more often in treated patients than in controls (33% vs 12% for the loss of HBeAg and 37% vs 17% for the loss of HBV DNA, $P = 0.0001$)^[3]. In a recent 9-year follow-up study, it was found that IFN treatment resulted in higher and earlier rates of cleared HBeAg and HBV DNA by hybridization in Chinese patients with chronic hepatitis B. Very few patients lost HBsAg despite sustained HBeAg clearance. There was no difference in incidence of hepatic complications between patients and controls and between those who did and did not clear HBeAg^[4]. T α -1 is currently registered for treatment of chronic HBV infection in China. In a randomized placebo-controlled trial conducted in Taiwan, complete virological response (with clearance of HBeAg and serum HBV DNA by liquid hybridization) was significantly higher in those who receive T α -1 ($n = 32$) for 6 months than the placebo group ($n = 32$, 40.6% vs 9.4%; $P = 0.004$), 18 months after entry, although complete response was similar at the end of treatment^[5]. In a recent study conducted in China, the safety and efficacy of T α -1 for 6 months was compared with combination of T α -1 and IFN- α (3MU qd \times 10 d then 3 \times weekly for 6 months) in the treatment of chronic HBV infection. Loss of HBeAg and HBV DNA was 27.8% in both groups at month 12. No significant side effect was observed in both groups^[6]. Recently, several other forms of immunotherapy such as DNA vaccines, therapeutic vaccine, antigen-antibody complexes, infusion of lymphocytes from immunized donors, and *in vitro* priming of autologous lymphocytes are being developed. This together with the use of nucleoside analogues, such as lamivudine and famciclovir, may become part of the armamentarium in the treatment of chronic HBV infection in the near future.

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Chemical cholecystectomy

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INTRODUCTION

Cholelithiasis is a commonly encountered disease in China. It was reported that the incidence rate is 7% by autopsy. Recent investigation of in natural populations disclosed an incidence rate of up to 10% by means of ultrasonography B, and the tendency is increasing yearly. Since Langenbuch first succeeded in the cholecystectomy for cholelithiasis in 1882, this procedure has now become a classical way of operation for cholecystolithiasis, and its efficacy has been clinically proven for over 100 years. Cholecystectomy seems to be a simple operation, but the risk is practically existing there^[1]. Thus, looking for a less invasive, easy and reliable procedure substitute cholecystectomy has become a research project of surgery. The small-incision cholecystectomy has been persistently reported in literature since Dubois reported it in 1982. But it is still controversial now. In 1984 Salomonowitz *et al*^[2] performed a chemical cholecystectomy, with the advantages of

less injury, low risk, nonoperative elimination of cholecystolithiasis, and clearing out the bed of recurrent cholelithiasis^[3]. It has attracted the attention and research of many authors.

CONCEPT

Chemical cholecystectomy is to use chemical method to destroy the mucous membrane of the gallbladder. As a result the reparation of fibrous tissue takes the place of cholecystectomy, so as to prevent the recurrence of cholecystolithiasis. Technically it includes 4 steps, such as percutaneous cholecystostomy, lithotomy occlusion of the cystic duct and perfusion of the hardener.

Percutaneous cholecystostomy

This technique often failed in early stage due to mobility of the gallbladder, and the complications of bile fistula often occurred. In recent years, with the application of ultrasonography B and CT, this operation has become a simple and reliable one. A puncture cholecystostomy is carried out under the guidance of percutaneous and transabdominal B ultrasound^[4]. Percutaneous-transhepatic cholecystostomy can be also performed under the guidance of ultrasonography B^[5]. The puncture point was usually located in intercostal space. At present this technique is seldom used clinically, yet it remains an important alternative therapy for the high risk elderly patients with a difficulty of cholecystectomy.

Percutaneous lithotomy

There are a variety of nonoperative ways of eliminating the gallstones. Roughly speaking they include chemically dissolution of stones, physical lithotripsy and instrumental lithotomy *etc*; All of which are performed through percutaneous cholecystostomy. Of them, vibrative-wave lithotripsy in the body, directly dissolving stones with litholytic agent and instrumental lithotomy *etc*. must be finished through the tract of transcutaneous cholecystostomy. In recent years the appearance of laser lithotripsy brings with it, the advantages of less injurious to gallbladder and safety *etc.*, but the equipment is too expensive to get the technique popularized and spread. And most of all the laser lithotripsy can not eliminate the causes of stone formation and recurrence rate is high after lithotomy. In general, the nonoperative procedure may have some severe complications, such as obstruction of the bile duct, infection, pancreatitis, *etc*. So its clinical application is greatly limited.

Occlusion of the cystic duct

Complete occlusion of the cystic duct is not only the premise of hardener perfusion, but also the crux of preventing the hardener from injuring the common bile duct and intestine, as well as the regeneration of the cystic mucous membrane. Both of the destruction of the mucous membrane of the cystic duct and the occlusion of the cystic duct are the critical point of a successful chemical cholecystectomy^[6]. There have been many ways that were used in blocking the cystic duct, such as cyanoacrylate, gel foam embolus and adhesives, *etc.*, since in 1984, Salomonowitz

first used aminoacrylic acid and the embolus made of collodion to occlude the cystic duct. But the shortcoming is that the embolus is easily dropped into the common bile duct, and it can not prevent the mucous membrane of the cystic duct from regenerating into the gallbladder, resulting in the growth of the mucosa of the cystic wall. In 1988, Becker *et al*^[7] successfully occluded the pig's cystic duct by bipolar radio frequency-electro-coagulation. While the permanent occlusion took 2 wk, so was the perfusing of the hardener into the gallbladder. At home, Xu *et al*^[8] reported 10 cases of cystic duct occlusion were performed by percutaneous cholecystoscopic micro-wave heat coagulation on human body. The result indicated that this type of cystic duct occlusion was due to local edema. The edema was most serious 24 h after heat coagulation, and it subsided obviously in 72 h. The occluded cystic duct may become unobstructed again. Therefore, the mucous inactive agent should be injected in to the gallbladder when edema of the cystic duct was most serious so as to make the cystic mucosa inactive. One injection was made every 4 h, and it was repeated for 5-6 times. A satisfactory result of inactivation of mucosa was achieved in all of the 10 cases. Chen *et al*^[9] succeeded in using microwave heat coagulation to instantly make the occlusion of the cystic duct in 8 human bodies. A microwave electrode was inserted into cystic duct through a cholecystoscope, but it needs to be further confirmed because of small sample size. In 1985, Getrajdman used rabbits to carry out his experiment. He tightly ligated the cystic duct with silk thread after laparotomy, so that the hardener can not leak into the common bile duct, and prevent the epithelial cells of the cystic duct from growing into the gallbladder. Guan *et al*^[10] used metal clip or silk thread to block the cystic duct of the white rabbit. The result suggested that there was no difference between metal clip and silk thread in fibrosis formation rate. Metal clip can block the cystic duct, and so providing the evidence of using metal clip to block the cystic duct during laparoscopic chemical cholecystectomy.

Perfusion of the hardener

The selection of the hardener may directly affect the success or failure of the chemical cholecystectomy. Therefore the hardener must meet the following criteria: (1) Can destroy the mucous epithelium completely; (2) To be easily cleaned out and not to result in too much necrosis of the tissue; (3) Nontoxic: Will not lead to damage of the organs in the body; (4) Noncarcinogenic^[11]. In 1984, Salomonowitz used dehydrated alcohol, tetracycline solution and heated contrast medium to destroy the mucous membrane, of rabbits' gallbladder, resulting in fibrosis of the mucous epithelium of the gallbladder wall. However it can not stop the regeneration of the mucous membrane of the cystic duct. Getrajdman (1985) proved that alcohol, tetracycline solution, methomethacrylate and trifluoroacetic acid can bring about fibrosis of the rabbits' gallbladder. Whereas the heated contrast medium and normal saline are ineffective. Peng *et al* carried out an animal experiment and pathologic investigation on the selection of the hardener. And he confirmed that the efficacy of the compound phenol is the best in destroying the epithelium and occluding the cavity of the gallbladder. Guan Hong Geng used with rabbits to do the experiment, and identified that 95% alcohol + 2 mol/L trifluoroacetic acid is the effective and safe mixture hardener for gallbladder. Up to date, according to the literature of home and abroad there are numerous hardeners can be chosen. Among them the followings are the most commonly used ones: 95% alcohol or dehydrated alcohol, 5% tetracycline solution, 2 mol/L trifluoroacetic acid, compound phenol solution, etc. Dehydrated alcohol and tetracycline solution are most frequently used in clinical practice. While tetracycline solution possesses a higher toxicity, and takes long time to destroy the mucous membrane. The dehydrated alcohol rarely affects the whole body, and needs less time to make the cystic mucosa inactive, so it has become a commonly used hardener.

PATHOGENIC CHANGES AFTER OPERATION

The hardener is absorbed by cystic mucous epithelium, leading to coagulation of cells' protein, cells' necrosis and inflammatory reaction, restoration of the fibrous scar tissues, and eventually, the

whole gallbladder to be "self cholecystectomy" due to fibrosis. In 1984, Salomonowitz performed an experiment on rabbits. Fibrosis of the wall of the gallbladder and occlusion of the cystic cavity occurred 2 wk after perfusion of the hardener. In 1985 Getrajdman proved that the complete destruction of the cystic mucosa of the rabbits and the fibrosis of the wall of the gallbladder occurred 6-8 wk after perfusion of the hardener. At home, Guan Hong Geng^[10] experimentally demonstrated that the pathological changes is characterized by epithelial exfoliation, necrosis and infiltration of inflammatory cells along with slight proliferation of fibrous tissues 2 wk after perfusion of the hardener. In 4-8 wk, mature fibrous tissue formed, and inflammatory reaction disappeared. Additionally observation of ultrastructure showed that a complete fibrous cicatrization of the gallbladder took place. Becker carried out a chemical cholecystectomy by way of percutaneous electro coagulation of the cystic duct, and found that the fibrosis of the cystic mucosa occurred 2-3 wk after the perfusion of the hardener. Reviewing reports in literature from home and abroad revealed, that the inflammatory reaction chiefly occurred within 2 wk after perfusion of the various kinds of hardener, and fibrous cicatrization 4-8 wk.

INDICATIONS AND CONTRAINDICATIONS OF CHEMICAL CHOLECYSTECTOMY

Indications include: Acute and chronic cholecystitis; gallstones, high risk elderly intolerable of cholecystectomy, or complicated with heart, lungs and kidney dysfunctions; hepatic cirrhosis with portal hypertension; patients unsuitable for cholecystectomy after cholecystostomy, and people who have had percutaneous cholecystoscopic lithotripsy and lithotomy. Contraindications: Gallbladder gangrene or perforation; malignant tumour of the gallbladder, patients with complications of intrahepatic extrahepatic stones in bile ducts, or common bile duct obstruction; gallbladder communicated with accessory hepatic duct, or fistula formation between gallbladder and other organs; ceramic gallbladder.

ADVANTAGES OF CHEMICAL CHOLECYSTECTOMY

In 1890 Langenbuch believed that cholecystectomy is of necessity not on account of the presenting gallstones, but that it is the cause of the gallstone formation. The traditional cholecystectomy has the disadvantages of large incision, numerous complications, especially for the high risk cases of elderly and the weak or those with heart and lung dysfunction, for whom the complication may reach up to 24%^[3]. Since nonoperative lithotomy doesn't eliminate the bed of the calculi, it is predisposed to recurrence of the gallstones. The calculi recurrence rate is 81%^[12] after cholelithotomy. The ejection rate of gallstones was low. The procedure was rather complicated treatment was difficult and expenditure was high. Various kinds of complications may occur during the process. Small incision cholecystectomy owns the advantages of small injury, rapid restoration of intestinal function, short duration of hospitalization, low cost and small scar of incision after healing compared with the traditional cholecystectomy. However, the lighting and exposure of the operative field are far from adequate due to small incision. The operative field and manipulative space are too narrow to limit its application, and poses severe potential risks. Laparoscopic cholecystectomy has the over smaller incision cholecystectomy, merits of smaller incision, less pain, quicker recovery and shorter hospital stay. Nevertheless it has a strict operative indication, the device is expensive, the cost is high. Further more the operators must be trained specifically. All of which renders it rather difficult and systemic intratracheal anesthesia is required to get popularized in the basic medical unit. Chemical cholecystectomy aims to wipe out the cystic cavity, make the gallbladder hardened, so that to prevent the calculi recurrence. This nonoperative cholecystectomy has substituted the operative cholecystectomy, and is as same as the efficacy of the operative cholecystectomy. If laparoscopic cholecystectomy can be combined with the chemical

cholecystectomy, laparotomy may be avoided. It makes minimal would, simplifies the therapeutic manipulation, shortens the operating time and hospital stay reduce the operative risk, as well as the adhesion of adjacent organs after operation. In the mean time, the recurrent bed of the gallstones can be eliminated. The requirement for device and technology, is not so high that it can be practised in basic medical units. Consequently it will get greatly developed in the future.

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Chinese diet in the causation and prevention of cancer

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The dramatic differences in the cancer patterns between China and North America, and among different regions in China, illustrate the profound effects of diet on cancer. Whereas cancers of the colon, breast, and prostate are major concerns in Western Countries, the most prevalent cancers in China are those of the digestive tract, stomach, esophagus, and liver (which account, respectively, for 23.0, 22.3, and 15.1% of the total cancer deaths). Nasopharyngeal cancer, which is rare among Caucasians, is common among Cantonese residing in Canton and Hong Kong. Knowledge about the dietary factors which contribute to the high or low incidence of these cancers is important for their prevention.

Dietary factors and viral or bacterial infection may act synergistically in causing human cancers. Consumption of aflatoxin-contaminated foods, such as *Aspergillus flavus* infected corn and peanuts, and HBV infection are the major risk factors for liver cancer in Qidong and many other areas. Both chronic hepatitis B surface antigen (HBsAg) carrier status and liver AFB₁-adduct levels were higher in patients with hepatocellular carcinoma than in controls. The viral and chemical factors work synergistically in the carcinogenic process, and in many cases the hepatocellular carcinomas have a characteristic codon 249 mutation of the p53 tumor suppressor gene. Similarly, consumption of salted fish (especially during weaning) and other preserved foods, in combination with EB virus infection, has been shown to be a major risk factor for nasopharyngeal cancer. Avoidance of these foods and prevention of viral infection are key measures in the prevention of these cancers.

The etiologies of the top two cancers in China, *i.e.*, stomach and esophageal cancers, are not as clear, although nitrosamines and nitrosamides have been strongly suspected. Consumption of salty foods and infection with *Helicobacter pylori* are believed to be

risk factors for stomach cancer, and consumption of moldy foods have been suspected to increase the risk for esophageal cancer. A common feature for the Chinese population at high risk to stomach, esophageal and other cancers is the infrequent consumption of fruits and vegetables, which contain micronutrients and phytochemicals. A case-control study on gastric cancer in Linqu, Shangdong indicated that frequent consumption of fresh fruits and vegetables, especially allium vegetables, has protective effect. Consumption of soybeans and soy products is also protective. Individuals with lower levels of plasma vitamin C and β -carotene had higher frequencies of intestinal metaplasia, a precancerous lesion of stomach cancer. A large scale nutritional intervention study on esophageal/gastric cardia cancer in Linxian, Henan, demonstrated that supplementation with α -tocopherol/ β -carotene/selenium for 5 years decreased the mortality rate of gastric cardia cancer and resulted in other health benefits. An ongoing intervention study on stomach cancer with dietary supplements as well as *H. pylori* eradication is being conducted in Linqu, Shangdong.

The traditionally rather low rates of colon, mammary, and prostate cancer in China are probably due to the high grain consumption, low intake of fat and meat, low total caloric intake, and high physical activity. The roles of possible cancer preventive agents, such as the polyphenols present in tea and soybeans, remain to be further investigated.

With the improvement of economic conditions and changes in dietary patterns in China, residents in Beijing, Shanghai, and other big cities are facing an increased risk for Western cancers, such as colon, prostate, and mammary cancers. This is the same problem experienced by Chinese in North America and in Taiwan. In order to reduce the cancer risk among Chinese inside and outside of China, I would like to make the following recommendations: (1) Chinese should keep the traditional high grain, low fat/ meat, and low sugar diet. Whole grains, such as brown rice, are far superior to refined grains because they contain micronutrients and fiber. A high grain and low fat/ meat diet will lower plasma cholesterol and derive beneficial effects in preventing cardiovascular diseases. For populations consuming refined grains and wheat flour, supplementation with micronutrients is very important to enhance public health. (2) The Chinese diet, especially the breakfast, is generally low in fresh vegetables and fruits. The consumption of these foods should be increased and increased availability of refrigerated or freshly frozen foods should be beneficial. The consumption of fruit juice should be encouraged. (3) The boiling/steaming cooking practice is healthier than grilling and baking. High temperature cooking is known to produce arylamines which are carcinogens. Boiling/steaming in well designed cookware can also save fuel. When stir-frying, excessive amounts of cooking oil should be avoided. (4) Fungal-contaminated and some ill-preserved foods should be avoided. Appropriate food inspections by governments are needed. These measures, together with cessation of smoking and increase in physical activity to maintain appropriate body weight, should effectively increase the health of the Chinese all over the world (support by NIH grants CA56673 and CA68871).

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Genetic polymorphism and human cancer

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It has been known for a long time that there are large variations in human susceptibility to cancers, and in an individual's response to cancer chemotherapeutic drugs. Understanding of the mechanisms of such variations is critically important for cancer prevention by identifying and protecting the susceptible subpopulations, as well as for cancer treatment by improving efficacy and safety of chemotherapy. The rapid advancement of molecular biology and the success of Human Genome Project in recent years have greatly stimulated this line of research. Age netic polymorphism is defined as a DNA sequence variation that exists in more than 1 percent of the population. It is now widely believed that genetic polymorphism could play an important role in cancer susceptibility and drug response. In this presentation, I am going to review the basic concepts of genetic polymorphism and commonly used approaches, as well as to discuss the problems and future directions. Finally, I will introduce our current studies on genetic polymorphism of carcinogen-metabolizing and DNA repair enzymes, which include identification and functional characterization of novel genetic variants, and ongoing collaborative projects on the risk of esophageal and gastric cancers in Chinese populations.

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Value of selective chemoembolization in the treatment of hepatic metastases in colorectal carcinoma

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Abstract

AIM: To explore the therapeutic effect of chemoembolization in hepatic metastases in colorectal carcinoma.

METHODS: Forty patients underwent chemoembolization of metastatic liver lesion from colorectal carcinoma. Selective angiography of the hepatic artery was performed to identify the feeding vessels of the metastatic lesion. The injected chemoemulsum consisted of 100 mg 5-fluorouracil, 10 mg mitomycin C and 10 mL lipiodol ultra fluid in a total volume of 30 mL. Gel foam embolization then followed until stagnation of blood flow was achieved. Patients were evaluated for response, over all survival, and side effects.

RESULTS: Overall median survival time from date of first chemoembolization was ten mo. Median survival time of cirrhotic patients with class A and B by Child-Pugh classification was 24 and 3 mo, respectively. The difference was significant, ($P < 0.01$). Patients with metastatic disease confined to the liver did better than those who also had extrahepatic disease, with median survivals of 14 and 3 mo, respectively ($P < 0.02$). There were significant differences in that median survival of patients with hypervascular metastases was longer than that of patients with hypovascular metastases. The most common side effects were transient fever, abdominal pain and fatigue. Three patients died within one mo from the procedure.

CONCLUSION: The therapeutic effect of systemic chemotherapy in hepatic metastases of large intestinal carcinoma was not satisfactory and there were more side effects, whereas the therapeutic effect of selective chemoembolization was promising and there were less side effects. Selective chemoembolization may be an effective first-line therapy in hepatic metastases of large intestinal carcinoma.

Key words: Colonic neoplasms; Rectal neoplasms; Liver neoplasms/drug therapy; Liver neoplasms/secondary; Chemoembolization, therapeutic; Fluorouracil/therapeutic use; Mitomycins/therapeutic use

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INTRODUCTION

The liver is the most common site of metastatic disease in large intestinal carcinoma, and hepatic involvement determines the survival duration and quality of life of affected patients. Approximately 20% of patients dying with metastatic disease have liver involvement exclusively, with an additional 40% having disease at other sites as well^[1]. Median survival ranges from 6 to 16. Eight mo in various series and is greatly influenced by the extent and surgical resectability of the metastases^[2]. Systemic therapy has not been very effective for metastatic large intestinal carcinoma. Intravenous 5-fluorouracil (5-Fu) with leucovorin is currently the most widely used chemotherapeutic regimen. The median survival was 11.5 mo^[3]. A recent meta-analysis of seven randomized trials evaluated tumor response and overall survival. These trials compared HAI hepatic arterial infusion using floxuridine (5-fluoro-2-deoxyuridine) with intravenous chemotherapy. Survival analysis showed a statistically significant advantage for HAI compared with controls who received no treatment^[4]. The rationale for regional chemotherapy or chemoembolization (CE) arises from the fact that metastatic carcinoma to the liver derives its blood supply primarily from the hepatic artery. Because of the vascular anatomy of the liver and the angiographic approachability of many hepatic tumors, embolization therapy with or without intra-arterial chemotherapy has been attempted for many of these lesions. Patients enrolled in these trials have generally failed systemic and/or intra-arterial chemotherapy. To assess the result of CE, we report a phase II trial using a combination of 5-Fu, MMC, lipiodol ultra-fluide and gel foam embolization in patients who have failed systemic chemotherapy for liver metastases from large intestinal carcinoma. The response, survival time, side effects, and prognostic factors were evaluated.

MATERIALS AND METHODS

Patients

Forty patients had hepatic lesions coexisting with functional disorders from histologically documented large intestinal carcinoma that had progressed or failed to systemic chemotherapy. Those who

Table 1 Patient characteristics

	Data
No. cases	40
Male: female ratio	23:17
Median age (range)	50 (41-61) yr
Child-Pugh class	
A	28
B	12
Sites of hepatic metastases	
liver, one lobe	4
Liver, > one lobe	24
Liver and other sites	12
Vascularity of liver lesions	
Hypovascular	11
Hypervascular	18
Indeterminate	11

had received previous intra-arterial chemot herapy were excluded. All patients had bidimensionally measurable disease by computer tomography (CT), ultrasound or magnetic resonance imaging, with no evidence of complete portal vein obstruction. The characteristics of 40 patients with stage IV large intestinal carcinoma were shown in Table 1.

Methods

Selective angiography of the hepatic artery was performed before CE to map the vascular anatomy and identify the primary feeding arteries of the metastatic lesions. Either the right or left hepatic artery was cannulated, followed by inject ion of the chemoemulsum, which consisted of 100 mg 5-Fu, 10 mg MMC, a nd 10 mL lipiodol ultra fluide, in a total volume of 30 mL.

Gelfoam embolization was then performed, until stagnation of blood flow was achieved. If the metastases was present in more than one lobe, each lobe was treated on a separate occasion,with an interval of four wk between the two procedures. Patients were hospitalized following CE until clinical recovery and stable liver function. Adjuvant medications included kefzol, morphine hydrochloride, metoclopramide, glucose, vit.B6, vit.C, and adequate intravenous hydration .

Follow-up

Laboratory studies including a complete blood cell count, coagulation parameters, chemistry, liver function tests, and carcinoembryonic antigen (CEA) levels were obtained before the procedure. These laboratory tests were followed during the patient's hospitalization and moly thereafter. A liver CT without contrast was obtained within 48 h following CE to determine the concentration of lipiodol ultra-fluide and serve as a baseline for measurements.The CT was repeated at 1, 3, 6, 9, and 12 mo afterwards.

Criteria for evaluation

Treatment responses, time of progression of disease, overall survival,and side effects were evaluated from the starting point of initial CE until time of progression or death. A partial response was defined as greater than 50 percent reduction in the sum of the products of the longest perpendicular diameters of the indicator lesions on CT. The response had to last at least three mo, and there must be no progression in any measurable lesion or appearance of new lesions. Survival was evaluated using the kaplan-Merier method and comparisons between groups with the log-rank method.

RESULTS

Forty patients with stage IV large intestinal carcinoma were treated in a phase II trial of CE of hepatic metastases. All patients progressed after treatment with 5-Fu-based systemic chemotherapy. Twenty-eight patients had metastatic disease that was exclusively confined to the liver. Eighteen patients with hypervascular and 11 with hypovascular hepatic lesions had liver function damaged. Median follow-up duration for the 40 patients was eight mo (range, 1-31). All patients were assessable for side effects and survival.

Treatment response was evaluated with follow-up CT scans

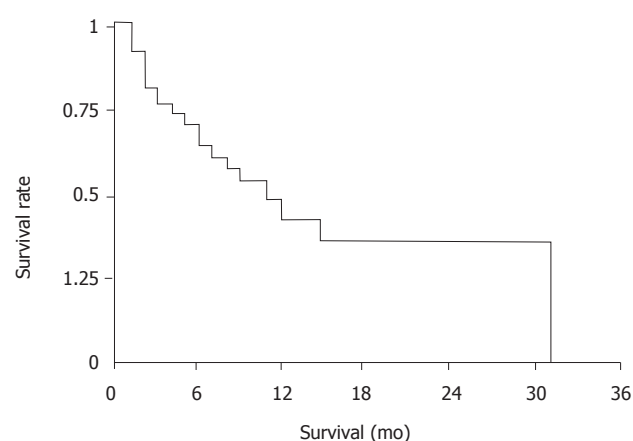


Figure 1 Actuarial survival after chemoembolization for large intestinal liver metastases of the 40 patients.

in 35 patients in this study. Eight patients had a partial response. Median duration of response was study. Eight patients had a partial response. Median duration of response was seven mo. An additional 14 patients had a more than 25 percent reduction in the sum of the products of indicator lesions. Median baseline CEA in 35 patients with an elevated level was 1088 ng/mL and dropped to a median of 175 mg/mL after CE. Eighteen of 29 patients had a more than 50 percent reduction in their CEA levels. In those 29 patients, median CEA reduction was 64 percent. Overall median survival from date of first CE procedure was ten mo (Figure 1).

Several side effects occurred first in most patients during the 4th-7th d following CE. These included abdominal pain, fever, and elevated transaminases lasting no more than 2 wk. All patients developed a fatigue syndrome lasting two to 4 wk. Six patients had pernicious ascites. One patient developed peritonitis and one had sepsis. Cholecystectomy was required for one patient because of necrotic cholecystitis. Three patients died from deterioration of the disease within one mo after the procedure. Comparisons between subgroups of patients by identifying several possible prognostic factors associated with survival revealed that there was no significant difference in overall survival between males and females. A significant difference in median survival of cirrhotic patients with class A and B ($P < 0.01$), by Child-Pugh classification was found, of 24 and 3 mo, respectively, as seen in Figure 2. Patients with metastatic disease confine d to the liver did better than those who also had extrahepatic disease, with median survival of 14 and 3 mo, respectively ($P < 0.02$), as seen in Figure 3. Patients with hepervascular metastases had a median survival of 11 mo and those with hypovascular metastases only 5 mo. There were significant differences in survival for different baseline levels of aminotransferase, alkaline phosphatase, and lactate dehydrogenase (LDH). Eleven patients with norm al baseline aminotransferase (≤ 25 u, karmen method) had a median survival of 14 mo and those with elevated levels only 5 mo ($P < 0.01$). When c omparing 24 patients with normal alkaline phosphatase (< 4.0 , Bodansky method) with 15 patients with higher levels, median survivals were 24 and 4 mo, respectively ($P < 0.01$). The difference was significant. 23 patients with normal LDH (< 450 u) had a median survival of 12 mo, which was significantly longer than those ten patients with higher levels, whose median survival was 2 mo ($P < 0.01$).

DISCUSSION

Hepatic involvement frequently determines the clinical status of patients with metastatic large intestinal carcinoma. There is no evident improvement in survival with systemic therapy of HAI compared with controls. CE has also been evaluated as a potentially beneficial approach in this setting. Hunt *et al*^[5] reported a prospective, randomized trial with three groups: no therapy, embolization alone, or intra-arterial 5-Fu with embolization using degradable starch microspheres (the CE group). Median survival from confirmation of metastases w as 9.6 mo for controls, 8.7 mo for the embolization group, and 13 mo s for the CE group. These

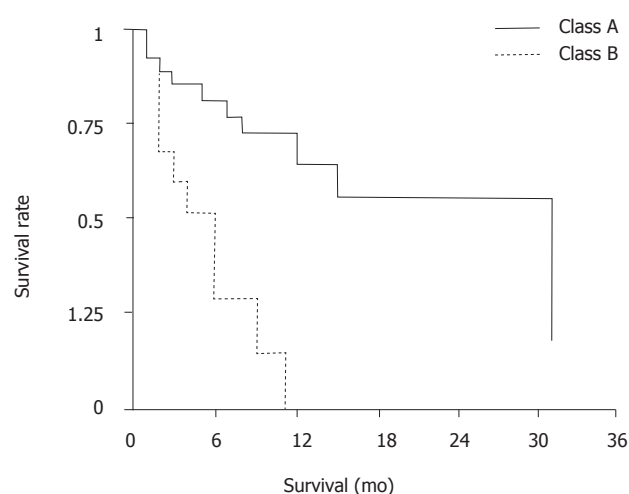


Figure 2 There was significant difference in survival between cirrhotic patients with class A and B ($P < 0.01$).

differences, however, did not reach statistical significance. Lang and Brown^[6] treated 46 patients by means of selective CE with doxorubicin and ethiodized oil. One year after treatment, 41 percent of patients were free of disease progression and 65 percent were alive. By the second year, the figures were 21 and 34 percent, respectively. In another recent study, 24 patients were randomized to receive embolization or CE using 5-Fu and recombinant alpha-2a-interferon. There was no significant difference between the two groups on survival time. The authors concluded that addition of more patients to this trial would be necessary. The principal goals of the current study were to evaluate the efficacy and toxicity of CE on hepatic metastases from primary large intestinal carcinoma and to identify the prognostic factors. Local administration of chemotherapeutic agents, both with HAI and CE, produces 10%-20% higher response rates than the conventional systemic chemotherapy. We prefer to use CT scan to evaluate the partial responses, rather than CEA or other criteria, such as estimation of tumor size or physical examination. Despite relatively high response rates were found in several studies of HAI, survival has not been clearly improved^[4]. Therefore, the importance of evaluating the response rate is questionable.

In our study, overall median survival from date of first chemoembolization was 10 mo. Patients with metastatic disease confined to the liver did better than those who also had extrahepatic disease, with median survivals of 14 and 3 mo, respectively ($P < 0.02$). There were significant differences in that median survival of patients with hypervascular metastases was longer than that of patients with hypovascular metastases ($P < 0.01$). There was significant difference in survival time between class A and class B cirrhotic patients, ($P < 0.01$), with that of class A longer than that of class B, suggesting that survival in patients with large intestinal liver metastases is closely related to Child-Pugh classification of hepatic

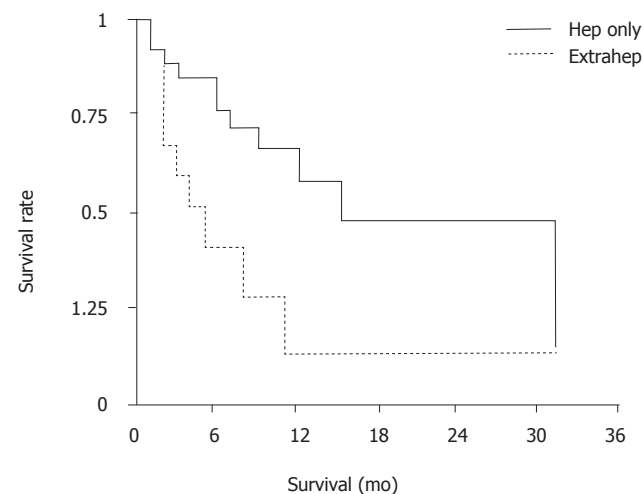


Figure 3 Median survival by site of metastases of patients with metastatic disease limited to the liver ($n = 28$) and of patients with more extensive disease ($n = 12$) was 14 and 3 mo, respectively ($P < 0.02$).

cirrhosis. The side effects of CE are worthy of appraisal. Some of them, such as abdominal pain and fever, are seen in almost all patients. However, they rarely last more than 5 d, and only need symptomatic treatment. There is also a significant elevation in hepatic transaminase level shortly after the procedure. The fatigue syndrome that follows CE improves progressively but can last more than one mo. On the other hand, there were infrequent but severe complications, including infections and gallbladder necrosis. The toxicities found in our study are consistent with those reported in the literature^[4,5].

In conclusion, selective CE can be used as the first line treatment for hepatic lesions of large intestinal carcinoma owing to its therapeutic efficacy, as well as less side effects.

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Experimental study of chemical cholecystectomy through abdominoscopic technology

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Abstract

AIM: To verify through animal experiment the validity of chemical cholecystectomy.

METHODS: Experimental animals used were healthy juvenile pigs. A 3cm incision was made at the right costal margin for passing the cold light source and some laparoscopic instruments into the abdominal cavity. The cystic duct was clamped with a silver clip and the gallbladder perfused with anhydrous alcohol (the sclerosing agent used). Gross observations and microscopic studies of the gallbladder, cystic duct, duodenum and adjoining liver specimens were made at the end of 2, 4, 6, 8, and 10 wk.

RESULTS: Coagulative necrosis and inflammatory reaction of the gallbladder and cystic duct appeared early, followed by extensive fibrosis and scar formation by the 8th week, and at the end of 10 wk complete fibrosis of the whole gallbladder occurred.

CONCLUSION: Chemical cholecystectomy is a safe, reliable, simple

and practical minor surgical technique.

Key words: Cholecystectomy, chemical; Gallbladder/pathology; Laparoscopy; Disease models, animal

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Sun SM, Xu JH, Sun SQ, Ma T, Wu MY, Wu LB, Chen K, Liu WX. Experimental study of chemical cholecystectomy through abdominoscopic technology. *World J Gastroenterol* 1998; 4(Suppl2): 38-40 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/38.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.38>

INTRODUCTION

Salomonowitz in 1984 introduced chemical cholecystectomy, in which the gallbladder mucosa was destroyed by a sclerosing agent. Thus, a cholecystectomy was substituted by postsclerosing fibrosis of the gallbladder, achieving the purpose of preventing the relapse of gallstones. The aim of this experiment was to prove the validity of chemical cholecystectomy as a practical, safe, reliable, simple, minor surgical technique for the treatment and prevention of gallstone in the gallbladder.

MATERIALS AND METHODS

Sclerosing agent: Anhydrous alcohol ($\geq 99.5\%$) was prepared by the Guangzhou Chemical Reagent Factory. The silver clips were produced by Shanghai Surgical Instrument Factory. Cold light source (XSL-1) was the product of the Shanghai Medical Optical Instrument Factory No.1 Branch.

Animal: 5 healthy, juvenile and hybrid pigs, each weighing 9-16 kg, provided by the animal experimental center, Medical College of Shantou University.

Methods

3% Pentobarbital was (30 mg/kg) injected into abdomen for general anesthesia, and a 3 cm oblique incision was made at the right lower costal margin for the introduction of the cold light source and laparoscopic instruments into the abdominal cavity. Then, under direct view, we found out the cystic duct, clamped it with a silver clip, punctured the bottom of the gallbladder to aspirate out the bile, installed a small catheter in it, rinsed the gallbladder with normal saline and finally measured the volume of the gallbladder. Now through the catheter we perfused into the empty gallbladder the anhydrous alcohol gently in a volume of about 1 mL less than the measured volume of the gallbladder. The sclerosing agent was left there for 4-5 min, before it was completely aspirated out, and then the gallbladder was rinsed with equal volume of normal saline;

Table 1 Histopathological changes

	Gallbladder mucosa	Proximal end of cystic duct	Distant end of cystic duct	Duodenum	Neighbouring liver tissues
No.1 (2 wk)	Coagulative necrosis, focal chronic inflammatory reaction, a great deal of inflammatory granulation tissues	Mucosal necrosis, chronic inflammatory reaction	Mucosa present, chronic inflammatory reaction	No change	No change
No.2 (4 wk)	Complete necrosis, chronic inflammatory reaction, granulation tissue and scar formation	Mucosal necrosis, chronic inflammation	Slight chronic inflammatory reaction	No change	No change
No.3 (6 wk)	Complete necrosis, replaced by inflammatory granulation tissue and scar formation	Mucosal destruction, granulation tissues	Chronic inflammatory reaction	No change	No change
No.4 (8 wk)	Mucosal coagulative necrosis, inflammatory granulation tissue and scar formation	Mucosal destruction, fibrous connective tissue	Inflammatory reaction	No change	No change
No.5 (10 wk)	Mucosa completely destroyed, dropping out, scar formation	Mucosal destruction, fibrous connective tissue	No pathologic change	No change	No change

we repeated the above procedure twice in a total duration of 20 min. The catheter was withdrawn, the abdomen was closed, and the animal was sent back to the animal room for observation.

Sample collection

Samples of the gallbladder wall, the proximal and distant end of the clamped cystic duct, common bile duct and the neighbouring liver tissues around the gallbladder bed (5 pieces from different sites) were collected in the 2nd, 4th, 6th, 8th and 10th week after the procedure, when the animals were sacrificed one after the another.

Gross Observation

We observed the skin and sclera for the presence of jaundice, the contour and size of the gallbladder, the gross appearance of the liver, duodenum and common bile duct of the animals.

Pathological examination

Specimens of the gallbladder, the proximal and distant ends of the cystic duct, common bile duct and the neighbouring liver tissues were routinely fixed, embedded, made into sections, stained with H-E and optical well studied under light microscope.

RESULTS

Gross observation

On the skin or sclera of each experimental pig, no jaundice were found. Their liver, common bile duct, and duodenum were all normal, but the gallbladder adhered to the omentum majus. Two wk after the procedure, an obvious atrophy of the gallbladder occurred; no scar or hydrops could be seen. At the end of 4 wk, the gallbladder was markedly atrophied with no scar or hydrops. Six wk after, the gallbladder atrophy became nearly complete and scar tissue could be seen, but there was still no hydrops. By the 8th week, gallbladder atrophy was complete and basically substituted by the scar. At the end of 10 wk, the scar replaced the whole gallbladder. The results of microscopic study of the sections were shown in Table 1.

DISCUSSION

The processes of histopathologic changes

The sclerosing agent was absorbed through the mucosal epithelial cells of the gallbladder, causing coagulation of cellular protein, cells necrosis, inflammatory reaction, and reparative fibrous scar tissues. Eventually the gallbladder became totally fibrotic ("self amputation")^[1]. The whole course of events needed some time for their completion. In a series of observation, we found that destruction and necrosis of all the mucosa of the gallbladder, inflammatory reaction accompanied by the formation of granulation tissue occurred in the first two wk. Chronic inflammatory reaction with a great deal of granulation tissue and scar formation occurred in the 4th-8th week. At the 10th week later, the inflammatory reaction reduced and scar tissue formation of the gallbladder became nearly complete. The mucosal changes of the proximal end of the clamped cystic duct was basically consistent with that of the gallbladder. In the 2nd-8th week the changes of the distant end of the cystic duct showed a chronic inflammatory reaction which disappeared completely at the end of 10 wk. No pathological change

of the duodenum and neighboring liver tissue could be found. The whole course of such pathological changes provided a pathological evidence for the clinical application of chemical cholecystectomy.

Occlusion of cystic duct

The complete occlusion of the cystic duct is not only the premise of the sclerosing agent perfusion but also can prevent from its injury to the common bile duct and intestine. Moreover, such a complete occlusion may check the extension of common bile duct mucosa into gallbladder cavity and lead to epithelial regeneration. The destruction of the cystic mucosa and the occlusion of the cystic duct are therefore crucial for a successful chemical cholecystectomy^[2]. There were many methods, which were used to occlude the cystic duct one after another since Salomonowitz first reported to use aminopropylenic acid and collodion as an embolus to occlude the cystic duct^[3], such as gelatin embolus and adhesives *etc*, but the disadvantage of these emboli were easy to drop out into common bile duct, and could not prevent the cystic mucosa from regenerating into the gallbladder. In 1985, Gertajdman used silk thread to ligate the cystic duct, and this can might avoid such shortcoming. Someone used microwave thermo-coagulation to occlude the cystic duct through a percutaneous chole-cystoscope; themicrowave thermo-coagulation can result in occlusion of the cystic duct immediately^[4,5], but this method needs special instruments and a minor operation. In China, Guan Hong Geng used metal clip to clamp the cystic duct without any complication^[1]. In our experiment we also used metal clips to block the cystic duct only, with no injury to the common bile duct and intestine, and the destruction of the proximal end of cystic duct mucosa was basically similar to that of the gallbladder mucosa. We believe that in this experiment the use of the metal clip to block the cystic duct is a reliable, simple and practical method, during chemical cholecystectomy.

Selection of the sclerosing agent

Selection of the sclerosing agent directly influences the result of chemical cholecystectomy, and the duration of perfusing is also a decisive factor. In 1985, Getrajdman proved that alcohol, tetracycline, metacrylic acid ester and trifluoroacetic acid could make rabbits gallbladder to be fibrosed, but thermo-contrast medium and normal saline were ineffective^[6]. From a review of the literature from abroad and home, many sclerosing agents can be chosen. Of them, the more commonly used are as follows: 95% alcohol or anhydrous alcohol, 5% tetracycline solution, 2 mol/L trifluoroacetic acid benzoic acid composita, *etc*. In this experiment we used anhydrous alcohol ($\geq 99.5\%$) only, and the perfusing time was only 20 min. The whole gallbladder mucosa could be destroyed completely. We believe that the anhydrous alcohol is a simple, easily available, effective and safe sclerosing agent.

Chemical cholecystectomy has many advantages, and may achieve the same efficacy of surgical cholecystectomy. This method needs only a 3 cm incision for passing a light source and some simple laparoscopic instruments under direct view. There is no need to make a pneumoperitoneum and to make use of a laparoscope. Moreover, it is a simple, relatively easy, less expensive, minor surgical procedure, and results in little postoperative visceral adhesion or other complications. Thus, it is our conviction that chemical cholecystectomy is a novel, simple and very effective technique for treating cholelithiasis even in not very well equipped

basic medical units.

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Retrovirus-ediated antisense RNA to *bcl-2* alter the biological behavior of stomach carcinoma MGC-03 cell lines

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Abstract

AIM: To demonstrate whether *bcl-2* gene can affect or alter biological behavior of a stomach carcinoma cell line MGC-803.

METHODS: To transduct a retrovirus containing *bcl-2* antisense RNA to MGC-803 cells and then to analyse the Bcl-2 protein expression in the cells by Western blotting. To observe the morphology alteration, detect the G1 phase arrest by FCM, inhibition of proliferation by MTT method and tumorigenicity in nude mice.

RESULTS: The MGC-anti-*bcl-2* cells shows contact inhibition, morphological alteration, from round or near round to shuttle like, decelerated growth rate, G1 phase arrest and weakened tumorigenicity in nude mice unlike the control (MGC-neo cells).

CONCLUSION: Our data show that antisense RNA to *bcl-2*, not only can induce apoptosis, but also reverse the biological behavior of MGC-803 cells. This would be a potential application to the gene therapy for stomach cancers.

Key words: Stomach neoplasms; Antisense RNA; *bcl-2* gene; MGC-803 cell lines; Gene therapy

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Cao GD, Wang SW, Wu SS, Li HF, Zhang WG. Retrovirus-ediated antisense RNA to *bcl-2* alter the biological behavior of stomach carcinoma MGC-03 cell lines. *World J Gastroenterol* 1998; 4(Suppl2): 41-44 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/41.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.41>

INTRODUCTION

bcl-2 gene, first detected as a putative oncogene located near to the breakpoint of t (14,18)(q32, q21) translocations in human follicular lymphoma^[10], was the first one shown to be involved in the regulation of apoptosis^[13]. Bcl-2 is expressed widely in tissues derived from all three germ layers, but its expression become more restricted during development^[6]. The *bcl-2* gene has been implicated in the oncogenicity of a wide variety of hematological malignancies and cancers including melanoma, breast, lung, prostate, gastric and bowel carcinoma. Overexpression of BCL-2 protein could promote cell survival or prevent apoptosis induced a variety of stimuli, including growth factor deprivation, γ -irradiation, glucocorticoids, heat shock, and multiple chemotherapeutic agents^[5,9,11]. There is strong *in-vitro* evidence that full phosphorothioated antisense oligonucleotides complementary to the open reading frame of the *bcl-2* mRNA can downregulate BCL-2 protein expression, which results in reduced cell viability and induces apoptosis^[1]. A phase I trial shows that in patients with relapsing non-Hodgkin lymphoma, *bcl-2* antisense therapy led to an improvement in symptom, objective biochemical evidence of tumor response, and down-regulation of the BCL-2 protein^[12]. All those reports were only concerned about the relationship between *bcl-2* to inhibition of apoptosis, and antisense *bcl-2* to apoptosis. Whether *bcl-2* antisense RNA or oligonucleotide can alter biological behavior of cells have not been reported. Here we report that retrovirus-mediated antisense RNA to *bcl-2* can alter the biological behavior of MGC-803 cells (a *bcl-2* positive stomach carcinoma), including alteration of morphology and cell cycle, and weakened tumorigenicity in nude mice.

MATERIALS AND METHODS

Plasmid construction, packaging and transduction

Human *bcl-2*, a 1.9 kb long *EcoR* I cDNA, were cloned into the retrovirus vector pLXSN. The reverse inserted recombinants were identified by *Bam*H I digestion and PCR methods using downstream primer of *bcl-2* and upstream primer of pLXSN vector near polycloning sites. Purified DNA of pLXSN vector or vector containing the antisense *bcl-2* cDNA were transfected into packaging cell lines PA317 using lipofectin according to the manufacturers instructions and G4 18 resistant colonies were obtained. To select the colonies with the highest titer, collect supernatants and used

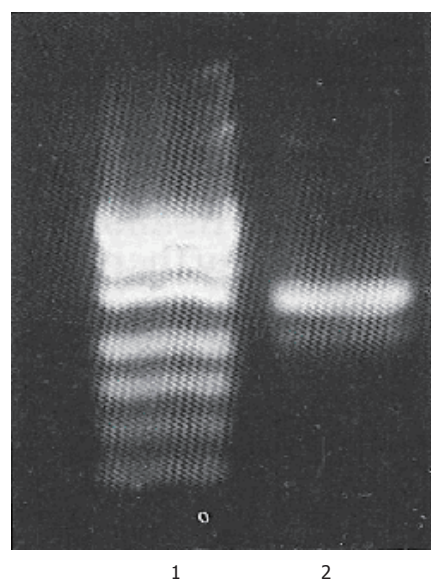


Figure 1 mRNA expression of MGC-803 cells analyzed by RT-PCR. Lane 1: pUC19/ MspI Molecular Markers. Lane 2: products of RT-PCR using primer of *bcl-2* and internal control GAPDH

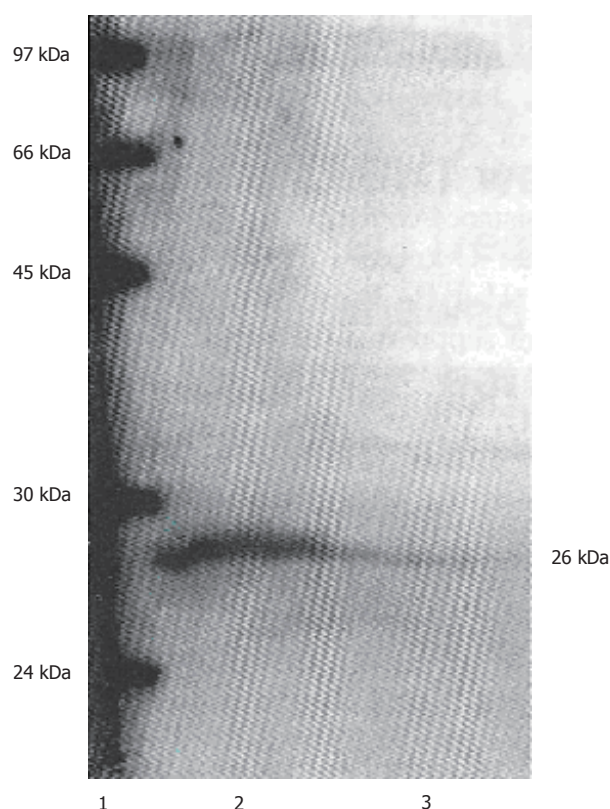


Figure 2 Western blotting of BCL-2 protein. Lane 1: Standard protein molecular marker. Lane 2: MGC-803 cells transduced with control virus (pLXSN vector). Lane 3: MGC-803 cells transduced with retrovirus expressing *bcl-2* antisense RNA.

to transduce stomach carcinoma MGC-803 cells. G418 resistant colonies were picked and propagated in the selective medium (400 $\mu\text{g/mL}$ of G418).

Western blotting

Exponentially growing cells were harvested into lysis buffer containing 50 mmol/L Tris, 2% SDS, 10% glycerol and 100 $\mu\text{g/mL}$ PMSF, boiled for 10 min and centrifuged at 10000 g. After determining protein concentration, 50 μg of protein were electrophoresed on 12% SDS-PAGE and transferred to nitrocellulose membrane by electroblotting. Membrane were blocked with 3% defatted milk powder and then incubated with an anti-*bcl-2* polyclonal antibody. Following incubation with a biotin-rabbit secondary antibody and SA-AP, antigen-antibody complexes were detected by adding BCIP and NBT.

Cell viability

Human stomach carcinoma MGC-803 transduced with virus expressing *bcl-2* antisense RNA and neo were plated in six-

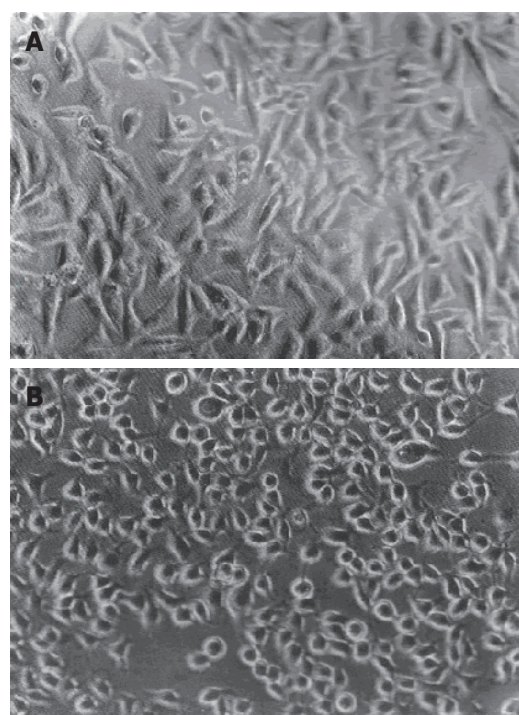


Figure 3 Morphological alteration of MGC-803 cells. (A) MGC-803 cells transduced with retrovirus expressing *bcl-2* antisense RNA. (B) MGC-803 cells transduced with control pLXSN virus.

well plates at a density of 5×10^4 cells/well. Cells number were measured by direct cell counting after being washed, trypsinized and stained with trypan blue every 24 h up to 4 d after plating. The experiment were performed in triplicates and reproduced three times.

Cell cycle analysis

Human stomach carcinoma MGC-803 transduced with virus expressing *bcl-2* antisense RNA and control pLXSN virus were plated in six-well plates at a density of 1×10^5 cells/well. Cells were collected at 70% confluence, or at 100% confluence with additional culturing for 24 h respectively, and then fixed with 75% ethanol at 4 $^{\circ}\text{C}$ overnight. After centrifuged and washed with PBS, the cells were digested with RNase A (20 $\mu\text{g/mL}$) at room temperature for 1 h, and then resuspended in solution containing 50 $\mu\text{g/mL}$ of propidium iodide, 0.3% sodium citrate, and 0.01% Triton X-100. Cell cycle were analyzed on the FACScan using lysis II software.

Tumorigenicity in nude mice

Four-week-old athymic nude mice were supplied by Chinese Institute of Cancer. The transduced MGC-neo and MGC-anti-*bcl-2* cells were propagated, trypsinized and resuspended in Hank's balanced salt solution at a concentration of 2.5×10^7 cells/mL. 5×10^6 of MGC-anti-*bcl-2* and MGC-neo cells were injected into the right and left flank of nude mice respectively. After sacrifice, the tumor mass were weighted. The significance of differences in tumor size between control and *bcl-2* antisense RNA virus transduced group was evaluated using paired *t* test.

RESULTS

Bcl-2 antisense RNA inhibit BCL-2 protein expression in MGC-anti-*bcl-2* cells

MGC-803 was a stomach carcinoma cell line which established by Shandong Institute of cancer, China in 1983. It has not been reported that whether MGC-803 cell express *bcl-2* mRNA and protein or not. RT-PCR was performed using GAPDH as internal control (Figure 1), and the mRNA proportion of *bcl-2* to GAPDH (BCL-2/GAPDH) analyzed by laser scanning is 0.25. A decreased level of BCL-2 protein was detected in MGC-803 cells after being transduced with retrovirus expressing *bcl-2* antisense RNA by Western blot analysis (Figure 2). Our results showed that MGC-803 cells expresses both *bcl-2* mRNA and protein in a high level,

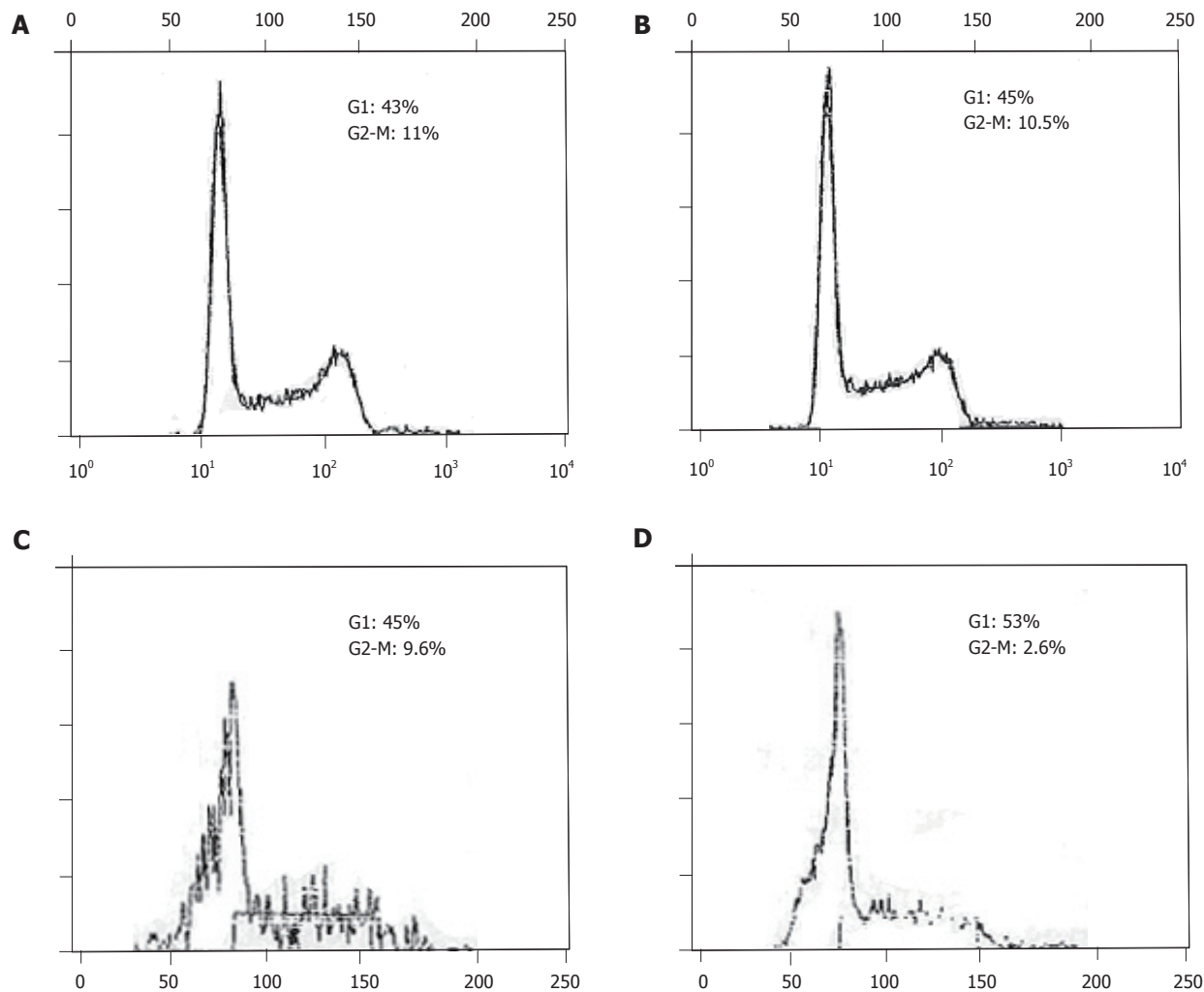


Figure 4 Cell cycle analyzed by fluid cytometry. A: MGC-neo cells in 60% confluence; B: MGC-anti-bcl-2 cells in 60% confluence; C: MGC-neo cells recultured for 24 h after reaching 100% confluence; D: MGC-anti-bcl-2 cells recultured for 24 h after reaching 100% confluence.

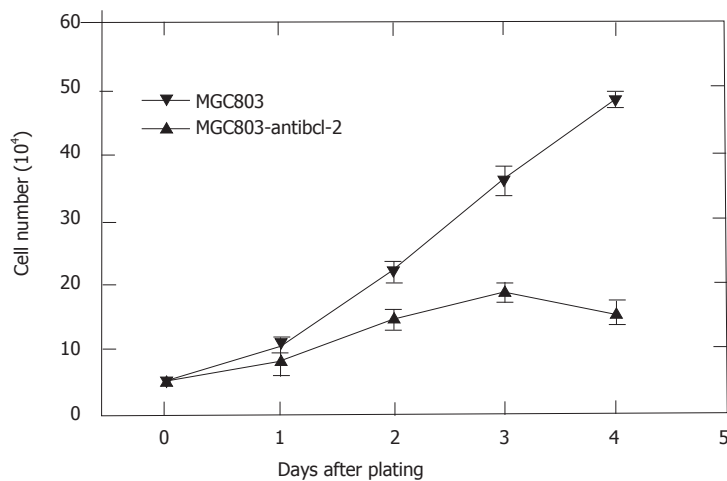


Figure 5 Growth curve of MGC-anti-bcl-2 and MGC-neo cells.

retrovirus-mediated bcl-2 antisense RNA was expressed and could down-regulate BCL-2 protein expression in MGC-803 cells.

Antisense RNA to bcl-2 alter morphology of MGC-803 cells

MGC-803 was an anchorage-dependent, round or a slightly flat cells. After being transduced with retrovirus expressing antisense bcl-2 RNA, morphology of MGC-803 cell altered, from round or slightly flat to shuttle-like, and it become larger than the parental MGC-803 or control MGC-neo cells (Figure 3). Contact inhibition was also observed in MGC-anti-bcl-2 cells. The result shows that MGC-803 cells transduced with retrovirus expressing antisense bcl-2 RNA was prone to differentiate. Vauk *et al.* (1988) reported that bcl-2 did not morphological transform NIH3T3 fibroblasts, and our data showed that bcl-2 antisense RNA also did not alter T-cell leukemia Jurkat morphologically (data not shown). The mechanism that bcl-2 antisense RNA alter morphologically MGC-803 cells remains for further investigation.

Antisense RNA to bcl-2 cause G1 phase arrest and inhibit proliferation

Cell cycle analysis of cells in logarithmic growth showed that antisense bcl-2 RNA had not altered the distribution of MGC-803 cells, the main proportion of MGC-anti-bcl-2 and MGC-neo cells in G1 and G2-M were as follows respectively: 45%, 10.5% and 43%, 11%. However, antisense bcl-2 RNA cause G1 phase arrest in MGC-anti-bcl-2 cells if cells were continued to culture for 24 h after reaching 100% confluent, the percentage of G1 and G2-M phase were 53%, 2.6%, and 45%, 9.6% for MGC-anti-bcl-2 and MGC-neo cells respectively (Figure 4). To study whether bcl-2 antisense RNA had effect on proliferation, the cell number was counted directly after being stained with trypan blue. The MGC-anti-bcl-2 cells grew slowly and ceased growing when it reached 100% confluent at the third day, while the control MGC-neo cells grew rapidly and continued growing even it was 100% confluent (Figure 5). All those data show that bcl-2 antisense RNA inhibit proliferation of MGC-803 cells, and cause G1 phase arrest.

Weakened tumorigenicity in nude mice

We tested the tumorigenicity *in vivo* of MGC-803 cells transduced with virus expressing antisense RNA to bcl-2 and with pLXSN virus as control in nude mice. Subcutaneous injection of MGC-anti-bcl-2 and MGC-neo cells into nude mice both resulted in the development of tumors, but the weight of tumors, 330.6 ± 69.4 mg and 496.5 ± 92.5 mg respectively, has significant difference ($P < 0.05$, $P = 0.028$). This indicated that the tumorigenicity of MGC-803 cells was weakened by retrovirus-mediated antisense RNA to bcl-2 (Figure 6).

DISCUSSION

In this report, we have investigated the effect of retrovirus mediated antisense RNA to bcl-2 on biological behavior of stomach carcinoma MGC-803 cell lines. The results of these studies shows that bcl-2 antisense RNA can inhibit the expression of BCL-2 protein

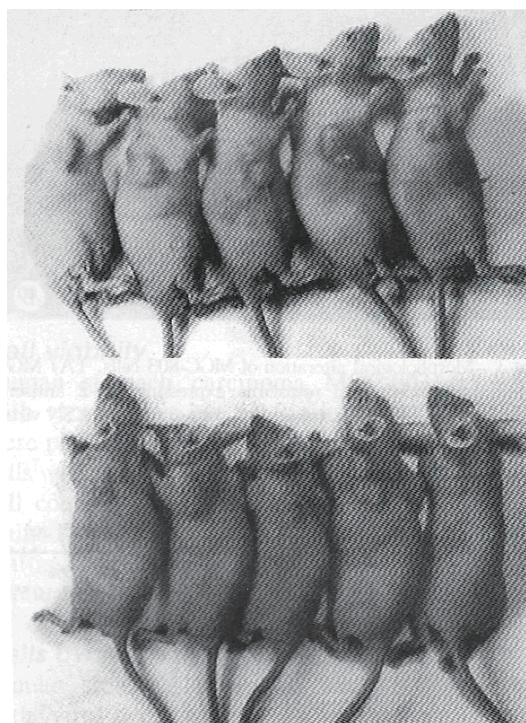


Figure 6 Tumorigenicity in nude mice. The left side is tumor formed by injection of MGC-anti-bcl-2 cells, and the right side is MGC-neo cells.

in MGC-803 cells, by which it cause morphological alteration, from round or a slightly round to shuttle-like, enlargement of cellular volume, G1 phase arrest, Contact inhibition and weakened tumorigenicity in nude mice. All these data indicate that bcl-2 antisense RNA can inhibit proliferation and alter the biological behavior of MGC-803 cells.

c-myc gene plays an important role in determinating the deovelpment of cells to proliferate, silent, differentiate or die depending on the stimuli given. *c-myc* can provide the first signal, leading to apoptosis or to progression, and bcl-2 may provide a second signal to inhibit apoptosis and allows *c-myc* to drive cells into the cell cycle^[2]. Bcl-2 has synergy with *c-myc* to promote proliferation of pre-B cells^[12] and to markedly enhance the tumorigenicity in athymic nude mice^[7]. The transduced retro virus can express bcl-2 antisense RNA, and downregulate BCL-2 protein expression in MGC-803 cells, thus the synergy between bcl-2 and *c-myc* was aborted and cause reversion of bilogical behavior. In addition, bcl-2 can modulate p53 fuction by altering p53 subcellular trafficking during cell cycle^[8] and block or delay the apoptosis

induced by p53, ICE and other apoptosis-promoting genes^[4]. All these data make us to hypothese that retrovirus mediated bcl-2 antisense RNA inhibit the expression of BCL -2 protein, and upregulation of genes which were associated with cell prolifera-tion or cell cycles caused by supression of BCL-2 protein alter the biological behavior of MGC-803 cells. The actual mechanism remains for further investigation.

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Breath hydrogen determination in patients following partial gastrectomy

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Abstract

AIM: The study was aimed at the unknown mechanisms of gastrointestinal symptoms and accompanied malnutrition in patients following partial gastrectomy.

METHODS: Thirty-six patients who had their gastric resection at least five years ago and forty-one normal controls were included in the study. Nutritional status as indicated by anthropometry measurements, glucose hydrogen breath test (G-HBT) before and after antibiotic treatment and mouth-cecum transit time (MCTT) with lactose hydrogen breath test (L-HBT) were simultaneously determined. The Student's *t* test was used for statistical analysis of all the data of the study.

RESULTS: Anthropometry measurements showed that decreased values (at least 10% lower than the ideal values) of body weight (BW), triceps skinfold thickness (TSF) and mid-arm circumference (MC) were observed in 63.2%, 94.7 % and 73.3% of the patients studied respectively. A positive result of 50g G-HBT was seen in 10 cases out of 26 patients (38.5%) who were undertaken the test. Six of the 9 patients with negative 50 g G-HBT were positive following a 80 g G-HBT. Hydrogen excretion in six patients with positive 50 g or 80 g G-HBT were significantly decreased after antibiotic treatment. Further studies of 25 L-HBT showed a significant difference of MCTTs either between the post-gastrectomy patients with or without chronic diarrhea, or between patient and control groups, *i.e.* an average MCTT of 58.8, 85.7 and 105.9 min in each group.

CONCLUSION: Malnutrition was common in patients a few years after their gastrectomies. About forty percent of positive G-HBT,

and effective antibiotic treatment and reduced MCTT determination were observed in these patients. The results suggested that bacterial overgrowth and increased small bowel transit may play a role in the development of gastrointestinal symptoms and related malnutrition in patients following gastrectomy.

Key words: Gastrectomy; Nutritional status; Glucose hydrogen breath test; Mouth cecum transit time; Lactose hydrogen breath test

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INTRODUCTION

Malnutrition with gastrointestinal symptoms including chronic diarrhea has been commonly observed in patients following partial gastrectomy. However, the causes of the symptoms and accompanied malnutrition are obscure^[1,2]. The present study was aimed at the target of unknown etiology of the entity using the method of breath hydrogen determination which has been well demonstrated as an indicator of carbohydrate malabsorption and also widely used for diagnosing bacterial overgrowth or determining small bowel transit time.

MATERIALS AND METHODS

Subjects

Thirty-six patients who had their gastric resection (partial gastrectomy) at least five years ago were included in the investigation. Forty-one healthy medical students and hospital staffs as control were included in the study.

A detailed history was taken and physical examination were performed for each patient and control subject. Indications for gastric surgery were stomach carcinoma, peptic ulcer diseases and their complications including massive upper gastrointestinal bleeding. Pre-and post operatively body weights were recorded.

Anthropometry measurements

Body weight (BW) as percent of ideal weight, tripeps skinfold thickness (TSF) and Mid-arm circumference (MC) were determined and normalized using age-and sex-specific reference tables of healthy Chinese adults^[3-5].

Glucose Hydrogen (H₂) breath test (G-HBT)

Breath excretion tests with glucose challenge were performed using the protocol as below: each patient and volunteer was first asked to have a dose of 50 g glucose (in 250 mL of warm water)

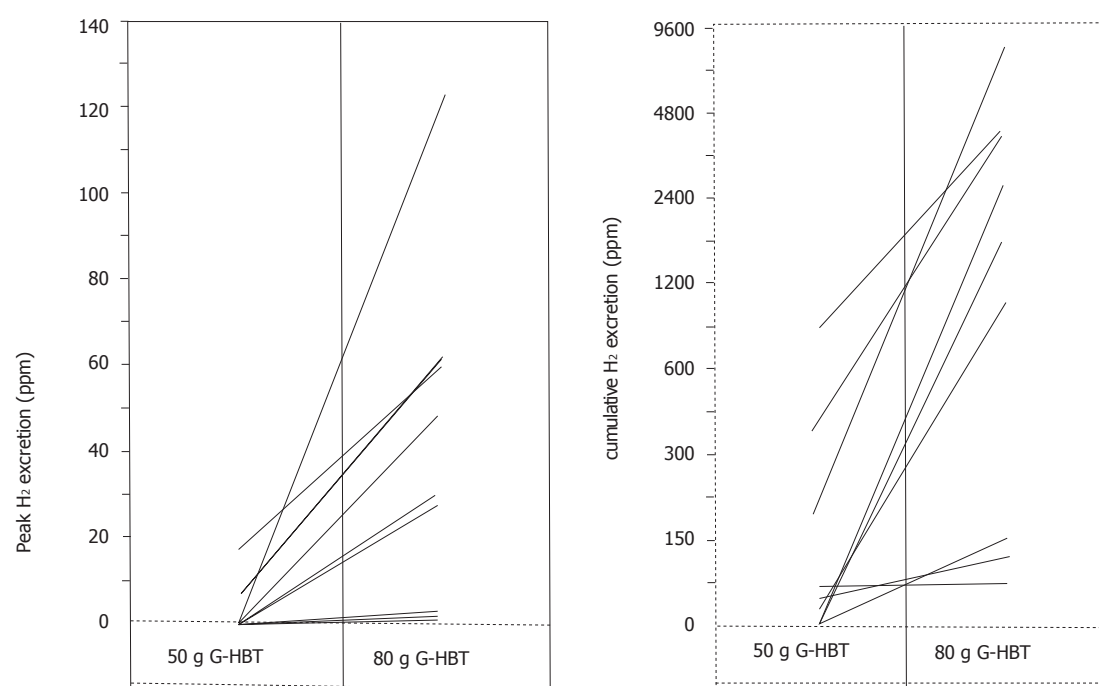


Figure 1 The result of 50 g and 80 g G-HBT.

Table 1 Evaluation of the nutritional status in patients following partial gastric surgery

% of ideal value	> 90	80-90	60-80	< 60
Nutritional status	Normal	Mild	Moderate	Severe
BW				
Diarrhea (n = 7)	3	3	1	0
Non-diarrhea (n = 12)	4	5	3	0
TSF				
Diarrhea (n = 7)	1	0	1	5
Non-diarrhea (n = 12)	0	0	1	11
MC				
Diarrhea (n = 7)	1	5	1	0
Non-diarrhea (n = 12)	4	4	4	0

$$WB(\%) = \frac{\text{Actual BW}}{\text{Ideal BW}} \times 100; MC (\text{cm}) = \text{Armce} (\text{cm}) - (0.314 \times \text{TST mm}) \text{ circumference}$$

(50 g G-HBT), and then H₂ was collected and determined at every 30 min interval as the method reported by Kotler, Metz and Kings *et al.*^[6-9]. The model CM₂ Microlyzer (Quin Tron Instrument Co. Inc., Milwaukee, Wisc. United States.) was used for H₂ determinations. Both peak H₂ concentration and its time of occurrence and cumulative H₂ excretion after glucose ingestion were recorded. The later indicator was estimated by calculating the area under the curve of H₂ concentration against time, with the following equation for the sum of the areas of consecutive trapezoids. $A = (1/2H_1 + H_2 + H_3 + \dots + H_{n-1} + 1/2H_n) \times t$. Where A stands for area, H stands for breath H₂ concentration in ppm (parts per million) and t is 30 min.

A further 80 g of glucose challenge (80 g G-HBT) was given next morning if the 50 g G-HBT showed a negative result, *i.e.* H₂ excretion was increased less than 20 ppm within 2 h after glucose ingestion. When 80 g G-HBT showed a negative result again, the study would be finished and was considered as a normal result. Antibiotic (terramycin 0.5 g four times every 6 h and metronidazole 0.2 g three times a d for a total of 3 d) were given orally for three d when 50 or 80 g of glucose loading showing a positive result, *i.e.* breath H₂ excretion increased at least 20 ppm more than fast H₂ concentration. A positive bacterial overgrowth (BOG) in the upper part of the small bowel was suggested only if HBT returned negative or there was a significant decrease of H₂ excretion after antibiotics administration. The patients stools studied were all cultured and found no growth of pathogenic organisms. For normal controls, only 50 G-HBTs was performed.

Lactose hydrogen breath test (L-HBT)

Lactose malabsorption was also determined among the patients and

volunteers next morning following G-HBT, or at least three d later if antibiotics were given during the study. The method using hydrogen breath test was as previously described^[10,11]. A positive result with lactose malabsorption was defined as H₂ output after 25 g of lactose loading increased 20 ppm higher than the fast level.

Mouth to cecum transit time (MCTT)

Transit time using 25 g L-HBT was only measured in patients and volunteers who had been document as lactose malabsorbers according to the criterion mentioned above. The time elapsing between lactose ingestion and the earliest 20 ppm rise of exhaled H₂ was considered to represent MCTT of the lactose column as it passed through the small bowels^[1,6,10].

RESULTS

Twenty-six patients with definite medical records were divided without diarrhea. Postprandial bloating and abdominal distention were seen in 8 cases, and borborygmus in 4 cases. Only 3 patients showed no significant gastrointestinal symptoms.

Anthropometrical measurements were taken in 19 out of above 36 patients, and most patients including non-diarrhea group showed lower results, *i.e.* BW, TSF and MC as expressed at least 10% lower than ideal value were seen in 63.2 (12/19), 94.7 (18/19) and 73.3% (14/19) respectively (Table 1). 50 g G-HBT were performed in all 36 patients and were positive in 10 cases (27.8%), including 4 with diarrhea and 6 without diarrhea. Nine patients with negative results of 50 g G-HBT were tested again with 80 g glucose. Six of the 9 patients became positive according to both peak and cumulative H₂ concentration determinations (Figure 1). In addition, Hydrogen excretions in six patients with positive results following either 50 g or 80 g of glucose loading were significantly decreased after antibiotics treatment (Figure 2). The symptoms of diarrhea, postprandial distention or borborygmus were all obviously improved. All six normal controls showed a negative result of 50 g G-HBT.

Twenty-five g L-HBTs were performed in fourteen patients, and H₂ excretion after lactose loading was significantly increased (more than 20 ppm) in thirteen patients with a positive rate of 92.3% (13/14) in contrast to 78% (32/41) of the normal volunteers ($P < 0.05$). MCTTs were determined in all above thirteen lactose malabsorbers. Six with permanent diarrhea had a 57.5 s of transit time. However, the rest seven without diarrhea and normal volunteers had 85.7 and 105.9 s respectively (Figure 3). Statistical analysis showed a significant difference between the two sub-groups and also between the patients and normal groups ($P < 0.05$).

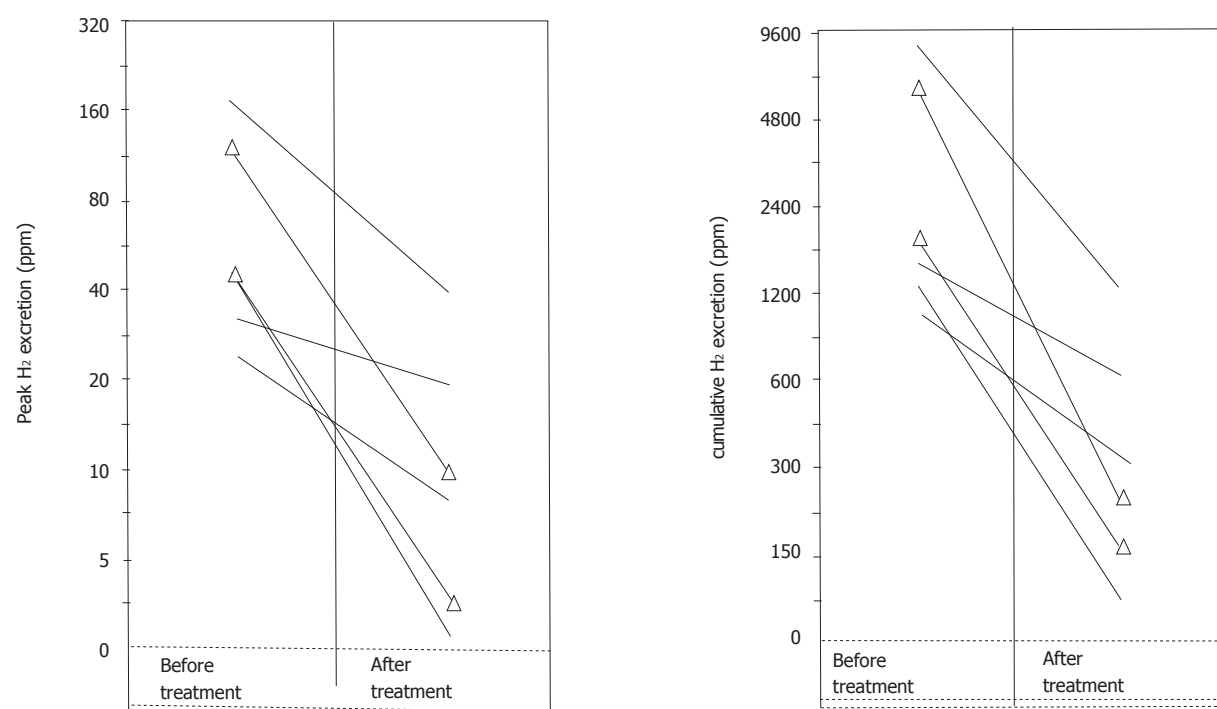


Figure 2 The result of 50 g and 80 g G-HBT after antibiotic ics treatment.

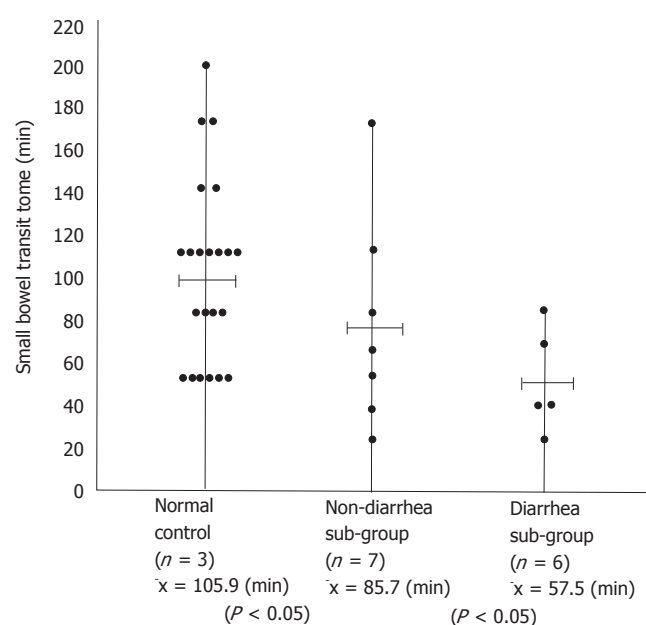


Figure 3 The results of small bowel transit time determination.

DISCUSSION

Malnutrition and accompanied gastrointestinal symptoms have been paid much attention in patients following partial gastrectomy, and were usually attributed to factors such as accelerated transit time, and bacterial overgrowth through the small intestine, and poor mixing of nutrients with digestive enzymes due to a reduced gastric surface following gastrectomy *ect*^[1,2]. The present study using HBT method documented a result consistent with the above hypothesis^[1,2]. The results showed that malnutrition in patients following partial gastrectomy was common, *i.e.*, most of the patients have decreased BW, TSF and MC value as compared to the reference table (Table 1). However, gastrointestinal symptoms including chronic diarrhea were only observed in less than one third of the patients. The fact that most of these malnourished patients have no remarkable clinical symptoms may further exacerbate their nutritional status, and therefore, a high incidence of malnutrition was observed in these gastrectomized patients in the investigation.

Though a few hypothesis it was proposed that the pathophysiology of this type of malnutrition is unclear^[1,2]. The 50 and 80 g G-HBT in the present study revealed more than one third of gastrectomized patients have increased H₂ excretion following glucose challenge. Interestingly, H₂ excretion in six patients had a remarkable decrease with clinical improvements after

antibiotic treatment (Figure 2). The results appeared to suggest a possible mechanism of bacterial overgrowth in the development of malnutrition and related gastrointestinal symptoms in the patients studied. However, there was no statistical difference of the occurrence of bacterial overgrowth between the sub-groups with or without chronic diarrhea. In combination with the fact that the anthropometric measurements were not different between these two sub-groups, we hypothesized that the mechanism of the entity must be multifactorial or individualized in different patients.

The study of 25 g L-HBT showed an accelerated SBTT (58.6 min) in diarrhea subgroup, as compared to 85.7 and 105.9 min in non-diarrhea patients and normal volunteers (Figure 3), indicating an altered MCTT may play a important role in addition to the BOG mechanism in the occurrence of diarrhea. Further more in the present study, a much higher incidence of lactose malabsorption which may reflect a lower quantity of lactase in the gut was seen in gastrectomized patients than in normal controls, and most interestingly all the patients with diarrhea were fallen into the positive group of 25 g L-HBT. All these facts that suggested a poor mixing of nutrients with digestive enzymes may participate in the development of chronic diarrhea and finally malnutrition after gastric resection.

We also obtained an increased positive result of HBT using 80 g glucose challenge (Figure 1). The result was were consistent with the conclusion that 80 g G-HBT may be a more sensitive and useful procedure than 50 g G-HBT for BOG diagnosis^[9].

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Effects of capsaicin on stress-induced duodenal injury

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Abstract

AIM: To determine whether capsaicin could protect against stress-induced duodenal ulceration.

METHODS: Fasted Sprague-Dawley rats were restrained in rigid plastic tubes and immersed in a water bath at 24 °C for 4 h. Thereafter, rats were killed, duodenum opened and discrete ulcers counted and aggregated area of ulceration (mm²) measured. Duodenal tissues were fixed in 10% formalin for histological examination. Duodenal CGRP content was measured by RIA after tissue extraction. All test drugs were given intragastrically. The following 4 groups of rats were subjected to water-restraint stress: (1) Control: saline or vehicle (1 mL solution: ethanol 10%, Tween 80 10%, saline 80% v/v/v), (2) Acute capsaicin administration (1.3 mg/kg), (3) Acute administration of CGRP 14 µg/kg, (4) Afferent sensory denervation caused by high dose of capsaicin (total 125 mg, sc) administered 2 wk prior to experiment. Data for each group represented the result of 6-8 experiments. Statistical evaluation and comparison of the data were performed by Student's *t* test and analysis of variance by Duncan's test.

RESULTS: Water immersion restraint stress caused severe duodenal ulceration with hemorrhage. Discrete duodenal ulcers numbered 3.6 ± 0.5 , and aggregated area of ulceration measured 5.1 ± 0.6 mm². Acute capsaicin pretreatment significantly reduced the number (1.6 ± 0.2) and area (2.0 ± 0.3 mm²) of duodenal ulcers ($P < 0.01$). Similarly, CGRP p retreatment significantly inhibited the number (1.4 ± 0.2) and area (1.7 ± 0.3 mm²) of duodenal ulceration. In contrast, denervation of sensory afferent nerves by chronic capsaicin treatment caused significant increase in ulcer number and area of ulceration as compared to control rats: 5.0 ± 0.4 and 7.6 ± 0.8 mm² ($P < 0.05$). Histological examination of the duodenum from animals subjected to stress confirmed macroscopic assessment of duodenal ulceration of mucosa, accompanied by acute hemorrhage. Duodenal CGRP content was reduced significantly in stressed animals when compared to non-stressed rats: 20.5 ± 2.9 pmol/g vs 31.6 ± 3.5 pmol/g ($P < 0.05$). Acute capsaicin pretreatment prevented reduction in duodenal CGRP content (29.8 ± 2.5 pmol/g) ($P > 0.1$ vs control). In contrast, chronic capsaicin treatment caused significant decrease in CGRP content to 5.8 ± 0.8 pmol/g ($P < 0.001$ vs control).

CONCLUSION: (1) Water immersion restraint stress caused duodenal ulceration. (2) Capsaicin and CGRP treatment protected against stress-induced duodenal ulceration. (3) Sensory denervation by capsaicin significantly altered the degree of duodenal ulceration in rats subjected to water immersion restraint stress.

These results validate this model of stress for development of duodenal ulceration and suggest those sensory afferent nerves and CGRP play a role in protecting the duodenal mucosa against stress injury.

Key words: Capsaicin; Stress ulcer; Duodenal ulcer; Rats; Disease models, animal

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Mucins and mucin binding proteins in colon cancer metastasis

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Abstract

AIM: To establish more directly the roles of the MUC2 mucin gene and the mucin binding protein galectin-3 in colon cancer metastasis.

METHODS: MUC2 levels were manipulated in highly metastatic human colon cancer cells using eukaryotic expression constructs designed to express a portion of MUC2 cDNA in the antisense orientation. Galectin-3 levels were also manipulated in human cancer cells using constructs designed to express the complete galectin-3 complementary DNA (cDNA) in either the sense or antisense orientation. Stable transfection was confirmed by a PCR-based approach and by Southern Analysis. Alterations in mRNA were determined by competitive RT-PCR and Northern Analysis. MUC2 apoprotein and galectin-3 protein levels were determined by Western Analysis. Liver colonization was assessed in athymic mice after splenic-portal inoculation or after spontaneous metastasis during cecal growth.

RESULTS: Stable integration of the MUC2 antisense construct into metastatic colon cancer cells (LS Lim6) resulted in an 80% reduction in MUC2-specific mRNA and a concomitant decrease in MUC2 apomucin protein. This was associated with a 50% reduction in synthesis of mature glucosamine labeled mucin, almost complete inhibition of secretion of sialyl Le-X and sialyl Tn antigens, and a 40% decrease in

binding of colon cancer cells to endothelial E-selectin. Reduction in MUC2 levels was associated with a marked decrease in liver colonization.

Introduction of galectin-3 antisense into metastatic Lim6 colon cancer cells resulted in an 80% reduction in galectin-3 specific mRNA by quantitative dot blot analysis (normalized to actin). Northern Analysis confirmed a decrease in the 1 kb product in these cells. There was a 13-fold reduction in galectin-3 protein by Western Analysis compared to parental cell line or vector-transfected controls. Similar results were obtained for another metastatic colon cancer cell line for HM7. Both total cellular and cell surface (FACS analysis) galectin-3 were reduced. Transfection of galectin-3 (sense) into low metastatic LS174 T cells resulted in a 4.5-fold increase in mRNA and a 10-fold increase in galectin-3 protein. Down-regulation of galectin-3 by antisense transformation resulted in a significant ($P < 0.001$) decrease in liver colonization (liver weight, number of tumor nodules and percentage of parenchyma replaced by tumor) by Lim6 and HM7, while introduction of galectin-3 (sense) into LS174T resulted in a significant increase in liver colonization after both splenic-portal and cecal injection. Tumor tissue levels of galectin-3 in metastatic foci correlated with levels in injected cells. Manipulation of galectin in these cell lines resulted in coordinately decreased (or increased) levels of MUC2 mucin, a major ligand for this lectin. Galectin-3 was also detected in the serum of 11/13 patients with colonic adenocarcinoma, with highest levels in those with distant metastatic disease.

CONCLUSION: These studies provide direct evidence that the MUC2 mucin gene and mucin binding protein galectin-3 play an important role in colon cancer metastasis.

Key words: Colonic neoplasms; Neoplasm metastasis; Mucins; Mucin binding proteins; MUC2 mucin gene; Galectin-3

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Genetic diagnosis and management of hereditary nonpolyposis colorectal cancer

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Abstract

AIM: To determine the frequency of the germline mutations of the mismatch repair (MMR) genes in hereditary nonpolyposis colorectal cancer (HNPCC) and the suspected-HNPCC families.

METHODS: We screened germline mutations of the mismatch repair genes (*hMLH1*, *hMSH2*, *hMSH3*, and *hMSH6*) in 35 Korean HNPCC families and 44 suspected HNPCC families by using polymerase chain reaction-single strand conformation polymorphism analysis followed by sequencing. For the definition of suspected HNPCC, two criteria (criteria I and II) were devised. Criteria I consisted of at least two first degree relatives affected with colorectal cancer with at least one of the following: development of multiple colorectal tumors including adenomatous polyp; at least one colorectal cancer case diagnosed before the age of 50; and occurrence of a HNPCC extracolonic cancer (endometrium, urinary tract, small intestine, stomach, hepatobiliary system, and ovary) in family members. Criteria II consisted of one colorectal cancer patient with at least one of the following: early age of onset (< 40 years); endometrial, urinary tract, or small intestine cancer in the index patient or a sibling (< 50 years); and two siblings with other integral HNPCC extracolonic cancers (one < 50

years). A question aire was mailed to members of the International Collaborative Group on Hereditary Nonpolyposis Colorectal Cancer to determine the mutation detection rate in mismatch repair genes from the families fulfilling these criteria.

RESULTS: In 35 korean HNPCC families, we found 11 germline mutations (31%), all in the *hMLH1* gene. In 44 korean suspected HNPCC families, we found 11 (25%) germline mutations, 7 in *hMLH1* gene, 2 in *hMSH2* gene, and 2 in the polycytosine repeat sequence of the *hMSH6* gene. Through the international collaborative study on the genetic diagnosis of suspected HNPCC, we were able to obtain data on 123 suspected HNPCC families from 8 different institutions. The mutation detection rate for families fulfilling the criteria I was 28% (19/67), while the mutation detection rate for families fulfilling criteria II was 9% (5/56).

CONCLUSION: Genetic testing should be an integral part of the management of HNPCC and suspected HNPCC families. The criteria I for the diagnosis of suspected hereditary nonpolyposis colorectal cancer have the advantages that they can be applied to nuclear families and include extracolonic cancers. Our results suggest that families fulfilling the criteria I should be offered genetic testing. The relatively low mutation detection rate in those families fulfilling criteria II suggests that using current techniques, genetic testing in these families is not a practical proposition. An international collaborative study under the revised criteria II is in progress. Also, our data indicates that genetic testing for *hMSH6* gene can be considered in suspected HNPCC families without mutations in the *hMLH1* and *hMSH2* genes.

Key words: Colorectal neoplasms/diagnosis; Colorectal neoplasms/therapy; Colorectal neoplasms/genetics; Mutations; Genetic test

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Park JG. Genetic diagnosis and management of hereditary nonpolyposis colorectal cancer. *World J Gastroenterol* 1998; 4(Suppl2): 51 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/51.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.51>

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Nutritional status in non alcoholic subclinical portosystemic encephalopathy

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Abstract

AIM: To understand the role of nutritional status in cirrhotic patients without clinical porto-systemic encephalopathy (PSE).

METHODS: We prospectively studied 51 non-alcoholic patients with cirrhosis without PSE (mean age: 58 ± 11 years; M: 29, F: 22) to compare with 20 healthy volunteers. The nutritional evaluation included serum prealbumin, albumin, transferrin, body mass index (BMI), mid-arm muscle circumference (MAMC), and grip power. The occurrence of subclinical PSE (SPSE) was defined as when N20-N65 inter-peak latencies of median nerve-stimulated somatosensory evoked potentials (SEPs) greater than 2.5 standard deviations of control means. Blood chemistries were tested within 12 h of SEP testing and nutritional evaluation.

RESULTS: Twenty-five, 17 and nine cirrhotic patients were grade d as Child-Pugh class A, B and C, respectively. Twenty-four (47.1%) cirrhotic patients developed SPSE. Cirrhotic patients with SPSE had lower serum albumin (2.8 ± 0.5 g/dL *vs* 3.1 ± 0.7 g/dL, $P < 0.001$) levels than those without SPSE. Prealbumin (10.6 ± 5.7 mg/dL *vs* 12.5 ± 5.8 mg/dL), transferrin (164 ± 46 mg/dL *vs* 178 ± 58 mg/dL), BMI (23.7 ± 2.7 kg/m² *vs* 25.3 ± 3.6 kg/m²), MAMC (22.2 ± 2.6 cm *vs* 22.7 ± 3.5 cm), and grip power (26.3 ± 6.4 kg *vs* 26.9 ± 6.8 kg) were not different between cirrhotic patients with and without SPSE. N20-N65 inter-peak latencies correlated with serum albumin levels ($P = 0.01$) but not with prealbumin, transferrin, BMI, MAMC, or grip power. Serum albumin, prealbumin and transferrin levels were different among cirrhotic patients in Child-Pugh classes A, B and C ($P < 0.05$). BMI, MAMC, and grip power were not different among patients in Child-Pugh classes A, B and C.

CONCLUSION: Our data suggest that serum is a simple test in the evaluation of nutritional status in patients with cirrhosis.

Key words: Liver cirrhosis/complication; Brain diseases/etiology; Nutritional status

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Diagnosis of *Helicobacter pylori* with emphasis on endoscopic diagnosis

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Abstract

Helicobacter pylori was successfully cultured and identified by Mash all *et al* in 1983. Various studies have since been performed. *H. pylori* infection was classified as a risk factor for stomach cancer (definite carcinogen group I) by the WHO/ IARC in 1994.

AIM: The detection of the organism is crucial for treatment and assessment after treatment.

METHODS: The reliability and specificity of the various methods available show almost no differences, and diagnostic methods include

both endoscopic and non-endoscopic techniques.

RESULTS: On endoscopy, mucosal changes such as erosions and redness are often observed in the pyloric glandular region of the stomach in the initial stage of infection, with subsequent progression to muddy color, atrophy, intestinal metaplasia and ulceration.

Diagnosis is often difficult by endoscopy alone, and mucosal staining with dyes such as phenol red is commonly used as auxiliary method. Histological examination and culture of biopsy specimens, as well as PCR and the rapid urease test are also necessary. Non-endoscopic methods include serum anti-Hp IgG antibody and the ¹³C urea breath test.

CONCLUSION: In Japan, diagnosis and evaluation of *H. pylori* eradication are performed according to the criteria published by the Japanese Society of Gastroenterology.

Key words: *Helicobacter pylori*; Helicobacter infection/diagnosis; endoscopy; gastric ulcer

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Hirakawa T. Diagnosis of *Helicobacter pylori* with emphasis on endoscopic diagnosis. *World J Gastroenterol* 1998; 4(Suppl2): 53 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/53.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.53>

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Infection of *Helicobacter pylori* in rats and mice: A one year study

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Abstract

AIM: To investigate the long term infection of *H. pylori* in the conventional laboratory rats and mice, and the serological responses of the infected-animals.

METHODS: Two strains of *H. pylori* (one vac positive and one vac negative) were separately isolated from two duodenal ulcer patients. The bacteria were considered as mouse-adapted strains after they have passaged through the mice 3 times serially. Groups of female BALB/c mice and Sprague-Dawley rats were separately inoculated with mouse-adapted vac⁺ or vac⁻ *H. pylori*. The animals were treated with omeprazole before and after the bacterial inoculation in order to increase the gastric pH. Then the animals were sacrificed 2 wk, 2, 6-7 or 12 mo after the bacterial inoculation. At sacrifice, blood was sampled for ELISA; mucosa from the corpus and the antrum were separately scraped off, and cultured in order to determine the colony forming units (CFUs).

RESULTS: *H. pylori* colonized the gastric mucosa in most of the

bacteria-inoculated mice and rats, and the colonization was rather constant 2 to 12 mo after *H. pylori* inoculation. In the mice, CFUs were around 200/mg scraped mucosa in the antrum and were around 100/mg in the corpus. There were no differences of colonization between vac⁺ and vac⁻ strain s. Two mo after the bacterial inoculation, the serum level of *H. pylori*-specific Ig in the mice infected by vac⁺ *H. pylori* was progressively and significantly increased up to 10-15 times higher than that in the uninfected controls, while was only slightly increased in the mice infected by vac⁻ *H. pylori*. In the rats, 2 to 12 mo after the bacterial inoculation, CFUs were around 1000/mg in the antrum, while only 2-52/mg in the corpus. Serum levels of *H. pylori*-specific IgG2a were persistently and significantly increased in the rats infected by vac⁺ *H. pylori* in comparison with the uninfected controls ($P < 0.05$ to < 0.001), while IgG1 in these *H. pylori* infected rats remained at control levels.

CONCLUSION: The conventional laboratory mice and rats can be infected by the mouse-adapted *H. pylori* strains. Serological response was significant in vac⁺ *H. pylori* infected mice, but not in vac⁻ *H. pylori*-infected mice. The significantly increased serum *H. pylori*-specific IgG2a antibody in the rats infected by vac⁺ *H. pylori* showed a strong predominance of an inflammatory Th1-type response.

Key words: *Helicobacter pylori*; Helicobacter infection; Rats; Mice

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Li H, Kalies I, Helander HF. Infection of *Helicobacter pylori* in rats and mice: A one year study. *World J Gastroenterol* 1998; 4(Suppl2): 54 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/54.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.54>

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Experimental study on the etiologic effect of pancreas divisum on chronic pancreatitis and the pathogenesis

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Abstract

AIM: To investigate the etiologic association of pancreas divisum (PD) with chronic pancreatitis and to clarify the pathogenesis.

METHODS: A PD canine model was established in 32 dogs. The dogs were randomly divided into 4 groups ($n = 8$). Group I: The communicating branch between the dorsal and ventral pancreatic ducts was partly ligated remaining about 1.0 mm diameter. Group II a: The communicating branch was amputated and completely ligated. Group II b: The dorsal duct was amputated and ligated at 2 mm distance to the minor papilla. Group III: A sham operation without any amputation or ligation was performed. before and after operation, the activities of serum phospholipase A2 (PLA2) and amylase (Ams) were assayed and the basal pressures of the ducts were measured when secretin was injected. Pancreatic ductography and the pathologic examination were performed.

RESULTS: (1) The activities of serum PLA2 and Ams in Group I, II a and II b were significantly increased 5 d-80 d after operation. (2) At sacrifice, the basal pressures of the ventral duct were significantly increased 30 min-60 min after provocation in Group I, II a and II b, especially in Group II b, the pressures returned to the normal level till 90 min. The pressures of the dorsal duct were significantly increased in Group II b but no difference in Group I and II a. (3) Light microscope observation: The fibrosis of interlobus and periductes, the destruction of acini and infiltration of inflammatory cell in dorsal and ventral pancreas were found in Group II b. But in Group I and II a, these findings were present only in ventral pancreas. (4) Electron microscope observation: In ventral pancreas of Group I and II a and the dorsal and ventral pancreas of Group II b, the rough endoplasmic reticulum of the acinar cells showed granules-scaling, fusion and relation. The zymogen granules decreased and the mitochondria was swollen.

CONCLUSION: A definite etiologic relationship was confirmed between PD and chronic pancreatitis. The pathogenesis was due to the functional obstruction of the minor papilla at the peak stage of secretion.

Key words: Pancreas divisum/complications; Pancreatitis/etiology; Pancreatitis/physiopathology; Disease models, animal; Chronic diseases

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Chinese fresh herbal medicine in prevention of virus hepatitis A

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Abstract

AIM: To illustrate the preventive effects of Chinese fresh herbal medicine. *Dandelion and Asiatic Plantation* against viral hepatitis A.

METHODS: We chose two epidemic areas where the disease was diagnosed as virus hepatitis according to the clinical and laboratory results and categorized as virus hepatitis A based on its characteristics of epidemiology. The first area is a natural farm village, where the people were asked to take the decoction of fresh herbal medicine dandelion and Asiatic Plantation. The second area is a town ship secondary school, where no such decoction was used.

RESULTS: After basic preventive measures (such as segregation of patients, disinfection of the epidemic spots, injection of placental gamma globulin to exposed children and students, publicity on health care and strengthening of water and excrement controls) taken at both areas, in the first location, a natural village with 26 families and 126 inhabitants, only 11 (8.7%) cases new occurred after administration of the fresh herbal medicine. Meanwhile, in the other location, a secondary school with a total of 578 people not taking the herbal medicine, there were 148 (25.6%) cases. The difference was remarkable between the two locations.

CONCLUSION: The effects of Chinese fresh herbal medicine *dandelion and Asiatic Plantation* are remarkable in preventing hepatitis A and controlling the spread of the disease. Its application is worthwhile promoting.

Key words: Hepatitis A/prevention and control; *Taraxaci mongolicum*/therapeutic use; *Plantago asiatica*/therapeutic use

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Role of oxygen free radical and other inflammatory mediators in acute necrotic pancreatitis

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Abstract

AIM: To study the role of oxygen free radical (OFR) and other inflammatory mediators in acute necrotizing pancreatitis (ANP).

METHODS: ANP model was induced by retrograde injection of 5% sodium taurocholate 2.0 mL/kg, rats were randomly divided into four groups: (1) control group, (2) ANP group, (3) ANP + NS group, (4) ANP + IL-2 group. Changes of SOD and MDA in plasma and pancreatic tissues and serum endotoxin, PLA₂ were studied. We

also studied the histologic changes of pancreas, liver and lung. The effects of interleukin-2 (IL-2) in the treatment of ANP were observed in this experiment.

RESULTS: Oxygen free radicals were involved in the aggravation of ANP and was associated with the increase of serum endotoxin and PLA₂. Those mediators were positively correlated with severe multiple organ damage. The results also suggested that IL-2 can inhibit the overexpression of OFR and endotoxin, and reduce the incidence of multiple organ damage in ANP.

CONCLUSION: OFR might play a major role in the pathogenesis of ANP, and IL-2 might have a potential role in the treatment of ANP.

Key words: Pancreatitis; Free radicals; Interleukin-2; Endotoxins; Superoxide dismutase; Malondialdehyde

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Wang WX, Zhao HP, Shou NY, Yang CW. Role of oxygen free radical and other inflammatory mediators in acute necrotic pancreatitis. *World J Gastroenterol* 1998; 4(Suppl2): 57 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/57.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.57>

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Short term and long term effects of Weisu granules triple therapy on peptic ulcer

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Abstract

AIM: To observe the short term and long term effect of Weisu granules triple therapy on peptic ulcer.

METHODS: Fifty-three cases of peptic ulcer were treated with triple therapy of Weisu granules, amoxicillin and metronidazole for 3 wk, and followed up 1 year to investigate the short term and long term effect. Thirty-two cases treated with Marzulene-S granules, amoxicillin and metronidazole triple therapy were used as control. Of the 53 patients, 46 were DU, 7 GU, 32 were men and 21 were women, aged 18-72 years. The clinical manifestations were fullness of the abdomen

(36 patients), upper abdominal pain (51), anorexia (26), eructation (35) and pantothenic acid (48). After treatment, the patients received gastroscopic examination and Hp were detected with urea test.

RESULTS: After 3 wk treatment with Weisu granules triple therapy, it showed that the rate of ulcer healing 81.1% (45/63) and Hp eradication 89.3% (42/47) in treatment group and 84.3% (27/32) and 92.1% (26/28) in control group ($P > 0.05$). The rate of adverse reactions was significantly lower in the treatment group (7.1%) than that in control group (11.2%) ($P < 0.05$). After one year follow up in treatment group 43 cases have cured. Hp recurrence was found in 7 cases (16.2%). Ulcer relapse rate was 5/42 (11.9%) in Hp negative group versus 7/11 (63.6%) in positive group. The difference was significant ($P < 0.01$).

CONCLUSION: The triple therapy of Weisu granules has better therapeutic effect on peptic ulcer.

Key words: Peptic ulcer/drug therapy; Weisu granules; Marzulene/therapeutic use; Amoxicillin/therapeutic use; Metronidazole/therapeutic use

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Short-term effects of the triple-therapy combined with ion therapy of Chinese herbal medicine on 50 cases of peptic ulcer

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Abstract

AIM: To improve the therapeutic effects of combined Chinese and western medicine in patients with peptic ulcer (PU).

METHODS: Ninety cases of patients with PU were divided into two groups. Fifty cases in group A were treated with triple therapy [Omeprazole 20 mg qd, Amoxicillin 1.0 g tid, Colloidal Bismuth Subcitrate (CBS) 110 mg tid] for 28 d and the ion therapy of Chinese

herbal medicines for 10-20 d; 40 cases in group B only with the triple-therapy as control.

RESULTS: By the 4th week the short-term effective rate (90% in group A versus 85.0% in B), or the ulcer healing rate (80.0% in group A versus 72.5% in B) showed no significant difference between group A and B ($P > 0.05$), but patients in group A recovered more quickly than in B (average 8.7 d versus 13.9 d, $P < 0.01$).

CONCLUSION: This therapy can release the symptoms of PU more quickly, and shorten the period of hospital stay.

Key words: Peptic ulcer/drug therapy; Amoxicillin/administration and dosage; Omeprazole/administration and dosage; Bismuth potassium citrate/administration and dosage

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Relationship between cell adhesion molecule CD15 and proliferating cell nuclear antigen expression in gastric cancer and precancerous lesions

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Abstract

AIM: Expression of cell adhesion molecule CD15 and proliferating cell nuclear antigen (PCNA) were examined in gastric cancer and precancerous lesions in order to study the correlation between CD15 and PCNA.

METHODS: CD15 and PCNA were detected respectively in 30 cases of normal gastric mucosa, 30 cases of intestinal metaplasia, 60 cases of atypical hyperplasia (22 mild cases, 21 moderate cases and 17 severe cases), and 95 cases of cancer tissues (63 well differentiated tumors, and 32 poorly differentiated tumors) by microwave-SP immunohistochemical technique.

RESULTS: The expression level of CD15 in gastric cancer was 81.1% (77/95), significantly higher than 55.0% (33/60) in atypical hyperplasia ($P < 0.001$). CD15 expression in poorly differentiated tumors was 84.4% (27/32), significantly higher than 79.4% (50/63)

in well differentiated ones ($P < 0.05$). Positive rate of CD15 in severe atypical hyperplasia was 82.4% (14/17), significantly higher than 36.8% (8/22) and 52.4% (11/21) in mild and moderate ones ($P < 0.05$). No difference was found between normal gastric mucosa and intestinal metaplasia, neither between severe atypical hyperplasia and well differentiated tumors. Positive rate of PCNA in the cases of CD15 positive expression was 81.1% (120/148), significantly higher than that of CD15 negative expression ($P < 0.001$). The level of CD15 expression was positively correlated to the level of PCNA expression ($r = 0.64$). CD15 expression in tumors penetrating through the serosa was 95% (38/40), significantly higher than 78.2% (43/55) in tumors not penetrating through the serosa ($P < 0.05$). Positive rate of CD15 in tumors with lymph nodes metastases was 92.6% (63/68), significantly higher than that in tumors with negative lymph node metastases ($P < 0.05$). Positive rate of PCNA that was not correlated with the infiltration and metastases of gastric cancer was increased progressively with the extension of gastric mucosal lesions.

CONCLUSION: CD15 expression correlated with gastric mucosal progression and differentiation, and with carcinogenesis, infiltration and metastases. It might be a good marker in diagnosis of early gastric cancer and the evaluation of malignancy, predicting the biological behavior of tumor and the prognosis of patients.

Key words: Stomach neoplasms; Precancerous lesions; Cell adhesion molecule CD15; Proliferating cell nuclear antigen

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Therapeutic effect of medicinal herbs and western drugs on hepatitis B virus

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Abstract

AIM: To investigate the therapeutic effect of chinese herbs and western drugs on inhibition of hepatitis B virus replication.

METHODS: There were 123 cases (patients with hepatitis B and carriers of HBsAg). They were either HBeAg positive or HBV-DNA (PCR) positive, or both. They were divided into four groups randomly. The first group was the interferon (IFN) group (the control group). The other three groups were the treatment groups. The first group (the α -IFN group) included 30 cases. 14 cases with normal liver function and 16 cases with abnormal liver function. The second group (treated with polyporus umbellatus polysaccharide and HBV vaccines) included 31 cases. 16 cases with normal liver function and 15 cases with abnormal liver function. The third group (treated with WuLinWan), included 30 cases. 15 cases with normal liver function and 15 cases with abnormal liver function. The fourth group (treated with polyporus umbellatus polysaccharide, HBV vaccines and WuLinWan), included 32 cases. 13 cases with normal liver function and 19 cases with abnormal liver function. All patients were treated for three mo. Afterwards, HBeAg, HBV-DNA (PCR) and liver function

were reexamined. The indicators for therapeutic effectiveness were that HBeAg and HBV-DNA (PCR) became negative. χ^2 test was used to analyse the results.

RESULTS: There were significant differences among the four groups. $\chi^2 = 13.877$, $P < 0.01$. In the first group, it was effective for one patient with normal liver function and 13 cases with abnormal liver function. The effective rate was 46.7%. In the second group, effective for one case with normal liver function and 8 cases with abnormal liver function, the effective rate was 29.0%. In the third group, effective for none with normal liver function and six with abnormal liver function. The effective rate was 20%. In the fourth group, effective for 2 with normal liver functional and 18 with abnormal liver function. The effective rate was 62.5%. There were significant differences between the first and the second group ($P < 0.05$); the first and the third group ($P < 0.05$); but $P > 0.05$ between the first and the fourth group. For subjects with normal liver function the effective rate was 7.0% (4/58). For subjects with abnormal liver function, the effective rate was 69.2% (45/65). There was significant difference between them. $\chi^2 = 49.69$, $P < 0.01$.

CONCLUSION: Combination of polyporus umbellatus polysaccharide, HBV vaccines and WuLinWan was proved to be effective for hepatitis B virus especially for patients with abnormal liver function.

Key words: Hepatitis B/therapy; Interferon/therapeutic use; Polyporus umbellatus polysaccharide; Wu Lin Wan/therapeutic use

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Experimental research of jaundice relieving and enzyme reduction by Chinese medicine compound oriental wormwood injection on toxic injury of liver in rats

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Abstract

AIM: To observe the effects of jaundice relieving and enzyme reduction by Chinese Medicine compound oriental wormwood injection (COWI) on toxic injury of liver in rats.

METHODS: The toxic liver injury models of rats were induced by intragastric perfusion of α -naphthalin-isothiocyanateyl (75 mg/kg·wk). Then models of rats were treated with COWI of three different doses (5 mL/kg·d, 10 mL/kg·d, 15mL/kg·d, respectively) sc.

COWI consisted of oriental wormwood, capejasmine, coptis, gentian, scutellaria and rhubarb. COWI originally has the effects of heat-clearing, detoxication, purging of fire and elimination of dampness. Serum alinine aminotransferase (SALT) and serum total bilirubin (STBIL) were measured at 24 h, 48 h, 72 h respectively after treatment with COWI on toxic injury of liver in rats.

RESULTS: Average levels of SALT and STBIL of treatment groups of three different doses were significantly lower compared with control groups ($P < 0.05$). The group treated with a dose of 15 mL/kg·d for 72 h achieved the best result comparably.

CONCLUSION: (1) The results demonstrate that COWI have effects of relieving jaundice and reducing SALT. (2) COWI is a treatment of choice for acute icteric hepatitis.

Key words: Hepatitis, toxic/therapy; Compound oriental wormwood injection; Disease models; Animal

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Present situation of diagnosis and treatment for Dieulafoy's disease

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Abstract

AIM: To present the fundamental conception, summarize the progress in diagnosis and treatment, and deepen medical workers' understanding of Dieulafoy's disease.

METHODS: 144 cases of Dieulafoy-s disease from home and abroad in recent 3 years have been reviewed in this paper by means of studying the literature. The summarization has been made in 5 respects retrospectively.

RESULTS: (1) Incidence: Of the 68 cases reported from abroad the incidence of Dieulafoy's disease was 3.7% among the total cases of massive upper gastrointestinal hemorrhage in the corresponding period. The male-female ratio was 6 to 1. The mean age of the patients was 65 years old. Almost half of the lesions located in the proximal portion of stomach. Moreover, lesions outside stomach was increasing in number, especially in rectum. There were 2 lesions in bronchi, amazingly. 76 cases have been reported at home in recent three years. The ratio of male and female was 7 to 1. The mean age was 49 years old. 51% of Dieulafoy's lesions were within a radius of 6 cm below the cardia in these patients. 13 of them accounted for 1.08% of the total cases with upper gastrointestinal hemorrhage during the corresponding period. (2) Pathology and pathogenesis: The pathological features were elliptical erosion or damage in mucosa with an artery nub (diameter 1 mm-3 mm) extruding the center of the lesion. The lesions lay within 6 cm area below cardia frequently. A few Dieulafoy-s lesions located in small intestine, large bowel, esophagus and bronchi. The pathogenesis: The artery going into gastric wall did not taper off normally but kept its constant diameter. A special damageable region was formed because the artery was fixed to the mucosa by Wanken fibre fasciculus. Break of constant diameter artery was brought about by mucosa damage

as a result of some harmful factors such as excessive drinking, bile reflux, intake of some medicine and shearing force arising from gastric peristalsis. (3) Clinical manifestations and diagnosis: The manifestations of Dieulafoy-s disease were massive haematemesis and melaena without any evident reason frequently, often followed by hypovolemic shock. Diagnosis was made by means of endoscopy, selective angiography, isotopic scan, ultrasonic endoscopy and laparotomy, ect. Emergency endoscopy should be the first of choice. Repeated examination or examination after gastric lavage should be done if necessary. Diagnostic rate was 25%-60% with endoscopy. Blood spurting from a small artery nub in Dieulafoy-s lesion was seen in 55%-66% of the patients. The rate of firm diagnosis was higher than before. (4) Treatments: Treatments for Dieulafoy-s disease were chiefly endoscopic therapy and surgery. The endoscopic therapy was carried out with injecting sclerosants or tissue glue, electrocoagulation, laser, microwave. A few of them were treated with endoscopic band ligation and clips. The curative effects have been improving. The stanching rate was 2/6-18/20. The efficacy rate of stanching was lower with spraying stancher without injection. The surgical way was usually wedge resection or laparoscopic wedge resection of the lesion. (5) Prognosis: The patients undergone endoscopic or surgical therapy often had a favorable prognosis. 93% of them were cured if exact bleeding lesion was found and proper measures were taken promptly. Few serious complications of endoscopic therapy were reported. Patients only undergone conservative treatment died mostly. The mortality of Dieulafoy's disease in this paper was 4.4%. Actually it may be higher, however.

CONCLUSION: Dieulafoy-s disease is a rare cause of gastrointestinal hemorrhage. The feature is a break of constant diameter artery in the lesion pathologically. The presentation of the disease is violent clinically. The common manifestations are massive haematemesis, melaena ad hypovolemic shock. The diagnosis depends mainly on endoscopy. Blood spurting from the small artery in Dieulafoy-s lesion is seen commonly. The curative effect with endoscopic injection is satisfactory generally. Wedge resection of the lesion should be adopted by surgery routinely. Most of the patients with a right diagnosis can be cured. The key to raise curative rate and decrease mortality are that every medical worker is aware of Dieulafoy's disease, and that emergency endoscopy are widely performed so that the diagnosis is made as soon as possible.

Key words: Dieulafoy disease/pathology; Dieulafoy disease/diagnosis; Dieulafoy disease/therapy

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Cell cycle-specific effects of tumor necrosis factor on human gastric cancer cell line

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Abstract

AIM: To study the effects of tumor necrosis factor (TNF) on

proliferation cycle of human gastric cancer cell.

METHODS: Exponentially dividing cells were collected. Cells were treated with TNF at 234 U/mL, harvested at every 24 h up to the 96 h, stained with propidium iodide, and analyzed for cell cycle distribution by flow cytometry. Percentages of cells in the different cell cycle phase were calculated.

RESULTS: The proliferation index (PI) of SGC-7901 dropped from 19.8% to 5.6% in 72 h ($P < 0.01$). When SGC-7901 cells were exposed to TNF for 72 h, the proportion of G-2M DNA content increased from 6.5% to 49.8% ($P < 0.01$). However, the proportion of G₀, G₁ and S phase DNA contents decreased from 73.7% to 44.6% ($P < 0.01$) and 19.8% to 5.6% ($P < 0.01$). The effects of TNF reduced 72 h later.

CONCLUSION: TNF can inhibit SGC-7901 cell proliferation and arrest cells in G-2M. The peak period is 72 h.

Key words: Stomach neoplasms; Tumor necrosis factor; Cell cycle; Flow cytometry

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Significance of detection of plasma nitric oxide, endothelin, endotoxin in patients with liver cirrhosis

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Abstract

AIM: To study the effect of nitric oxide (NO) endothelin (ET) and endotoxin in the decompensatory stage of hepatic cirrhosis due to hepatitis.

METHODS: Thirty-six patients with decompensatory stage of hepatic cirrhosis were in study group, and 30 cases of normal persons in control group. We measured plasma levels of NO metabolite (namely NO₃/NO₂), ET, endotoxin of every case. We classified the 36 patients as degree A, B and C according to Paugh-Child criteria and then measured the levels of NO₃/NO₂, ET and endotoxin.

RESULTS: The plasma NO₃/NO₂ levels in the patient (mean, 7.79 ± 2.07 μmol/L) were significantly higher than that of normal

persons (mean, 3.87 ± 0.73 μmol/L, $P < 0.01$) ; The plasma ET levels in the patients (mean, 99.89 ± 13.20 pg/mL) were significantly higher than that of the normal persons (mean, 42.34 ± 6.27 pg/mL, $P < 0.01$), and differences of plasma endotoxin between patients (mean, 0.476 ± 0.222 eu/mL) and normal persons (mean, 0.142 ± 0.081 eu/mL) were also significant ($P < 0.01$). At the same time, we observed that NO₃/NO₂, ET and endotoxin had positive correlations with each other. $r = 0.609^b$, 0.613^b , 0.523^a , respectively ($^bP < 0.01$, $^aP < 0.05$). The plasma NO₃/NO₂, ET levels increased significantly with the progress of degree A, B and C. NO₃/NO₂ levels between degree B, C, A and control group had no significant difference ($P > 0.05$), but differences of NO₃/NO₂ between degree A and C, B and C were very significant ($P < 0.01$).

CONCLUSION: It was suggested that NO, ET and endotoxin have some role in pathogenesis of hepatic cirrhosis. And that NO₃/NO₂ and ET may increase with liver function deterioration.

Key words: Liver cirrhosis; Nitric oxide/blood; Endothelial growth factors/blood; Endotoxins/blood; Hepatitis

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Double blind randomized control trial of occult blood bead test and gastroscopy-pathology screening for upper digestive tract cancer

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Abstract

AIM: To observe diagnostic value of occult blood bead and gastroscopy-pathology for upper digestive tract cancer in high risk area.

METHODS: At the beginning 4970 subjects received the occult blood bead (OBB) test and 817 underwent gastroscopy, 40 persons of those screened were found to have cancers, 30 of which had early lesions (15 had carcinoma *in situ*). Meanwhile, a double blind randomized control study of the mass screening was conducted. Subjects over 30 years of age were persuaded to participate. Two-hundred and eight people accepted the OBB test, gastroscopy and

histopathological assessment.

RESULTS: The double blind randomized control study of the mass screening found 4 cancers (2 early and 2 moderate and advanced). All these four patients fell in the OBB positive subjects and there was no cancer missed.

CONCLUSION: It demonstrates that if the OBB is adequately carried out, missing of upper GI tract cancer is unlikely. We believe that there would inevitably be missed cancers in large samples. The OBB had to stay in the gastric juice in the fundus to ensure a positive color change. The authors believe that until more simple and effective methods of screening for upper GI tract cancers are introduced, the OBB test can be an easy, inexpensive and reliable means of screening. It is suitable for use in developing countries and areas to screen for cancerous lesions in the upper GI tract. The OBB gastroscopy screening for esophageal and gastric cancer is reliable and practical.

Key words: Esophageal neoplasms/diagnosis; Stomach neoplasms/diagnosis; Gastroscopy; Mass screening; Occult blood bead

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Pathologic analysis of 4451 cases with digestive tract cancer

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Abstract

AIM: To analyse pathological characteristics of 4451 cases of digestive tract cancer, and study its clinical significance.

METHODS: All cases were unselected patients of digestive tract cancer who were diagnosed and operated in our hospital during the period 1983-1997, and the diagnosis confirmed by pathological examination. Comparison was made between different age groups (young < 30, middle 30-40, old 40-70, very old > 70) on the basis of location of the primary cancer.

RESULTS: All patients aged from 7-87 years, mean 61 years, the

ratio of male to female is 2:1. The distribution of age is young (3.5%), middle (9.5%), old (70%), very old group (17%). Distribution of cancer is esophagus 17.1%, cardiac and gastric cancer, 50.7%, and carcinoma of large intestine, 31.6%. In the old and very old age groups well-differentiated and poorly differentiated squamous cell carcinoma of the esophagus, well-differentiated and poorly differentiated adenocarcinoma, myxoadenocarcinoma, papillary adenocarcinoma were significantly higher than those of young and middle age groups ($P < 0.01$, $P < 0.05$, $P < 0.05$). Cardiac and gastric cancer have similar pathological presentations with adenocarcinoma predominates and adenosquamous carcinoma and squamous carcinoma occur infrequently. The incidence of poorly differentiated adenocarcinoma (79% of all cancer of the same location) and ring cell carcinoma (90% of all cancers of the same pathological type) is high in cardia and stomach among all cases. The metastatic rate of cardiac and gastric cancer is 11%; The recurrence rate of residual gastric cancer is 8% with high malignancy and poor prognosis. Precancerous lesions existed in 687 cases; The ratio to all cases is 1:6.5. There are 193 cases of early cancer (4.3% of all cases).

CONCLUSION: It is valuable to perform screening test to examine routinely (such as barium-air double contrast radiography, rectal touch, endoscopy + biopsy), as well as to get a timely pathological diagnosis for the detection and management of gastrointestinal tract carcinoma and early cancer, especially for young and middle age groups.

Key words: Digestive system neoplasms/pathology; Carcinoma, squamous cell/pathology; Adenocarcinoma/pathology; Precancerous conditions/pathology

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Long-term follow-up of patients with liver carcinoma after hepatic arterial infusion and embolization

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Abstract

AIM: To study the long-term effect of intervention therapy on liver carcinoma.

METHODS: Thirty-six patients with middle and late stage unresectable hepatic carcinoma were studied, 31 men and 5 women, age 28 to 68 years. Primary including liver carcinoma 34 cases and 2 cases metastatic carcinoma. The diagnosis was confirmed by selective hepatic arterial angiography through percutaneous femoral artery puncture catheterization follow Seldinger technique. Chemotherapeutic drugs include EPI 40-60 mg, MML 30-40 mg, CDPP 150-300 mg. Embolic agent include: Alcohol 5-8 mL, Lipidol oil

10-15 mL and gelatin gelfoam particles 20-40 cap.

RESULTS: Symptoms got improved and masses were reduced in size in 32 patients (90%). AFP turned negative in 18 cases. 32 cases were followed-up. The longest follow-up time is 8 years. 18 patients died 8-12 mo after operation. 6 patients died 1-2 years after operation. 3 patients died 2-8 years after operation. 5 patients survived longer than 8 years.

CONCLUSION: Hepatic arterial infusion and embolization was a palliative therapy for liver carcinoma. The arteries supplying the tumor were embolized, leading to ischemic necrosis and destruction of tumor tissue, whereas normal hepatic tissue was not damaged from it. When the size of the tumor is huge, we should control the dose of embolic agent and perform operation stage by stag so that to increase therapeutic efficacy, and improve the survival rate. HAIE is better than surgical resection.

Key words: Liver neoplasms/therapy; Embolization, therapeutic; Hepatic artery; Perfusion, regional

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Observation of morphological changes and cytoplasmic movement in apoptosis process

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Abstract

AIM: To investigate the relationship between morphological changes and cytoplasmic movement in apoptosis process of tumor cells.

METHODS: Human esophageal carcinoma Eca-109 cells cultured *in vitro* were treated with cisplatin (DDP, 10) for 24 h, 48 h and 72 h, respectively. A part of cells were grown in cover-glasses. Growth, death and morphological changes of the cells before and after being treated with DDP were observed under inverted microscope. The treated cells were collected and made into smears. The smears and cover-glasses were stained with HE, and observed under light microscope. Parts of cells were made into specimens routinely to be

examined with transmission electron microscope. Cells that were not treated with DDP were used as control ones.

RESULTS: Eca-109 cells treated with DDP displayed shrinkage, budding, nuclear fragmentation and formation of apoptotic bodies. Some cells stuck out irregular microspikes or pseudopodia-like protrusions. Sometimes it was seen that these protrusions existed at one pole of the cells while condensed nucleus and cytoplasm existed at the other pole. Nuclear fragments together with a part of the cytoplasm protruded into the surface of the cell. When cells were treated with trypsin-EDTA in PBS, it was observed that the cells which were still adherent to plates retracted more slowly than control cells. Observation under electron microscopy showed that microvilli were not seen on the surface of apoptotic cells and were substituted by circular or semicircular protuberances in which there were a little subcellular structures or/and nuclear fragments.

CONCLUSION: Cisplatin may induce apoptosis in human esophageal carcinoma Eca-109 cells. The process of apoptosis may be accompanied by cytoskeletal damage and abnormal cytoplasmic movement.

Key words: Apoptosis; Esophageal neoplasms/pathology; Microscopy, electron, scanning transmission

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Side effects and complications of hepatic arterial infusion and embolization of liver carcinoma in aged patients and its management

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Abstract

AIM: To study postoperative morbidity and treatment of hepatic arterial infusion and embolization of hepatic carcinoma in the elderly.

METHODS: There were 125 patients, 98 men and 27 women, aged from 60 to 78 years. All the diagnosis were made according to the standard of the Country's Study Group for the treatment of liver cancer. Hepatic arterial infusion and embolization were performed after hepatic arterial angiography using Seldinger puncture technique.

RESULTS: Side-effect: (1) Nausea, Vomiting occurred in 51 patients after the procedure, lasting 2-4 d. It was improved after inhalation of O₂ and metoclopramide injection im. (2) Pain of right-upper abdomen: presented in 95% mitigated by use of analgesics. (3) Fever, occurred in 123 patients, relieved by using: indomethacin. Complications: (1) Liver abscess: occurred in 5 patients. Chief manifestations were severe pain of right-upper abdomen, fever, ameliorated after one week adequate antibiotic treatment. If the abscess is huge, percutaneous puncture and drainage should be carried out intraabscess injection of antibiotics as well time. (2) Upper gastro-intestinal Hemorrhage (U.G.H.): The catheter should be positioned just above the lesion (pass through gastroduodenal artery) as much as possible. If U.G.H. is present, injection of H₁-receptor antagonist is indicated. (3) Right pleural effusion: Usually permission

can be achieved by conservative therapy. (4) Lipoid pneumonia: cure is induced by adequate antibiotic therapy. (5) Cholecystitis: occurred in 1 patient. Symptomatic relieve after antibiotic therapy. (6) Myocardial poisoning of E.P.I. presented in one patient: inhalation of O₂ instantly and myocardial-protection therapy were taken, and the patient got improved. (7) Damage of liver function: A.L.T rise in 30 patients, decreased to normal after liver-protection therapy. (8) Acute pancreatitis: recovered quickly after symptomatic treatment. (9) Paralytic intestinal obstruction: presented in one patient 2 d following the operation, and diminished after decompression of gastrointestinal luminal pressure and the usage of gastrointestinal tract peristaltic drugs.

CONCLUSION: HAE is a little-damaged and good-effecting therapy for liver carcinoma and can be carried out repeatedly. But the complication would be descend the treatment effect. How to avoid and treat the complication is important. Control the Indication. Potentiate nursing of perioperation, advance operator's inserting catheter level could be decrease the complications.

HAE is of therapeutic value for hepatic carcinoma, and of little injury which can be carried out repeatedly. Nonetheless complications after the intervention affect the result of it. Consequently much emphasis should be drawn on the avoidance and timely management of complications by the physician. In order to avoid the various complications, the following measures are required; be strict with indications pay more attention to perioperative care, and be skillful in performing the cannulation technically.

Key words: Liver neoplasms/therapy; Embolization, therapeutic; Hepatic artery; Perfusion, regional; Postoperative complications

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Huang FG, Li Y, Xie XD. Side effects and complications of hepatic arterial infusion and embolization of liver carcinoma in aged patients and its management. *World J Gastroenterol* 1998; 4(Suppl2): 70 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/70.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.70>

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Clinical study on surgical treatment of esophageal carcinoma in patients after subtotal gastrectomy

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Abstract

AIM: To study the cause and surgical treatment outcome of esophageal carcinoma in patients after sub-total gastrectomy.

METHODS: Seventeen patients with esophageal carcinoma after sub total gastrectomy was studied. Of the 17 patients, 15 were male and 2 were female. The lesions (of gastrectomy) included 13 cases of gastroduodenal benign pepticulcer and 4 cases of cardiac carcinoma. The types of gastrectomy performed were: B I in 2 patients, B II in 11 patients and proximal subtotal gastrectomy in 4 patients. The interval between subtotal gastrectomy and esophageal carcinoma for benign lesions was from 7 to 27 years (mean 16.2 years) and malignant lesion within one year for three patients, and four years for 1 patient. Recurrent anastomatic carcinoma was 2 and 11 years. Of these cases, five lesions located at upper thoracic segment; 10 at middle thoracic segment and 4 at lower thoracic segment. In operation group (13 cases) incisions include right postero-lateral thoracotomy, upper abdominal and left neck incision. The lesions were resected, and transverse and descending colon were brought to the neck to make anastomosis with esophagus. Anastomosis of celiac colon with the remaining stomach were performed in five patients. In 3 patients the lesion was removed through thoraco-abdominal incision the remaining stomach, with spleen and caudal portion of pancreas were moved into the left thorax and anastomosis of esophagus with the remaining stomach above the aortic was performed, and Roux-en-Y

jejunojejunostomy as well. One patient for esophagogastrctomy up the aortic and Roux-en-Y esophagojejunostomy in three patients. One patients only received laparotomy. Four patients (nonoperation) received chemotherapy and radio-therapy.

RESULTS: For nonoperation group, one patient with early lesion survival 4 years, the other three patients died of metastatic carcinoma within one year. In the whole group of patients who underwent surgery 7 out of 13 patients died, including two patients died from the operation (serious pulmonary infection. Pneumomycosis and ARDS). 3 patients survival 1 year and sixteen mo, 1 patient 3 years. Another six years and two mo. Six patients are still alive, two of them more than two years, one survival more than nine years and one mo, and two more than ten years. The results of treatment were satisfactory.

CONCLUSION: The incidence rate of esophageal carcinoma in patients with subtotal gastrectomy is 5.54 per cent (17 vs 307). It is almost certain that esophageal carcinoma is associated with subtotal gastrectomy. Not only are these patients predisposed to carcinogenicity, but also there is a dose-effect relationship between them. Esophageal carcinoma is strongly correlated with subtotal gastrectomy B II or proximal subtotal gastrectomy. After the initial subtotal gastrectomy type B I or Roux-en-Y jejunojejunostomy is the choice of procedure for alimentary tract reconstruction. Transplanting the remaining stomach together with spleen and caudal portion of pancreas into the left thoracic cavity, and esophago-gastrectomy with remaining stomach and Roux-en-Y jejunojejunostomy forms a new operative way which we recommended as an ideal procedure.

Key words: Esophageal neoplasms/surgery; Gastrectomy; Anastomosis, Roux-en-Y

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Wu XY, Zhang XF, Yin FS, Lu HS, Guan GX. Clinical study on surgical treatment of esophageal carcinoma in patients after subtotal gastrectomy. *World J Gastroenterol* 1998; 4(Suppl2): 71 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/71.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.71>

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Determination of plasma nitric oxide, molitin and their significances in ulcerative colitis

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Abstract

AIM: To investigate the concentration changes of plasma nitric oxide (NO) and molitin (MTL) and the relationships between NO, MTL and ulcerative colitis (UC).

METHODS: The plasma concentration of nitrite/nitrate (stable end products of NO, standing for NO) and molitin of 18 patients with UC and 11 control subjects were respectively measured with Cadmiun-reduction chromatography and development process (Greiss) and RIA (Radioimmuno assay). Evaluation was made using Student's *t* test for unpaired data and correlative analysis performed. $P < 0.05$

was considered significant statistically.

RESULTS: The concentration of plasma NO and MTL in control group were $21.34 \pm 5.86 \mu\text{mol/L}$, $348.42 \pm 124.32 \text{ ng/L}$; respectively whereas in UC group were $46.76 \pm 10.43 \mu\text{mol/L}$, $581.24 \pm 176.58 \text{ ng/L}$ respectively. The concentration of plasma NO and MTL in UC groups were significantly higher than those in controls ($P < 0.01$, $P < 0.05$, respectively). The concentration change of plasma NO in UC group significantly correlated with the change of MTL ($r = 0.482$, $P < 0.05$); there is no significant correlation in control group ($r = 0.376$, $P < 0.20$), however.

CONCLUSION: Nitric oxide and molitin are both involved in the pathophysiologic process of ulcerative colitis. Moreover, there may be some positive interactions between NO and MTL in the pathogenesis of UC.

Key words: Colitis, ulcerative/blood; Nitric oxide/blood; Motilin/blood; Radioimmuno assay

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Surgical treatment of residual stomach cancer with a new technique of alimentary tract reconstruction

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Abstract

AIM: To summarize the experiences of surgical treatment of residual stomach cancer and introduce a new technique of alimentary reconstruction.

METHODS: Between January 1973 and December 1996, 39 residual gastric cancer were treated at our department. Of the 39 patients, 34 were male and 5 were female. Thirty-five were with residual cardiac cancer, one residual gastric greater curvature cancer and three were residual stomach anastomotic cancer. Absolute radical resection was performed in 12 patients (30.8 per cent), relative radical resection in 8 patients (20.5 per cent), palliative resection in 6 patients (15.4 per cent) and one patient had laparotomy. Twelve patients were treated with inguinal lymph nodes chemotherapy. The pathohistological findings were: residual cardiac cancer in 23 cases, residual stomach greater curvature cancer in 1 case, residual stomach anastomotic cancer in 2 cases. Poorly differentiated carcinoma: 8 cases, mucous adenocarcinoma 3 cases and adenocarcinoma 15 cases. Sixteen patients had lymph nodes metastasis and 10 had no lymph nodes metastasis. Of the 16 patients, fourteen had N1 lymph nodes involvement, 13 N2 lymph nodes involvement and 6 had N3 lymph nodes involvement. According to TNM classification, 1 patient belonged to early residual stomach cancer, 1 to stage I, 7 to

stage II-a, 6 to stage III-b and 7 to stage IV. Twenty-two patients received combined resection of total residual stomach and adjacent organs. Of these, 14 patients had combined resection of five organs, four organs (4), three organs (4) and total resection of residual stomach (4). The esophago-jejunostomy for gastric substitution or Roux-en-Y jejunojejunostomy for alimentary reconstruction were performed in ten patients. Tomoda and Roux-en-Y were carried out in 11 and 5 patients, respectively.

RESULTS: Thirteen non-resected patients died between six months and two years from diagnosis, mean survival length 10⁴ mo. In the whole group of patients who underwent surgery 12 out of 26 patients died. 6 patients survived over one year, 2 patients two years, one patient four years, two patients five years and the longest length of survival was nine years, mean length of survival 2.5 years. Fourteen patients are still alive. Including, two patients over half a year, 4 over one year, 4 over two years and 4 over five years (two patients are still alive for more than ten years). The overall operative mortality for this group was zero, the results of treatment were satisfactory.

CONCLUSION: Incidence rate of residual stomach cancer was 1.85 per cent (39 vs 2110). Combined resection of total residual stomach and adjacent organs and elimination of lymph nodes (D⁺₂, D₃) are necessary for residual stomach cancer. Esophago-jejunostomy for gastric substitution and Roux-en-Y jejunojejunostomy for alimentary reconstruction is proved to be a suitable modality, and worth of recommending.

Key words: Stomach neoplasms/surgery; Adenocarcinoma/surgery; Neoplasm, residual

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Evaluation of the effect of three antibacterial therapies on eradication of *Helicobacter pylori*

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Abstract

AIM: To evaluate the effect of three kinds of anti-*Helicobacter pylori* (Hp) therapies on eradication of Hp.

METHODS: One hundred and fifty-one patients with confirmed presence of Hp were enrolled into the study, and were randomly divided into three groups A, B and C. Group A took Denol 120 mg tid, Amoxycillin 500 mg bid, Cimetidine 400 mg bid, and Metronidazole 200 mg tid; Group B Ranitidine 300 mg bid, Denol 120 mg tid, Furazolidonum 100 mg tid, Amoxycillin 500 mg bid; and group C Losec

20 mg qd, Amoxycillin 500 mg bid, Denol 120 mg tid, Famotidine 200 mg bid, respectively, for 2 wk. Endoscopy and ¹⁴C-UBT were repeatedly performed 4 wk after antimicrobial therapy ended.

RESULTS: The eradication rates of *H. Pylori* in Group A, B and C were 93.3% (36/39), 92.1% (35/38) and 95.0% (38/40), respectively, and there was no significant difference in the eradication rates between the three groups ($P > 0.05$). The ulcer healing rates in group A, B and C were 90.0% (9/10), 92.3% (12/13) and 91.0% (10/11), respectively, and there was no significant difference between the treatment groups, either. The incidence of drug-induced side-effect was similar among the three groups.

CONCLUSION: All the three anti-*H. Pylori* remedies are the treatment of choice in eradication of Hp.

Key words: *Helicobacter* infections/drug therapy; Amoxici llin/therapeutic use; Cimetidine/therapeutic use; Organometalic compounds/therap eutic use; Omeprazole/therapeutic use

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Qian JZ, Chen PD, Wu LF. Evaluation of the effect of three antibacterial therapies on eradication of *Helicobacter pylori*. *World J Gastroenterol* 1998; 4(Suppl2): 74 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/74.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.74>

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Investigation of emotional disturbance in patients with functional gastrointestinal disorders

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Abstract

AIM: To investigate the relation between functional gastrointestinal disorders (FGID) and emotional disturbance.

METHODS: According to the diagnostic criterion of FGID, 118 cases of FGID patients were divided into 5 subgroups; 61 cases of functional dyspepsia; 27 cases of irritable bowel syndrome; 12 cases of functional esophageal motility disorders; 11 cases of chronic constipation; 7 cases of psychogenic vomiting. Each patient gave a self evaluation using Self Rating Anxiety Scale (SAS) and Self-Rating Depression Scale (SDS). The standard scores were calculated

according to self-evaluation. The score levels of SAS above 50 and SDS above 53 were used as diagnostic standard for emotional disturbance. The scores of SAS and SDS of FGID patients were compared with normal model of our country, and among subgroups of patients as well.

RESULTS: The scores of SAS and SDS of FGID patients were obviously higher than the normal model of our country, but no significant difference among subgroups of FGID patients. Every subgroup of FGID patients had one or more items reached or higher than the diagnostic standard of emotional disturbance.

CONCLUSION: Emotional disturbance of anxiety and depression commonly existed among FGID patients. The corresponding measure of therapy should be taken in order to achieve expected results.

Key words: Gastrointestinal diseases/psychology; Gastrointestinal diseases/diagnosis; Affective disorders/diagnosis; Psychiatric status rating scales

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Investigation of intra-arterial chemotherapy infusion and embolization combined with abdominal chemotherapy for advanced gastric cancer

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Abstract

AIM: To explore the feasibility and clinical benefit of intra-arterial chemotherapy infusion and embolization (GAI + GAE) combined with abdominal chemotherapy for advanced gastric cancer.

METHODS: Ninety-eight patients with advanced gastric cancer were randomized into three groups according to gender, age, pathological classification, and clinical staging. Group A was treated with GAI + GAE combined with abdominal chemotherapy, Group B with abdominal chemotherapy, and Group C with intravenous chemotherapy. Group A was followed up for gastric mucosa change by gastroscopy.

RESULTS: The response rate for Group A, B and C was 71.88%, 38.71% and 14.29%, respectively. The median survival duration for Group A, B and C was 16, 10 and 8 mo, respectively. The response rate and median survival duration of Group A were significantly different from those of Group B ($P < 0.01$) or Group C ($P < 0.01$), 5 patients in Group A had complete remission. The main side effects were gastrointestinal toxicity and inhibition of bone marrow. An injury to gastric mucosa was detected by gastroscopy within 2 wk after treatment in group A. Tissue repair took place by the 2nd week. And normal gastric mucosa returned in 4 wk.

CONCLUSION: GAI + GAE combined with abdominal chemotherapy was an effective modality for advanced gastric cancer.

Key words: Gastric neoplasms/drug therapy; Chemoembolization, therapeutic; Infusions, intra-arterial; Peritoneal cavity; Randomized controlled trials

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Combination of arterial infusion chemotherapy and radio therapy in the treatment of 36 cases of middle and late stage esophageal cancer

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Abstract

AIM: To assess and compare the therapeutic effect, clinical responses and survival time between radiotherapy alone and radiation combined with arterial infusion chemotherapy for medium and late stage esophageal carcinoma.

METHODS: Altogether 36 cases of medium and late stage histopathologically confirmed esophageal cancer, were given radiotherapy of DT 60-70 G y (6-15 mV x-ray/6-7 wk), with concurrent arterial infusion chemotherapy by means of percutaneous punctural catheterization of left bronchial artery, left gastric artery, or esophageal artery. Chemotherapeutic drugs (5-Fu, mytomycin, adriamycin, cisplatin *etc.*) were injected through the catheter once every 3-4 wk, twice a course. In the mean time, 38 cases were given

radiotherapy alone as control group.

RESULTS: There were 18 cases (CR + PR + MR) in control group (38 cases). The effective rate was 47.4% (36 cases). There were 24 cases (CR + PR + MR) in therapeutic group. The effective rate was 66.7%, which was significantly higher than control group. After following up for 18 years, the survival rates was 26.3% (control) and 47.12% (the therapeutic), respectively, the however, as for the one year survival rate the therapeutic group was much higher than the control group.

CONCLUSION: Though the present observation in clinic. It is proved that radiation combined with arterial infusion chemotherapy is superior to radiotherapy alone. On efficacy and survival for medium and late stage esophageal cancer.

Key words: Esophageal neoplasms/therapy; Antineoplastic agents, combined/therapeutic use; Doxorubicin/administration and dosage; Mitomycins/administration and dosage; Fluorouracil/administration and dosage

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Experimental and clinical study of Danshen on treatment of peptic ulcer

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Abstract

AIM: To study the therapeutic efficacy and adverse reaction of Danshen on treatment of reserpine induced ulcer of rats, and effect of Danshen on treatment of peptic ulcer.

METHODS: Sixty rats were randomized into two groups after twenty-four hour fast, thirty rats were given subcutaneous injection of Danshen 10 mL/kg, thirty controls were treated with normal saline 10 mL/kg. One hour later, all rats were given subcutaneous injection of reserpine 5 mg/kg each. Eighteen later, observation was made on acute injury of gastric mucosa, gastric mucosal blood flow, gastric acid secretion and free radical of oxygen for all rats. 120 patients with peptic ulcer were randomized into two groups, 90 received intravenous drip of Danshen 40 mL and 5% glucose solution 250 mL in the morning, and an additional of Danshen 10 mL orally before,

for one course of 4 wk. Thirty received ranitidine 150 mg, twice daily for one course of 4 wk.

RESULTS: The index of ulceration, gastric mucosal blood flow, gastric acid secretion, SOD, MDA in Danshen group were 20.37 ± 9.89 mv, 194.5 ± 39.61 mv, 14.06 ± 5.61 meq/L, 262.57 ± 106.6 ng/mL, 49.64 ± 23.27 nmol/g tissue, respectively. In group control they were 65.81 ± 36.25 mv, 52.27 ± 11.6 mv, 31.13 ± 7.24 meq/L, 54.36 ± 23.31 ng/mL, 289.61 ± 30.27 nmol/g tissue ($P < 0.01$). The healing rate of ulcer. In Danshen group was 86.7%, negative rate of *Helicobacter pylori* (Hp) was 57.1%, epigastric pain disappeared in an average of 6 d. Relapse rate is 27.8% in one year. In controls they were 76.7%, 5%, 10 d, 72%, respectively.

CONCLUSION: Danshen can increase gastric mucosal blood flow, reduce gastric acid secretion, eliminate free radical of oxygen, destroy Hp. Danshen is effective in short-term treatment of peptic ulcer. The relapse rate is low in one year.

Key words: Peptic ulcer/drug therapy; *Salvia miltiorrhiza*/therapeutic use; Gastric acid/secretion; Gastric mucosa/blood supply

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Liu RJ, Wang YS, Li ZQ, Tang XK, Nie Q, Xia PJ, Guo Y, Zhang W. Experimental and clinical study of Danshen on treatment of peptic ulcer. *World J Gastroenterol* 1998; 4(Suppl2): 78 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/78.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.78>

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Clinical study of therapeutic effect of dong fang gan kang No.1 on fatty liver

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Abstract

AIM: To observe the therapeutic effect of traditional Chinese medicine Dong Fang Gan Kang No.1 on fatty liver, and compare it with western medicine.

METHODS: A total of 398 patients with fatty liver were divided into two groups, the therapeutic ($n = 360$) and control group ($n = 38$). The therapeutic group consisted of several subgroups based on causes: pure obesity (225), alcohol (63), hepatitis (48), diabetes (24). The control group consisted of 38 cases. For therapeutic group 20 mL oral liquid of Dong Fang Gan Kang No.1 which was processed by the hospital from Chinese herbs was taken 3 times a day. For control subjects 77 mg Yi Gan Ling, 1.8 g Duoxikang, 0.2 g Vitmi C were taken 3 times a day. The average course was 3 mo. Comparasion and analysis of the results were carried out between the two groups.

RESULTS: In therapeutic group, the cure rate is 62.8% (226/360) notable effective 23.3% (84/360), general effective 10.6%(38) ineffective 3.3% (12). Total effective rate 96.7%. The alcoholic subgroup achieved best result with a total effective rate 98.4%, the cure rate 73.0% (46), notable effective 20.6% (13), general effective 4.8% (3), ineffective 1.6% (1). The day diabetic subgroup had the least satisfactory result with a total effective rate 8 3.3%, the cure rate 45.8% (11), notable effective 20.8%(5), general effective 16.7% (4), ineffective 16.7% (4). Where as in control group the total effective rate 13 (34.2%), the cure rate 0% (0), notable effective 5.3% (2), general effective 28.9% (11) ineffective 65.8% (25). Results from therapeutic group was significantly preferential to that of control group.

CONCLUSION: Dong Fang Gan Kang No.1 is an effective treatment for fatty liver, especially for alcoholic fatty liver, but less effective for diabetic fatty liver. Western medicine is of little therapeutic effect for fatty liver as well as plasma lipid.

Key words: Fatty liver/drug therapy; Composite (TCD)/the rapeutic use; Obesity/complications; Hepatitis/complications; Diabetes mellitus/complications

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Effect of cold upon upper gastrointestinal hemorrhage resulting from liver cirrhosis and its mechanism

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Abstract

AIM: To study the effect of cold upon 98 cases (89 males, 9 females) of upper gastrointestinal hemorrhage resulted from liver cirrhosis and its regularity and mechanism.

METHODS: From April 7 to October 8 and October 9 to April 6 in 1992-1996, we performed a statistical morbidity of upper gastrointestinal hemorrhage resulted from liver cirrhosis. In the same period, at the temperature of 20-30 °C and 5-15 °C, we studied the nailfold microcirculation of 151 cases of liver cirrhosis and analyzed its 16 kinds of values and its sensitivity to the change of temperature.

RESULTS: Among the 98 patients with liver cirrhosis, the morbidity of upper gastrointestinal hemorrhage happened in 72 cases from October 9 to April 6 (73.0%), showing a concentrated tendency; While that happened in 26 cases from April 7 to

October 8 was (26.5%), showing a disperse tendency and there was a significant difference when compared with each other ($P < 0.01$). After performing examinations of nailfold microcirculation of 115 patients with liver cirrhosis, we found that, the numbers and length of capillary and the velocity of blood flow in capillary of nailfold microcirculation measured at temperature 5-15 °C ($7.9 \pm 1.8/\text{mm}$, $109 \pm 24 \mu\text{m}$, $387 \pm 161 \mu\text{m/s}$) were less than that measured at temperature 20-30 °C ($9.6 \pm 2.1/\text{mm}$, $138 \pm 31 \mu\text{m}$, $808 \pm 213 \mu\text{m/s}$, $P < 0.01$). It showed that the effective blood circulatory volume blood in shallow tissues had reduced to some extent. So we deduced that in deep tissues would increase relatively.

CONCLUSION: In cold weather, the patients with liver cirrhosis will suffer from upper gastrointestinal hemorrhage easily. The mechanism is that the change of temperature effects the redistribution of blood of the human body. When the weather temperature drops in the surroundings of the subjects, the effective blood circulatory volume of shallow tissues reduces to some extent; while that of deep tissues increases relatively. This will result in the pressure of portal vein system and its collateral circulation increase. The esophagogastric varices can easily break and hemorrhage.

Key words: Gastrointestinal hemorrhage/etiology; Gastrointestinal hemorrhage/physiopathology; Liver cirrhosis/complications; Cold upon

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Li ZZ, Wei CD, Wang Y, Xing C, Guo H, Cai W, Liu H. Effect of cold upon upper gastrointestinal hemorrhage resulting from liver cirrhosis and its mechanism. *World J Gastroenterol* 1998; 4(Suppl2): 80 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/80.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.80>

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Early diagnosis of hepatitis A virus-micro-blotting immuno-binding assay

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Abstract

AIM: To establish a quick and easy method for detecting the anti-HAV IgM level in sera of HAV patients during acute periods.

METHODS: To use micro-blot immuno-binding assay (MBIMA) was used to detect the titration of Goat-anti-Human (GaH) IgM-HRP and titration of IgM in sera of healthy people. RIA method and MBIBA methods were used to detect the IgM level in sera in 114 HAV

patients and 48 non-HAV patients.

RESULTS: Titration of IgM and GaH IgM-HRP in healthy people were 1:1000 and 1:1600, respectively; The IgM level in sera in 114 patients was positive by RIA method and that in 112 patients was positive by MBIBA method; the IgM level in sera in 48 non-HAV people was negative by both methods; the duration of RIA and MBIBA were 2-d and 6-h, respectively.

CONCLUSION: The positive and negative coincidence rates of RIA and MBIBA in detecting the serum IgM level in patients were 98.24% and 100%, respectively; the MBIBA method was much easier and quicker than RIA and might be used widely in clinical practice.

Key words: Hepatitis A/diagnosis; Hepatitis A/immunology; Hepatitis A virus; IgM/analysis

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Wang RH. Early diagnosis of hepatitis A virus-micro-blotting immuno-binding assay. *World J Gastroenterol* 1998; 4(Suppl2): 81 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/81.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.81>

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Research of application with pressure controllable simple enemator for colon diseases in the course of diagnoses and treatment

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Abstract

AIM: On the basis of the principle of gas state change ($P_1 \times V_1 / T_1 = P_2 \times V_2 / T_2$) and of communicating vessel. A pressure controllable simple enemator made by ourselves (PCSE) can be applied to contrast examination, to pressure determination and to reduction of intussusception.

METHODS: A PCSE was made up of a humidistat bottle, a bigeminy bulb, a manometer *etc.* 108 cases (age 16-72 years) with barium air double contrast radiography had been cleaned enema before examination. Some cases were examined after colonofiberscopy. Colon cavity would be perfused with thin colloidal suspension (100 mL-200 mL) and with compressed air (12.5 kPa, 3, 4 times). The pressure in colon cavity could be determined. The dilation change of colon could be observed and photographed. Some cases were injected 654.2 20 mg into the muscles respectively 5 min before examination. 26 cases (age 4 /12-6 years) of intussusception were reduced by simple compressed air, *etc.* If the pressure showed too high or the complaints were bitter, it was necessary to air to

decrease pressure.

RESULTS: The success ratio of contrast examination arrived at 99%. Small lesions such as polyps, cancer and so on could be showed and be correctly diagnosed (the positive accordion rate compared with colonoscopy was 94%). The scope and character of obstructive lesions could be determined more clearly. The buffer capacity of unobstructive colon cavity was large enough. Under 3.9 ± 0.8 kPa MDP (Moderate degree pressure), dilatation diameter of colon cavity was 5.8 ± 1.4 cm. Safety exam pressure (SEP) could be mainly determined by speed of pressure change and acuity of complaints. The abdominal symptoms such as pain and so on could be relieved with 654.2 injected, which could be helpful to accomplish examination; but it had little influence on pressure and calibre of examination. In contrast to incomplete obstructive lesions, the influence to pressure and calibre in complete obstructive lesion had significant difference ($P < 0.01$). The success ratio of the reduction of intussusception was 92%. All RP (reposition pressure) among which 18 cases' were 9.3-12.0 kPa are 8.0-16.0 kPa. The pressure fluctuation (2.7-4.0 kPa) would be helpful for the intussusception to be reduced.

CONCLUSION: Being cheaply and manipulated easily, the PCSE can be applied accurately and safely to barium air double contrast examination and effectively to the treatment of reduction of intussusception with air enema. Colon moderate dilatation can be regulated easily, lesions can be clearly manifested. Near machine manipulation will be available for better co-operation between examiner and patient to smoothly complete examination and treatment. It will be spread and applied in different grade hospitals of different levels.

Key words: Intussusception/diagnosis; Intussusception/therapy; Barium/diagnosis use; Enema

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Analysis of long-term therapeutic effects of cisapride and domperidone on functional dyspepsia

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Abstract

AIM: To compare the long-term therapeutic effects of cisapride and domperidone Ddt on functional dyspepsia (FD).

METHODS: Randomly choosing 40 patients treated with cisapride and 32 patients treated with domperidone, of whom the symptoms of FD completely disappeared after the 4 wk treatment, respectively. And the symptoms of FD completely disappeared. In the cisapride group, 21 were men, 19 were women, aged 19-72 years, average age 38 years, their disease course ranged from 1 mo to 13 years, average 27 mo. Among them, 19 with dysmotility-like dyspepsia, 4 with gastroesophageal reflux-like dyspepsia, 10 with ulcer-like dyspepsia, 7 with complex dyspepsia. In the domperidone group 17 were men, 15 were women, age 19-74 years, average age 39 years, their disease course ranged from 1 mo to 14 years, average course 26 mo. Among them, 16 with dysmotility-like dyspepsia, 3 with gastroesophageal reflux-like dyspepsia, 9 with ulcer-like dyspepsia, 4 with complex dyspepsia. All of the patients were treated either with

cisapride (5 mg, twice per day) or domperidone (10 mg, twice per day) and maintained the treatment for 12 mo. During this period, observation was made of the recurrence of satiety, epigastric pain, epigastric distention, early satiety, nausea, vomiting, anorexia, belch which appeared after they had meals, and as well as side effects. The patients' symptoms were compared and analysed.

RESULTS: After 12 mo's treatment, epigastric pain recurred in 1 patient, respectively; in the cisapride group. Epigastric distention, early satiety. The recurrence rate was 7.5%. In the domperidone group, early satiety recurred in 3 patients, heartburn in 1, epigastric pain in 2, epigastric distention in 4. The recurrence rate was 31.2%, and the symptoms were more severe ($P < 0.01$). Side effects: In the cisapride group, loose stool occurred in 1 patient, stool frequency increased in 1. The occurrence rate was 5.0%. In the domperidone group, loctorrhea, abnormal menstruation, agitation, drowsiness, loose stool and palpitation occurred in one patient, respectively. The occurrence rate was 18.7%.

CONCLUSION: Ddt cisapride has better therapeutic effects than domperidone, and it can significantly decrease the recurrence of functional dyspepsia.

Key words: Dyspepsia/drug therapy; Piperidines/therapeutic use; Domperidone/therapeutic use

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Liang ZG, Quan HB. Analysis of long-term therapeutic effects of cisapride and domperidone on functional dyspepsia. *World J Gastroenterol* 1998; 4(Suppl2): 83
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Emergency management of left colon with stage I resection

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Abstract

AIM: Emergency resection of left colon with intra operative lavage and primary anastomosis.

METHODS: After the satisfactory exploration of abdominal cavity, the corresponding mesenteries, the splenic flexure and hepatic flexure were freed sufficiently. The proximal portion of the lesion was ligated, and placed outside the incision in case an extensive operation was needed, which was often the case in tumor patients. If a small lesion is to be removed, ligation and fixation of the proximal portion of the lesion can be performed through catheterization. Feces in shape were taken out of the bowel lumen, and a large-diameter tube was connected with it. A 22-Foley catheter was connected through the base of freshly amputated appendix or through an enterotomy of terminal ileum into cecum. Saline solution of body temperature was infused through the Foley catheter for lavage until the effluent

from the lavage was clear. Usually it took 3-8 liter saline solution on average. After completion of lavage the Foley catheter was removed, and appendectomy was performed or the enterotomy is closed. The diseased colon was removed, the bowel end-to-end anastomosis was carried out routinely. A drainage tube was positioned near the anastomosis site. After completing anastomosis, the fecal material in the distal colon was evacuated through a proctoscope. All the patients received broad-spectrum parental antibiotics.

RESULTS: In this study, left colectomy was performed in 10 cases. Segment resection of left colon and local anastomosis in 5 cases. Low anterior resection was in 3 cases. One patient died from MOF(multiorgan failure). Anastomosis occurred in one case. After drainage the leakage closed. Pelvic abscess in 1. Wound infection in 2. All but one patients ranged recovered. The duration of postoperative hospital stay ranged from 8-60 d, Mean 12 d.

CONCLUSION: Compared with traditional one or three-stage resection method, this technique is reliable and safe for patients who need urgent nonelective resection of left colon.

Key words: Colon/surgery; Enema; Colectomy

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Li WY, Huang WZ, Wu F. Emergency management of left colon with stage I resection. *World J Gastroenterol* 1998; 4(Suppl2): 84 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/84.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.84>

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Evaluation of the hepatitis B virus in hepatitis B surface antigen by hepatitis B virus deoxyribonucleic acid measured with polymerase chain reaction

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Abstract

AIM: To evaluate whether the negative HBsAg inpatients carry HBV in the department of gastroenterology in our Hospital.

METHODS: The HBV DNA was measured with PCR technique in 119 negative HBsAg digestive inpatients and compared with negative HBsAg hepatitis inpatients.

RESULTS: The results showed that 52.1% of the digestive inpatients in the department of gastroenterology were positive HBVM (HBsAg, anti-HBs, HBeAg, anti-HBe and anti-HBc), and 30.3% HBV DNA was positive in the patients. These two indexes were markedly lower compared with hepatitis. The difference of the rate of positive HBV DNA in the two groups was only in the HBV infective model of negative HBVM.

CONCLUSION: The results suggested that there were HBV carriers in negative HBsAg inpatients in the department of gastroenterology, and positive HBVM patients of the two groups actually come from the same group.

Key words: Hepatitis B virus; DNA, viral; HBsAg; Polymerase chain reaction

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Zheng Z, Yang SW, Xiao W, Sun P, Li XJ, Hu YQ. Evaluation of the hepatitis B virus in hepatitis B surface antigen by hepatitis B virus deoxyribonucleic acid measured with polymerase chain reaction. *World J Gastroenterol* 1998; 4(Suppl2): 85 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/85.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.85>

E- Editor: Li RF



Magnetic resonance imaging of pancreatic adenocarcinomas

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Abstract

AIM: To compare the efficiency of the different MR sequences in the diagnosis of pancreatic adenocarcinomas and to assess the MRI findings.

METHODS: 70 patients with pancreatic adenocarcinoma proved by surgically or clinically underwent MR imaging with a 1.5 T superconducting unit. MR imaging sequences included T₁WI, T₂WI, fat-suppressed T₁WI, dynamic FMPSPGR and delayed contrast-enhanced T₁WI. The MR images were viewed. We analyzed of the

quality and quantity MR sequences.

RESULTS: The tumors could be seen more clearly on FT₁WI and 72.22% appeared as obvious hypointense. FT₁WI was the most effective sequence in the detection of small non-contour-deforming pancreatic carcinoma. Dynamic FMPSPGR and delayed contrast-enhanced T₁WI were more sensitive sequences in the demonstration of dilated biliary ducts. Blood vessels around pancreas could be shown distinctly on dynamic FMPSPGR. Metastasis of retroperitoneal lymph node could be defined clearly on T₁WI. T₂WI was the most sensitive sequence in the display of liver metastasis. MRCP was very useful for obstructive jaundice.

CONCLUSION: MR images are useful in the diagnosis of pancreatic adenocarcinomas.

Key words: Pancreatic neoplasms/diagnosis; Adenocarcinoma/diagnosis; Magnetic resonance imaging

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Liu AL, Lang ZJ, Ding ZQ, Fu WL. Magnetic resonance imaging of pancreatic adenocarcinomas. *World J Gastroenterol* 1998; 4(Suppl2): 86 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/86.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.86>

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Expression of p53, bcl-2, epidermal growth factor receptor in carcinoma and polypoid lesion of the gallbladder and their clinicopathological significance

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Abstract

AIM: To explore the relationship between gallbladder carcinoma and polypoid.

METHODS: The expression of p53, bcl-2, EGFR protein were examined by immunohistochemistry in benign lesions and carcinomas in gallbladder.

RESULTS: The study revealed that overexpression of p53, bcl-2,

EGFR protein were detected in 0, 4, 3 in 21 cases of chronic calculus cholecystitis, 1, 5, 3, in 20 cases of adenomyomatosis, 7, 11, 7 in 23 cases of adenomas and 16, 14, 11 in 25 cases of adenocarcinomas of the gallbladder respectively. There were significant differences in single or multiple oncogene expression rates between groups but not in chronic cholecystitis to adenomyomatosis or in mixed double oncogene expression rate between adenomas and adenocarcinomas.

CONCLUSION: These results suggested that oncogenic changes of p53, bcl-2, EGFR may play a role in tumorigenesis of gallbladder carcinoma, adenomyomatosis is not an important precancerous lesion of gallbladder carcinogenesis but adenomas.

Key words: Gallbladder neoplasms/pathology; Adenomyomatosis; p53 gene; bcl-2 gene; Gene expression; Epidermal growth factor receptor

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Sun XF, Chi BE, Luo L. Expression of p53, bcl-2, epidermal growth factor receptor in carcinoma and polypoid lesion of the gallbladder and their clinicopathological significance. *World J Gastroenterol* 1998; 4(Suppl2): 87
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Effect of nitric oxide on gastric carcinoma metastasis

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Abstract

AIM: To observe the effect of nitric oxide in peripheral blood during the process of gastric carcinoma metastasis.

METHODS: Twenty-four patients including 21 males and 3 females suffered from gastric carcinoma. The average age was 56 (from 44 to 68). They were divided into two groups: carcinoma group (without metastasis; $n = 8$) and metastasis group (with local or/and distance metastasis; $n = 16$). Their serum were collected pre-operation for detecting the metabolite of nitric oxide-nitrite. Forty volunteers as the normal control group were venupunctured to detect the concentration of nitrite simultaneously. The nitric oxide was measured by a method

of cadmium reduction through detecting the concentration of nitrite. The values were expressed as $\bar{x} \pm s$. The data were analyzed with analysis of variance and q test. Statistical significance was defined as $P < 0.05$.

RESULTS: The average nitric oxide concentration of metastasis group was $50.62 \pm 7.8 \mu\text{mol/L}$, the concentration of gastric carcinoma group was $70.76 \pm 9.7 \mu\text{mol/L}$, and that of the normal control group was $80.78 \pm 14.50 \mu\text{mol/L}$. The nitric oxide concentration of metastasis and carcinoma groups were decreased significantly compared with the normal control ($P < 0.01$, $P < 0.05$). The difference between metastasis and carcinoma group was significant ($P < 0.05$).

CONCLUSION: The concentration of nitric oxide may have an inhibited effect on the process of gastric carcinoma metastasis, and the decrease of nitric oxide concentration would be harmful to the treatment of gastric carcinoma.

Key words: Stomach neoplasms; Nitric oxide; Neoplasm metastasis

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Treatment of rectal carcinoma with a specially designed anus-protected localized negative pressure type cryoprobe

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Abstract

AIM: To perform cryosurgery for 100 rectal carcinoma with a specially designed anus-protected localized negative pressure type cryoprobe observed its clinical curative effects.

METHODS: One hundred cases of rectal carcinoma (56 men, 44 women) were diagnosed by finger examination, rectal scope and biopsy. Clinically, three types were found: cauliflower type 43 cases, ulcer type 48 cases, 9 cases and diffused type, pathologically, 84 cases malignant adenoma, 13 cases colloid carcinoma, 2 cases squamous carcinoma and one with metastasis from post-operative urinary bladder carcinoma recurrence. Seventy-three advanced cases showed signs of intestinal obstruction because of circular stricture of the carcinoma, 17 cases in middle stage and 10 cases in early stage. Cryosurgery was performed with a specially designed anus-protected localized negative pressure type cryoprobe (the patent No.

is ZL92235996.2.). The diameter of the freezing zone was about 4 cm.

RESULTS: Patients in early and middle stages received cryosurgery 1-3 times. The carcinoma disappeared and no cancer cells was found in biopsy, and there was no recurrence in the 5-year follow-up. The 5-year survival rate was 100%. The cryosurgery was ineffective in 2 cases with liver metastasis and ascites. The other patients in late stages lived one year to 4 years and 3 mo after cryosurgery, averaging 2 years and 7 mo. One day after the cryosurgery the intestinal obstruction were remitted in late stage patients, with an effectiveness rate of 100%.

CONCLUSION: The tumor tissues can be killed by cryosurgery. The diameter of the freezing zone was about 4 cm, which could reach the lymph nodes of the pelvic cavity and the nodes near the lower intestinal mesentery vessels. There was no local stimulus, compression and distention. Cancer cells could be frozen to death before blood metastasis occurred. If it is combined with chemical therapy, the clinical effects may be even better.

Key words: Rectal neoplasms/therapy; Rectal neoplasms/pathology; Cryosurgery

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Pharmacokinetics of 7 cephalosporines antibiotics in dog's bile

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Abstract

AIM: Study the pharmacokinetics of 7 cephalosporine antibiotics in bile of dogs so as to select appropriate antibiotics for biliary infection.

METHODS: Experimental dogs were administered separately with i.v. cefoperazone, ceftriaxone ceftazidime, cefazolin, ampicillin, cefuroxime, and cefmetazone. Drug concentrations in the bile of the dogs were measured by microbiological method. With 3p₈₇ software, the maximum of concentration (C_{max}), peak time (T_{peak}), half-life (T_{1/2β}), clearance (CL), apparent

volume of distribution (V_a) of each antibiotic were calculated were in bile.

RESULTS: C_{max} of cefoperazone was the highest (2464 ng/L); C_{max} of ceftriaxone was lower than cefoperazone, but T_{1/2β} ceftriaxone was the longest (6024 min). The C_{max}, T_{1/2β} of cefazolin, ceftazidime, ampicillin was lower than the former two but they were significantly higher than cefuroxime ceftriaxone and cefoperazone was the first choice.

CONCLUSION: Among this group of seven antibiotics, in the treatment of biliary infection, ceftriaxone is the first choice, and cefoperazone is the second one. cefamedin and ampicillin are not so good as the former two, but they have advantages of low cost, and still can be used in treating biliary infection while cefuroxime and cefmetazone are not accessible.

Key words: Biliary infection/drug therapy; Cephalosporins/therapeutic use; Cephalosporins/Pharmacokinetics

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Sun GH, Zhao SJ, Huang XR, Xu BF, Zhan CL. Pharmacokinetics of 7 cephalosporines antibiotics in dog's bile. *World J Gastroenterol* 1998; 4(Suppl2): 90 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/90.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.90>

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Diagnosis and treatment of malignant leioblastoma of small intestine

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Abstract

AIM: To report 6 patients with malignant leioblastoma of small intestine verified by surgery and pathology.

METHODS: There were 3 males and 3 females, aged from 38 to 73 ye ars. The tumor body were distribued mainly over duodenum (1 patient), jejunum (2), and ileum (3). Three patients underwent radical resection for malignant leioblastoma of small intestine and three palliative resection for the cancer. In two patients with hepatic metastasis, ligation of hepatic artery, the shock chemot herapy and hepatic artery thrombalization were performed. All of 6 patients were treated with Chinese medicine and immunopotentiator after operation.

RESULTS: One patient was lost to follow-up. Three patients died at 26 mo, 32 mo and 51 mo, respectively. One patient received second operation for recurrent cancer, and died at 2 mo after the operation. One patient have been living for 8 mo.

CONCLUSION: Based on our clinical experience of diagnosis and treatment, hypotonic duodenography and B ultrasonography were thought to be the first method for malignant leioblastoma of small intestine in grass-raot hospitals, and a tool for early diagnosis of intestine cancer. The malignant leioblastoma of small intestine should be resected radically as for the gastrointestinal carcinoma. If the hepatic metastasis was found, malignant leioblastoma of small intestine was not only resected, but also treated with ligation of hepatic artery, the shock chemotherapy and hepatic artery trombolization. The effect was excellent, and two patients have lived more than two years.

Key words: Small intestine neoplasms/surgery; Small intestine neoplasms/pathology; Small intestine neoplasms/diagnosis; Jejjoblastoma

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Qiu SQ, Wang JY. Diagnosis and treatment of malignant leioblastoma of small intestine. *World J Gastroenterol* 1998; 4(Suppl2): 91 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/91.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.91>

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Study on gastroscopic feature of gastritis like carcinoma of stomach

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Abstract

AIM: To analyse the gastroscopic features of gastritis-like carcinoma of stomach.

METHODS: The clinical and gastroscopic and pathological features in 22 patients with gastritis-like carcinoma of stomach were compared and analysed.

RESULTS: Five features of gastritis-like carcinoma of stomach have been obtained: (1) gastric cavity became smaller, gastric angle disappeared, and gastric peristalsis reduced; (2) gastric mucosa was rough and luster disappeared and projecting partides or congestive hydrops like angleworm on the surface of mucosa were seen; (3) there were white patches on the erosive surfaces of gastric mucosa; (4) old and new hemorrhagic spots coexisted. (5) the precancerosis were found by the previous gastric tissue biopsy.

CONCLUSION: The above five features were the suspicious ambiguous lesions of gastritis-like carcinoma of stomach.

Key words: Stomach neoplasms/pathology; Stomach neoplasms/diagnosis; Gastroscopy; Gastritis/diagnosis

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Diagnosis and treatment of spontaneous rupture of liver carcinoma with bleeding

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Abstract

AIM: To study the diagnosis and treatment for spontaneous rupture of liver carcinoma with bleeding.

METHODS: 22 patients (19 males 86%, and 3 females 14%) , with spontaneous rupture of liver carcinoma with bleeding treated between 1980 and 1995 were reviewed. The patients consisted of exploratory laparotomy was performed in 16 cases (73%), of them, hepatectomy in 5 cases (31%), hepatic artery ligation in 2 cases (13%), suture and packing with omentum in 9 cases (56%), and conservative therapy in 6 cases (27%).

RESULTS: The survival time of the 16 patients with operation ranged from 1 to 15 mo, with a mean survival of 5 mo, and the longest one survived 15 mo after liver resection. In non-resectable cases conservative cases, the survival time was only 1 to 3 mo.

CONCLUSION: Abdominal paracentesis, along with a physical examination of the abdomen will be useful in diagnosis of spontaneous rupture of liver carcinoma. The selection of the procedure for the treatment of spontaneous rupture of liver carcinoma will be decided, according the patient's condition, such as hepatic function, extent of the hepatoma. It is very important to accomplish hemostasis and reverse hemorrhagic shock. The therapeutic procedures including hepatectomy, hepatic artery ligation, suture and packing with omentum may be used in some late cases, especially in the aged.

Key words: Liver neoplasms/diagnosis; Liver neoplasms/therapy; Spontaneous rupture

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Clinical study on therapeutic effect of three cycle natural therapy on chronic hepatitis B and C

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Abstract

AIM: To observe the therapeutic effect of three-cycle natural therapy that include injecting self-blood plus Chinese medicine at acupuncture points, moxaing at acupuncture points and taking Chinese medicine on chronic hepatitis B and C.

METHODS: According to diagnostic standard of chronic virus hepatitis of the sixth, national prevention and treatment plan of virus hepatitis in 1990' chose group A: 439 patients with typical chronic hepatitis B, 298 male and 141 female, 337 aged 18-40 years and 102 aged 41-65 years; Group B: 294 patients with non-typical chronic hepatitis B, 202 male and 92 female, 75 aged 18-40 years and 219 aged 41-65 years; Group C: 102 patients with chronic hepatitis C, 67 male and 35 female, 69 aged 18-40 years and 33 aged 41-65 years. The course of the disease of all patients was longer than six mo. Virology mark materials HBV-DNA and/or HCV-RNA were all positive. And ALT was innormal or innormal repeatedly. The clinical manifestations were tired, poor appetite, abdominal distention, disorder of the hepatic zone, and so on. According to determination of treatment based on differentiation of symptoms and signs with Chinese-western method, we chose different medicine and treated the patients with acupuncture, moxa and medicine of three-cycle natural therapy, one a week.

RESULTS: After 2 courses or 24 times of treatment with three-cycle natural therapy, group A: HBsAg (+) 439 before treatment and 383 after treatment, the negative conversion rate was 12.8%. HBeAg(+)

439 before treatment and 167 after treatment, the turned negative conversion rate was 62%. HBV-DNA (+), 439 before treatment and 205 after treatment, the turned negative conversion rate was 53.3%. Of the 261 with ALT innormal before treatment and 3 after treatment, the turned negative conversion rate was 98.9%. Of the 122 with A/G innormal before treatment and 12 after treatment, the negative conversion rate was 90.2%. Of the 105 with HA innormal before treatment and 9 after treatment, the negative conversion rate was 91.4%. And 439 patients in Groups A, very effective in 331, 89 improved and ineffective in 19 with a total effective rate of 95.7%.

Group B: HBsAg (+) 294 before treatment and 264 after treatment, the negative conversion rate was 10.2%. HBV-DNA (+) 294 before treatment and 51 after treatment, the negative conversion rate was 82.7%. Of the 228 with ALT innormal before treatment and 10 after treatment, the negative conversion rate was 95.6%. Of the 169 with A/G innormal before treatment and 21 after treatment, the negative conversion rate was 87.6%. of the 108 with HA innormal before treatment and 11 after treatment, the negative conversion rate was 89.8%. And 294 patients in group B, very in 94 effective, 144 improved, and ineffective in 56 with a total effective rate of 81.0%.

Group C: HCV-RNA (+) 102 before treatment and 17 after treatment, the negative conversion rate was 83.3%. Of the 75 with ALT innormal before treatment and 4 after treatment, the negative conversion rate was 94.7%. Of the 42 with A/G innormal before treatment and 5 after treatment, the negative conversion rate was 88.1%. Of the 45 with HA innormal before treatment and 4 after treatment, the negative conversion rate was 91.1%. And 102 patients in Group C very in 38 effective, 54 improved, and ineffective in 10 with a total effective rate of 90.2%.

CONCLUSION: Three-cycle natural therapy has good therapeutic effect in chronic hepatitis B and C. Because a few patients were so fatter or thinner, taller or shorter that correctness of the acupuncture points was affected. The result of treatment was also affect. After correcting the acupuncture points and one more course, a good result was obtained.

Key words: Hepatitis B/therapy; Hepatitis C/therapy; Drugs, chinese herbal; Acupuncture; CTM-WM therapy

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Analysis of the relationship between ultrasonography and laparoscopic cholecystectomy

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Abstract

AIM: To assess the clinical value of ultrasonography in diagnosis of gallstone(s) before laparoscopic cholecystectomy.

METHODS: 61 patients with gallstone(s), 42 women and 19 men with age from 23 to 80 years, average 49.68. After fasting 12 h, patients were taking supine position or left lateral decubitus position, occasionally erect, scanned with 3.5 MHz sector transducer. According to previous literature gall stone(s) and gallbladder were evaluated. Before operation all the 61 cases were diagnosed by ultrasonography, among them 36 cases also evaluated by oral cholecystography. The intervals between ultrasonography and laparoscopic cholecystectomy were as follows: The shortest was 1 d (16 cases), the longest 44 d (1 case), 55 cases less than 10 d in 55 cases, 6 cases more than 11 d, the average 6.13 d.

RESULTS: In 61 patients with gallstone(s) the accurate rate diagnosed by ultrasonography and oral cholecystography was 100% and 38.88% respectively. The positive rate of ultrasonography was significantly

higher than oral cholecystography. Among 61 cases laparoscopic cholecystectomy was performed in 37 cases (60.11%), laparoscopic cholecystectomy with removal calculi in 14 cases (22.95%) and conversion to conventional cholecystectomy in 10 cases (16.39%). All three types of treatment completed successfully, no complications encountered, and follow-up to date the quality of life was good in general. There was no difference ($P > 0.05$). During the operation time and staying in hospital between laparoscopic cholecystectomy and laparoscopic cholecystectomy with removal calculi. But the operation time and staying in hospital were significantly longer in conventional cholecystectomy than that of the two groups ($P < 0.05$). The number or size of gallstone(s), normal or large gallbladder demonstrated that no influence for laparoscopic cholecystectomy or laparoscopic cholecystectomy with removal calculi. Whereas in cases with multiple or large gallstone(s) the possibility from laparoscopic cholecystectomy conversion to conventional cholecystectomy increased significantly. Among 14 cases with dilatation of common bile duct 8 cases (57.14%), converted to conventional cholecystectomy it showed that dilatation of common bile duct, especially present stone the majority of them would convert to conventional cholecystectomy.

CONCLUSION: Preoperative laparoscopic cholecystectomy ultrasonography provides a detailed information. This can help the surgeons to select patients and make surgical plan. Therefore, before operation ultrasonography plays an important role and is quite requisite for laparoscopic cholecystectomy.

Key words: Gallstones/ultrasonography; Gallstones/diagnosis; Gallstones/surgery; Laparoscopic cholecystectomy

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Clinical analysis of 83 cases from 365 cases of cerebrovascular accident complicated by upper alimentary tract hemorrhage

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Abstract

AIM: To inquire into various relation between cerebrovascular accident and upper digestive tract hemorrhage for physicians to enhance clinically vigilance; avoid and decrease occurrence of serious complication to cut down the death rate.

METHODS: There were 83 patients from 365 cases with cerebrovascular accident (cerebral hemorrhage, cerebral thrombosis and subarachnoid cavity hemorrhage) complicated with hemorrhage in upper digestive tract, their materials were clinically analysed as following: (1) the morbidity difference of cerebral hemorrhage, cerebral thrombosis, subarachnoid cavity hemorrhage and complicated hemorrhage; (2) relation between complicated cerebral hernia of three groups and upper digestive tract hemorrhage; (3) the relation between original basic gastric disease or *Helicobacter pylori* (Hp) infection and complicated hemorrhage; (4) the rule of usual onset time of cerebrovascular accident complicated by hemorrhage.

RESULTS: (1) The incidence rate of cerebrovascular accident complicated hemorrhage was obviously higher than cerebral

thrombosis and subarachnoid cavity hemorrhage ($P_1 < 0.01$ and $P_2 < 0.02$) in comparison with latter two, there were no marked differences ($P_3 > 0.05$), morbidity of 365 cases was 22.75%; (2) in 83 cases of complicated hemorrhage there were 48 cases complicated by cerebral hernia, in 282 cases of uncomplicated hemorrhage, there were 41 cases complicated by cerebral hernia, there was marked difference between the groups ($P < 0.01$). It showed that cerebral hernia was closely associated with complicated hemorrhage. The incidence of complicated hemorrhage complicated by cerebral hernia was 57.83%, but uncomplicated hemorrhage complicated by cerebral hernia was 14.53% only; (3) In 83 cases of complicated hemorrhage, there were 34 patients with various gastric condition or Hp test culture +++ before the onset (40.96%); (4) In 83 cases of complicated hemorrhage, 70 cases occurred in a week (84.34%) and most of the onset occurred at night.

CONCLUSION: (1) Cerebral hemorrhage is the most commonly complicated by the upper digestive tract hemorrhage, the cerebral thrombosis more common ly and the subarachnoid cavity hemorrhage less commonly; (2) Cerebral hernia is closely associated with complicated hemorrhage; (3) The patients with original basic gastric disease or Hp positive would be subject to the induced the upper digestive tract hemorrhage; (4) Most of the complicated hemorrhage occur in a week and at night.

Key words: Cerebrovascular disorders/complications; Gastrointestinal hemorrhage/etiology; Gastrointestinal hemorrhage/prevention and control; Gastrointestinal hemorrhage/therapy

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Expression of bcl-2 and c-myc protein in gastric carcinoma and precancerous lesions

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Abstract

AIM: To observe the expression of bcl-2 and c-myc protein in gastric carcinoma and precancerous lesions.

METHODS: Ninety-three specimens of biopsy were collected, 5 cases with gastric epithelial dysplasia (GED) from 21 chronic superficial gastritis (CSG), 23 cases with GED and intestinal metaplasia (IM) from 34 chronic atrophic gastritis (CAG) and 22 mucosa tissues adjacent to the primary cancer (MA) with GED and IM from 38 gastric carcinomas (GC). Bcl-2 and c-myc were determined with streptavidin peroxidase immunohistochemical method.

RESULTS: Immunostaining was found in cytoplasm in all the bcl-2 positive cells and most c-myc positive cells, while in a few c-myc positive cells, brown-yellow granules could be found in cytoplasm and in nuclei. The positive rates of bcl-2 and c-myc oncoprotein were 100%, 60.8% in CSG with GED, whereas in CSG without GED, were zero and 75.0% respectively. The positive expression rates of

bcl-2 and c-myc were 34.8% and 73.9%, in CAG with GED and IM and zero and 63.9% in CAG without GED and IM. In gastritis, the positive rates of bcl-2 in with GED and IM were significantly higher than that in CAG without GED and IM ($P < 0.05$ - $P < 0.001$), but the significant difference of c-myc expression in both was not found ($P > 0.05$). The positive expression rates of bcl-2 and c-myc were 47.4% and 76.3% in GC, 54.5%, 81.8% in MA with GED and IM and zero, 25% in MA without GED and IM, respectively. The positive rates of bcl-2 and c-myc in GC and MA with GED and IM were significantly higher than that in MA without GED and IM ($P < 0.001$). In this study, the coexpression rates of bcl-2 and c-myc oncoproteins were 60%, 34.8%, 54.5%, respectively, in with GED and IM of CSG, CAG and MA. No positive staining was found in without GED and IM ($P < 0.001$). However, expression of bcl-2 and c-myc was independent of age and sex of the patients ($P > 0.05$).

CONCLUSION: The mutation of *bcl-2* and *c-myc* genes may be an early molecular marker of gastric carcinogenesis, more biological characteristics and feature of gene expression of cancer cells were found in gastric epithelial dysplasia and intestinal metaplasia. Therefore, co-detection of bcl-2 and c-myc expression may be of special importance to early recognize the occurrence of gastric carcinoma and judge prognosis.

Key words: Stomach neoplasms; Precancerous lesions; *bcl-2* gene; *c-myc* gene; Gene expression

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Hemodynamic study of hepatitis B virus carriers

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Abstract

AIM: To a study the real state of health of HBV carriers (ASC for ahort) in the view of hemodynamics.

METHODS: The nailfold microcirculation of 60 patients with HBV (51 cases males, 9 females, the average age 29.5 ± 11.9 years) was studied by MCX-5A systemic micro-circulation instrument. And the hepatic hemodynamics and hemomicirculation state of 118 patients with HBV (90 males, 28 females, the average age 29.2 ± 11.4 years) were studied by RG-2B systemic rehohepatography. In 9 patients with HBV, we performed hepatic biopsies. All the results were compared with that in normals.

RESULTS: After a close clinical observation and pathological study

of liver in 60 cases of what is called HBV carriers, we found that the single and general integral values of their nailfold microcirculation (0.38 ± 0.32 , 0.89 ± 0.52 , 0.97 ± 0.69 , 2.24 ± 0.96) were significantly different from the values of healthy group (0.17 ± 0.09 , 0.49 ± 0.27 , 0.55 ± 0.31 , 1.21 ± 0.47), ($P < 0.01$). And its abnormal rate (55.0%) was markedly higher than the abnormal rate of healthy group (3.3%) ($P < 0.01$). The values of h_s , h_a/h_s , t_a of the rehohepatography in 118 cases of the patients ($0.0949 \Omega \pm 0.0297 \Omega$, 0.226 ± 0.103 , $0.223 s \pm 0.045 s$), were significantly different from the values of healthy group ($0.1230 \pm 0.0258 \Omega$, 0.165 ± 0.080 , $0.175 s \pm 0.022 s$), ($P < 0.01$). And its abnormal rate (36.5%) was markedly higher than the abnormal rate of healthy group (0). ($P < 0.01$). After performing hepatic biopsy in 9 cases of the patients, we found chronic persistent hepatitis in 5 cases and chronic active hepatitis in 2 cases, and only 2 cases have no significant pathologic damage.

CONCLUSION: Most clinical HBV carriers have a mild to middle hepatic damage and they belong to sub-healthy state. Nearly none of them is healthy.

Key words: Hepatitis B virus; Hemodynamics; Microcirculation; Liver/ pathology

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Wang XL, Guo H, Li ZZ, Jia SY, Zhang ZR, Liu H. Hemodynamic study of hepatitis B virus carriers. *World J Gastroenterol* 1998; 4(Suppl2): 98 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/98.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.98>

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Clinical analysis of the efficacy of interferon alpha treatment of hepatitis

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Abstract

AIM: To study the efficacy of interferon alpha treatment in patients with chronic hepatitis and combined with other type virus.

METHODS: From 1996 to 1998, about 44 cases were diagnosed as having chronic hepatitis B, about 11 cases, combined with other type hepatitis virus infection, 30 cases as control, established on the basis of abnormal serum ALT (more than 1.5 times than normal value) for at least 6 mo and positive serologic makers of hepatitis B virus (HBsAg and HBeAg), and positive HBV DNA detected by polymers chain reaction patients were treated with 300 mu of interferon alpha three times a week for 6 mo.

RESULTS: Of 85 patients, male: female was 5:1, averaging 40.3 years in age (26-61) 44 cases were only with hepatitis B, 11 cases were with complex infection. In 55 cases who had interferon treatment, 23 positive HBeAg had seroconversion of HBeAg to negative (41.8%), 5 of the controls were converted to negative

(16.7%) ($P < 0.01$); 18 HBV-DNA positive to negative (32.7%), 1 of the controls to negative (3%) ($P < 0.01$); 14 HBsAg positive to negative (25.5%), 3 of the controls to negative (1%) ($P < 0.01$). All the results had significant difference. In 44 cases of chronic Hepatitis B, 23 cases positive HBeAg had seroconversion of HBeAg to negative (51%) and in the 11 cases of complex infection the number was 0, ($P < 0.01$). The result had significant difference. The ALT was 127.9 ± 10.2 μ /L before treatment. 20 cases (36.4%) had increased ALT after treatment for a short time; the average ALT was 207.9 ± 10.2 μ /L. Half a year after treatment, 8 cases (14.5%) had HBeAg positive again, 5 cases (9.1 %) had HBVDNA positive, again.

CONCLUSION: Interferon treatment on Hepatitis B and combined with other type Hepatitis virus infection can increase cure rate. (HBeAg negative conversion rate was 41.8%, HBV-DNA was 32.7%). Interferon alpha treatment for chronic Hepatitis B had higher efficacy than the complex infection, HBeAg negative conversion rate was 51.0%, HBV-DNA was 31.0%. The time for treatment is in the beginning when the liver function gets better. The liver functions will get worse within a short period of time after treatment. Half a year after treatment, some cases reverse.

Key words: Hepatitis B/therapy; Hepatitis, viral/therapy ; Chronic diseases; Interferon α /therapeutic use

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Zhu Y, Wang YL, Shi L. Clinical analysis of the efficacy of interferon alpha treatment of hepatitis. *World J Gastroenterol* 1998; 4(Suppl2): 99 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/99.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.99>

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Diagnosis and treatment of gastrojejunal fistula and nutrition support action

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Abstract

AIM: To explain the diagnostic standard and therapeutic methods and lay emphasis on the importance to the treatment of nutrition support during the period of before and after operation through analysis of treatment of seven patients with gastrojejunal fistula (GJCF) and in combination of medical references concerned.

METHODS: Seven patients, all male averaging 32 years in age

(21-45), their primary illness was duodenal bulb ulcer; suture of perforation and large gastrectomy had been operated. GJCF had been found from 4 mo to 12 years after operation (averaging 52 mo), the chief symptom is abdominal pain, diarrhea, vomiting fecaloid substance and loss of body weight. GJCF had been diagnosed by barium enema examination.

RESULTS: Five patients were cured by primary excision of GJCF through TPN support before operation (including TPN and TEN after operation). Two patients died, one died of burst hemorrhage of upper digestive tract, the other died of fistula without TPN.

CONCLUSION: The common reason for GJCF is duodenal bulb ulcer and stoma ulcer perforated colon after large gastrectomy. It is mainly related to high acid. A diagnosis is based on personal illness and ex-operation history. Barium enema examination is the main method to diagnose. The key to successful operation is to improve the patients' nutrition condition before and after operation during the period of treatment.

Key words: Gastrojejunal fistula/diagnosis; Gastrojejunal fistula/therapy; Gastrojejunal fistula/surgery; Nutritional support

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Jiang ZM, Zhang SY, Li YG, Wang XR, Jia RM, Jiang YK, Hao SM, Liu YS. Diagnosis and treatment of gastrojejunal fistula and nutrition support action. *World J Gastroenterol* 1998; 4(Suppl2): 100 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/100.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.100>

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Analysis of the clinical effectiveness of the HCPT combination chemotherapy in treating 38 cases of late malignant tumour of digestive tract

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Abstract

AIM: To study the effectiveness and toxic reaction of the HCPT combination chemotherapy in treating late tumour of digestive tract.

METHODS: In the combination chemotherapy plan of the carcinoma of esophagus stomach, large intestine, HCPT dose was 20 mg each time, twice each cycle, 21 d was one cycle, three cycles was one course of treatment, total dose was 120 mg. 8 mg of Shudan (on dansetron) is injected by intravenous 15 min before chemotherapy. 20 mg of Benadryl was injected by intramuscular after chemotherapy; increasing fluid infusion when PDD was used; detoxifying by CF when high dose MTX and 5-Fu were used at the

same time urine was alkalized.

RESULTS: 38 patients had been treated for one course of treatment, effective rate: carcinoma of esophagus was 44.4%, carcinoma of stomach 42.9%, carcinoma of large intestine 37.5%. Clinical observation showed: if HCPT is used rationally in combination chemotherapy of late tumor of digestive tract, we can obtain satisfactory effectiveness can be obtained, and also the toxic reaction of HCPT is mainly that hemogram decreases at II degree, and reaction of digestive tract is light.

CONCLUSION: HCPT's price is cheaper, it's effectiveness is exactly. It's toxic reaction is also light. Therefore, the plan of the HCPT combination chemotherapy has an important practical value in the chemotherapy of the late tumor of digestive tract.

Key words: Esophageal neoplasms/drug therapy; Stomach neoplasms/drug therapy; Colonic neoplasms/drug therapy; Rectal neoplasms/drug therapy; Camptothecin/therapeutic use

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Liao ZJ, Wu GS, Li J, Sun CX. Analysis of the clinical effectiveness of the HCPT combination chemotherapy in treating 38 cases of late malignant tumour of digestive tract. *World J Gastroenterol* 1998; 4(Suppl2): 101 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/101.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.101>

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Study on P53 protein and C-erbB2 protein expression in primary hepatic cancer and colorectal cancer by flow cytometry

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Abstract

AIM: Quantitative study on P53 protein and C-erbB2 protein in primary hepatic cancer and colorectal cancer.

METHODS: The expression of P53 protein and C-erbB2 protein was quantitatively detected using flow cytometry in 15 primary hepatic cancer and 22 colorectal cancer.

RESULTS: The positive expression rates and the average expression of P53 protein and C-erbB2 protein in primary hepatic cancer were 26.6%, 0.69FI, 20%, 0.73FI, respectively. The positive expression rates and the average expression of P53 protein and C-erbB2 protein in colorectal cancer were 36.3%, 0.86FI, 31.8%, 0.71FI, respectively. The percentage of positive expression rates of cancer cells were different from one case to another.

CONCLUSION: The quantitative study method on P53 protein and C-erbB2 protein expression in primary hepatic cancer and colorectal cancer by flow cytometry was established. Flow cytometry is a new procedure by which we can quantitatively analyse the expression of P53 protein and C-erbB2 protein in hepatic and colorectal cancer.

Key words: Liver neoplasms; Colorectal neoplasms; P53 protein; C-erbB2 protein; Flow cytometry

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Luo F, Kan B, Lei S, Yan LN, Mao YQ, Zou LQ, Yang YX, Wei YQ. Study on P53 protein and C-erbB2 protein expression in primary hepatic cancer and colorectal cancer by flow cytometry. *World J Gastroenterol* 1998; 4(Suppl2): 102 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/102.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.102>

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Analysis of 20 cases of leiomyoma of alimentary tract

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Abstract

AIM: Through analysing 20 cases of leiomyoma of the alimentary tract to investigate its clinical features and the value of all kinds of adjuvant examinations.

METHODS: Twenty in patients with leiomyoma of the alimentary

tract, whose tumor was operatively removed and the diagnosis confirmed by pathological examination in our hospital from Oct. 1989 to march 1995.

RESULTS: The chief symptoms and signs of leiomyoma of the alimentary tract are abdominal pain, abdominal mass, hemorrhage of the alimentary tract and incomplete intestinal obstruction. There is no specific examination for it.

CONCLUSION: The incidence of leiomyoma of the alimentary tract is low, and it has no characteristic clinical symptoms. Unique examinations are not available, making the diagnosis rather difficult. The confirmative preoperative diagnosis rate is low, while the misdiagnosis rate is high.

Key words: Digestive system neoplasms/diagnosis; Digestive system neoplasms/pathology; Leiomyoma/diagnosis; Leiomyoma/pathology

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Sun SM, Xu JH, Ma T, Guo GH, Jing SB, Zhuang QW. Analysis of 20 cases of leiomyoma of alimentary tract. *World J Gastroenterol* 1998; 4(Suppl2): 103
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Clinical analysis of therapeutic effect of traditional Chinese medicine on peptic ulcer

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Abstract

AIM: To analyse the therapeutic effect of Jieyu yuyang san, Xia qi xiaoshi yutong san, Yangyin yuyang zhentong wan on three kinds of peptic ulcer.

METHODS: Two thousand two hundred patients with peptic ulcer were treated for 6 mo. Seven hundred and twenty affective ulcer patients (is mainly refered to duodenal ulcer) were treated with Jieyu yuyang san, Eight hundred and thirty dietary ulcer (is mainly refered gastric ulcer) patients were treated with Xiaqi xiaoshi yutong san. Six hundred and fifty mixed ulcer patients (mainly refered to duodenal ulcer with detachment of gastric mucosa, pyloric obstruction with pancreas cancer patients complicated with retrograde flow of bile) were treated with Yangyin yuyang zhentong wan. Of the 2200 patients, 1320 were men and 880 were women, aged 20-56 years. Of them, patients aged 20-39 years accounted for 850 (38.64%) and aged 40-56 years accounted for 1150 (52.27%). The disease course

ranged from 6 mo to 30 years, and 550 of them (25%) had a course of 6 mo to 3 years, 1650 of them (75%) had a course of 3-30 years. The clinical manifestations were bloated stomach, chest distress, eructation and back flow of acid (720); stomachache, tenderness of abdomen, anorerxia and vomitting swallow of gastric acid 830; stomachache, cold stomach, vomiting water, like hatness, like pressure (650). After 20-90 d treatment, the improvements of gastric and duodenal mucosa and disappearance of crater were analysed.

RESULTS: After the whole course treatment, 382 affective ulcer patients were recovered, 120 had avident effect, 204 got improved, and 14 ineffective with a total effective rate of 98%; 450 of dirtary ulcer patients were recovered, 240 very effective, 108 improved, and 32 ineffective with a total effective rate of 96.2%. 301 mixed ulcer patients were recovered, 209 very effective, 107 improved, and 33 ineffective with a total effective rate of 95%. By gastroscopy and radiography, ulcer crater disappeared and 1702 ulcer patients were recovered. In 2121 patients symptoms disappeared, and 79 patients ineffective with a total 96.4% and cure rate 77.6%. Before treatment, the I, II, III degree peptic ulcer included 720, 830, 650 patients and 14, 32, 33, respectively after treatment. After treatment, peptic ulcer were symptomatically significantly improved and ulceration were significantly diminished or healed.

CONCLUSION: The three kinds of medicine have good therapeutic effects on peptic ulcer including disappearance of ulcer crater and restore of gastric mucosa.

Key words: Peptic ulcer/therapy; Stomach ulcer/therapy; Duodenal ulcer/therapy; Drugs, Chinese herbal/therapeutic use

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Zhang ZQ, Zhang HP, Ha CL, Li XZ, Lu GQ, Chen GL, Zhang GH. Clinical analysis of therapeutic effect of traditional Chinese medicine on peptic ulcer. *World J Gastroenterol* 1998; 4(Suppl2): 104 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/104.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.104>

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Molecular clone constructed by the fragment of chromosomal DNA from *Helicobacter pylori*

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Abstract

AIM: *Helicobacter pylori* (Hp) was related to chronic gastritis and peptic ulcer. The fragment of chromosomal DNA from Hp amplified by PCR was cloned, which is significant on the basic research and clinical test for the positive control.

METHODS: Primer pairs were designed from the fragment of

Hp chromosome and the fragment was amplified by PCR, then the amplified product was inserted to pBluescript SK vector and transformed into *E. coli* DH5 α . The constructed clone of Hp DNA was certified by PCR, restriction endonuclease digestion and DNA sequencing.

RESULTS: PCR product was showed to be 203 bp electronic band, consistent to that of Hp standard strain. Analysis of Hp-DNA sequence was similar to known Hp sequence.

CONCLUSION: The Hp DNA clone is used as the positive control in the Hp test.

Key words: *Helicobacter pylori*; DNA, bacterial; Molecular cloning; Chromosome

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Pan XY, Lin WY, Wang SW, Cao GD, Liu Y. Molecular clone constructed by the fragment of chromosomal DNA from *Helicobacter pylori*. *World J Gastroenterol* 1998; 4(Suppl2): 105 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/105.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.105>

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Clinical research on plasma motilin levels and cutaneous electrogastrogram in patients with functional dyspepsia

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Abstract

AIM: To investigate the relationship between plasma motilin, cutaneous electrogastrogram (EGG) and functional dyspepsia, and to further investigate the etiology of the disease.

METHODS: Samples from peripheral venous blood were collected 12 h after fasting and 30 min after the testmeal in the morning in 30 dyspeptic patients and 30 volunteers, respectively. EGG were recorded concurrently for every person. The students' *t* test was used to analyse the result.

RESULTS: The plasma motilin level in the dysmotility-like dyspepsia at fasting was significantly lower than that of the control ($P < 0.01$); both of the plasma motilin levels at fasting and postprandial state of the other three types of functional dyspepsia were significantly higher than those of the normal subjects ($P < 0.01$); The gastric electrical dysrhythmia rates of all patients were significantly higher than those of the control whether at fasting state or postprandially ($P < 0.005$); The gastric electrical amplitude of the patients after the test meal was significantly lower than that of the control ($P < 0.025$ and $P < 0.005$).

CONCLUSION: The abnormality of the plasma motilin concentration and the gastric electrical activity leading to gastric hypomotility might be the essential pathophysiological mechanism of functional dyspepsia.

Key words: Dyspepsia/Etiology; Dyspepsia/Classification; Motilin/Blood; Electrogastrogram

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Niu CY, Gui YF, Wang ZF. Clinical research on plasma motilin levels and cutaneous electrogastrogram in patients with functional dyspepsia. *World J Gastroenterol* 1998; 4(Suppl2): 106 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/106.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.106>

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Effect of cholecystectomy on retrograde flow of bile in pylorus

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Abstract

AIM: To observe the effect of cholecystectomy on retrograde flow of bile in the pylorus.

METHODS: Thirty patients with gallbladder stone were diagnosed by B ultrasound and received cholecystectomy. Of them, there are 11 men and 19 women aged 32-65 years. The average age is 43.3 years. There are 7 patients with single gallbladder stone of 0.7-3.0 cm in diameter, 14 patients with 2-5 gallbladder stones of 0.4 cm and 2.0 cm in diameter, and 9 patients with silt filling gallbladder stones. The doctor who operated on the patients checked everyone 30 d before and after operation, with JF-IT 30 model of fiber duodenoscope. So the doctor could observe the degree of retrograde flow of bile in pylorus as well as the bile remains in bulbus duodenum.

RESULTS: Before the gallbladder was resected, 7 patients had a small amount of retrograde flow of bile in the ostium pylorus, two patients had moderate amount, 21 patients had no. After cholecystectomy, 8 patients had a small amount of retrograde flow of bile in ostium pylorus. The patients with moderate amount of retrograde flow of bile were 15, and 4 had a great amount of retrograde flow of bile into their stomachs. Only 3 without any retrograde flow of bile. Before the patients' gallbladders were resected, there was a little remains in the bulbus duodenum in 25 patients, moderate amount in 5. Then after cholecystectomy, there are 4 patients with a little remains, 19 with moderate amount, and 7 with a great amount of bile remained in bulbus duodenum. The degree of retrograde flow of bile in ostium pylorus was positively proportionate to that of bile remains in bulbus duodenum.

CONCLUSION: After cholecystectomy, the bile remains in the bulbus duodenum increase evidently, which increase pressure of the bulbus duodenum and the pylorus. This makes the function of sphincter muscle of pylorus decline, and the function of pyloric shutting is restricted.

Key words: Cholecystectomy; Bile reflux; Cholelithiasis/surgery

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Primary hepatic carcinoma with extrahepatic metastasis and secondary hepatic carcinoma

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Abstract

AIM: To distinguish primary hepatic carcinoma with extrahepatic metastasis from secondary hepatic carcinoma (SHC).

METHODS: Eighty-nine in patients with confirmed primary hepatic carcinoma with extrahepatic metastasis and secondary hepatic carcinoma in the period of November 1992 to May 1996, were reviewed, the shape diameter number of intrahepatic cancer nests, serum AFP, CA19.9 and CEA levels were compared.

RESULTS: There were 17 cases (19.1%) PHCEHM and 72 cases (80.9 %) SHC in this group. There were 9 cases (52.9%) with pulmonang metastasis, 3 cases (17.6%) with bone metastasis and 5 cases (29.4%) with other organ metastasis. In SHC there were 30 hepatic metastasis (41.7%) from gastric carcinoma 27 cases (37.5%) from lung carcinoma, 8 cases (11.1%) from pancreas carcinoma, and 7 cases (9.7%) from other carcinoma. Examination by CT scan showed in primary hepatic carcinoma that single cancer nests in

10 cases (58.8%), satellite cancer nests in 7 cases (41.2%); and in secondary hepatic carcinoma single cancer nest in 3 cases (4.2%), satellite cancer nests 8 cases (11.1%), the other 61 cases (84.7%) were multicancer nests with equalsize. In primary hepatic carcinoma 15 were AFP positive, and CA19.9 + CEA were the negative, CA19.9 + CEA of the rest 2 cases were positive, including 1 cholangiocellular cancer all was AFP negative, and 1 mixed hepatocellular cancer was AFP positive. In SHC CA19.9 + CE A were positive, AFP negative in 69 cases, AFP positive in 3 cases.

CONCLUSION: The results indicated that of the cases with intrahepatic and extrahepatic cancer nests 80.9% were SHC. Cases with intrahepatic single cancer nests, and serum AFP positive and CA19.9 + CEA negative, were in generall PHC, or else SHC. It was difficult to distinguish AFP-positive SHC, cholangiocellular carcinoma and mixed hepatocellular cancer accounting 5.6% (5/89) totally, which should be identified by pathological examination of extrahepatic or intrahepatic cancer nests. These results can serve as a reference for clinicians to make differential diagnosis of primary hepatic carcinoma with extrahepatic metastasis from secondary hepatic carcinoma.

Key words: Liver neoplasms/diagnosis; Liver neoplasms/secondary; Neoplasm metastasis; Lung neoplasms/secondary; Stomach neoplasms/secondary

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Study on cellular immune function of advanced alimentary tract cancer in perioperative period

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Abstract

AIM: To study the immune functions of patients with alimentary tract cancer in the perioperative period.

METHODS: In our study, T cell subsets and NK cells (NKC) in the peripheral blood were tested in 133 alimentary tract cancer patients, including 102 treated with radical surgery and 31 unresectable patients in the perioperative period.

RESULTS: There were a higher level of CD8+ ($P < 0.05$) and a lower level of NKC, CD3+ and CD4+ ($P < 0.01$). Ratio of CD4+/

CD8+ cell was reduced in patients before and surgery compared with those in normal subjects ($P < 0.05$). The results showed that cellular immune function of patients was significantly depressed, and further depressed one week after operation. This means surgery and anesthesia can damage the immune function of the patients. The levels of CD3+, CD4+, CD8+, CD4+/CD8+ and NKC in patients with radical treatment were higher before surgery than those three week after operation ($P < 0.05$). This demonstrated that removal of cancer led to the elimination of TDSF. There is no change for patients with unresectable cancer which indicated the immune function was depressed seriously.

CONCLUSION: (1) It is suggested that alimentary tract cancer must be treated with radical surgery, and advanced cancer should be treated with palliative surgery. So the load of cancer and TDSF could be eliminated or reduced. (2) Surgery and anesthesia may impair the immune function. So lessening influence from surgery and anesthesia so as to restore cellular immune function of the patients is of great importance for treatment.

Key words: Digestive system neoplasms/immunology; Digestive system neoplasms/surgery; Immunity, cellular; Intraoperation period

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Experimental and clinical research of predicting chronic hepatitis progressing into serious hepatitis

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Abstract

AIM: To seek early indicator of chronic hepatitis developing into serious hepatitis.

METHODS: Liver of rat damaged by D-Galactosamine was used as Dynamic observation of tumor necrosis factor (TNF), F-protein (FP), serum bilirubin (SB), prothrombin time (PT), and alanine aminotransferase (ALT) were performed. Pathological change of the liver tissue have been quantitatively analysed by the analysis instrument of image. The relationship between pathological changes of and laboratory markers were analysed using multilinear correlation, multivariate regression and stepwise logistic regression analysis by computer.

Clinical research based on patients of chronic active hepatitis B (All of the patients with middle degree or over chronic Hepatitis B according to the new standard). Apart from the above serum markers interleukin-2 receptor (SIL-2R) and gene mutation of HBV pre C have been detected. SAS software was used for analysis.

RESULTS: According to the result of clinical and experiment research, and combination with clinical practice. A predictive formula could be draw up for chronic Hepatitis B developing into serious hepatitis. By dynamic observation and application of different parameters into this formula, we can predict the tendency of chronic hepatitis developing into serious hepatitis.

CONCLUSION: The predictive formula will be of reference value for clinicians to predict whether chronic hepatitis will develop into serious hepatitis.

Key words: Hepatitis/Diagnosis; Hepatitis/Physiopathology; Liver/Pathology; Chronic diseases

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Study on bacterial translocation of intestine and endotoxin concentration of plasma in obstructive jaundice

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Abstract

AIM: To observe intestinal bacterial translocation and plasma endotoxin concentration in obstructive jaundice.

METHODS: Sixty Wistar rats with an average weight of 220-250 g were used in the experiments. The animals were randomized to undergo ligation and division of the common bile duct (CBD) or sham ligation. The *Escherichia coli* (O₅₅B₅) were labeled by fluorescein at a final concentration of (5×10^6 cfu/L). Specimens of distal

myenteric lymph nodes (MLN), liver, spleen were obtained on the 7th postoperated, blood was collected and endotoxin was measured.

RESULTS: There was a significant ($P < 0.01$) increase in mean (s.e.m) serum bilirubin and significant ($P < 0.05$) improvement on endotoxin concentration. There was no evidence of colonization in MLN, liver, spleen in control rats. In contrast, 20 of 30 CBD-ligated rats labeled *E.coli* in MIN was found in and damage of intestinal mucosa occurred in rats with experimental obstructive jaundice.

CONCLUSION: Bacterial translocation from gastrointestinal tract and endotoxin to the blood stream are central to current theories of sepsis. Our study suggests that the gut is a primary source of infection in obstructive jaundice.

Key words: Jaundice; Endotoxin/blood; Bacterial translocation; Intestine/microbiology

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Reversal of devazepide on antagonistic effect of CCK-8 on morphine on electrical and mechanical activities of rat duodenum *in vitro*

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Abstract

AIM: To study the antagonistic effect of cholecystokinin octapeptide (CCK-8) on morphine and its mechanism.

METHODS: The method of simultaneously recording the electrical and mechanical activities of rat duodenum *in vitro* was adopted.

RESULTS: The results showed that the average amplitude and number of spike potentials (SPA and SPN), after injection of acetylcholine (Ach, 300 nmol/L) of 22 duodenal segments *in vitro* respectively increased from 0.70 ± 0.07 mV ($\bar{x} \pm s$) before injection to 0.94 ± 0.09 mV, and 2.71 ± 0.23 to 3.88 ± 0.15 ,

followed by the increase of the average amplitude of contractions (CA) from 16.40 ± 1.00 mm to 24.44 ± 1.63 mm. This SPA, SPN and CA were reduced to 0.59 ± 0.06 mV, 2.71 ± 0.09 and 13.54 ± 1.04 mm after administration of morphine (330 nmol/L), respectively. But the SPA, SPN and CA were respectively increased to 0.81 ± 0.07 mV, 3.52 ± 0.13 and 22.73 ± 1.00 mm after injection of CCK-8 (0.7 nmol/L). Using CCK-A receptor antagonist (Devazepide, 10 nmol/L), the SPA, SPN and CA were reduced to 0.54 ± 0.05 mV, 2.66 ± 0.18 and 13.67 ± 0.66 mm, respectively. Moreover, all of them showed extremely significant differences ($P < 0.001$) when the latter was compared with the corresponding item of the former.

CONCLUSION: The results firstly demonstrated that CCK-8 could antagonize the effect of morphine which inhibited the potentiation of Ach on the electrical and mechanical activities of rat duodenum *in vitro*, whereas devazepide could reverse the anti-morphine effect of CCK-8. It is suggested that the antagonistic effect of CCK-8 on morphine was mainly mediated by CCK-A receptor, and thus provide a new clue for the clinical treatment of disturbances in intestinal movement function.

Key words: Duodenum/Physiology; Duodenum/drug effects; Cholecystokinin/Pharmacology; Morphine/Pharmacology; Devazepide/Pharmacology

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Xu MY, Lü HM, Wang SZ, Shi WY, Yang DX, Yang CX, Yang LZ. Reversal of devazepide on antagonistic effect of CCK-8 on morphine on electrical and mechanical activities of rat duodenum *in vitro*. *World J Gastroenterol* 1998; 4(Suppl2): 112 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/112.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.112>

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Clinical investigation of ulcerative colitis patients treated by integrated traditional Chinese and Western medicine

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Abstract

AIM: To observe the therapeutic effects of ulcerative colitis managed by integrated Traditional Chinese Medicine (TCM) and Western therapy and compared by conventional interventions solely.

METHODS: Ninety ulcerative colitis patients were randomly divided into two groups. (1) Group I: 48 cases treated by integrated TCM and western medicine, 40 were men and 8 were women, aged 23-50 years with 31.6a in average and the disease course ranged from 5 mo to 15a, 3.76a in average, with 11 cases less than 1a, 22 cases 1a-5a, 13 cases 5a-10a and 15 cases more than 10a. Endoscopic examinations revealed 16 cases with scattered ulcerative lesions on intestinal mucosa, 16 cases with slight mucosal erosions and 14 cases with mucosal congestion and edema. (2) Group II: 42 cases treated solely by conventional therapy as control, 36 were men and 6 were women, aged 21-48 years with 30.3a in average with the disease course ranged from 6 mo-14a, 3.55a in average, with 9 cases less than 1a, 21 cases 1a-5a, 11 cases 5a-10a and 1 case more than 1a.

Endoscopic examinations revealed 16 cases with scattered ulcerations on the intestinal mucosa, 15 cases with slight mucosal erosions, 13 cases with mucosal congestions and adema. Two groups were demographically comparable, their general status, clinical symptoms and endoscopic signs were similar without significant differences ($P > 0.05$). Patients in Group I were treated by integrated TCM and western medicine based on an overall analysis of the illness and patient condition and conventional western interventions were used solely in the controlled Group II. The efficacy and clinical results were observed and compared meticulously.

RESULTS: The results were investigated 2 wk afterward with 39 cases of immediate cure (81.3%), 8 cases of improvement (16.7%) and 1 case of ineffectiveness (2%), *i.e.* with 98% total effective rate in Group I. Comparatively there were 27 cases of immediate cure (64.3%), 9 cases of improvement (21.4%) and 6 cases of ineffectiveness (14.3%) *i.e.* only 86.9% total effective rate in Group II. Statistical analysis were performed with significant differences between these two groups, $P < 0.01$.

CONCLUSION: It is concluded that the therapeutic results are much better in cases treated by the integrated TCM and western medicine.)

Key words: Colitis, ulcerative/drug therapy; TCM WM therapy; Endoscopy

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Hu QY, Hu XY, Jiang Y. Clinical investigation of ulcerative colitis patients treated by integrated traditional Chinese and Western medicine. *World J Gastroenterol* 1998; 4(Suppl2): 113 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/113.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.113>

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Clinical application and evaluation of CT in the diagnosis of esophagus and gastrointestinal tract diseases

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Abstract

AIM: To detect the examined methods of esophagus and gastrointestinal tract with CT scan and evaluate its clinical application.

METHODS: 83 cases esophagus and gastrointestinal tract patients were examined with CT scan. All were confirmed by surgical and pathological findings. They included 28 cases in the esophagus, 32 cases in the stomach, 1 cases in the small intestine, 22 cases in the large intestine. Preparation before examination esophagus patients had 10-20 mL of the oral administration of 5% urografin 5-10 min after 3 g of the oral administration of puvis efferve scientiae compositae. Stomach patients had 350-500 mL of the oral ad ministration of mineral water and turned round the body in examined-bed 2-3 times. Intestine patients had 350-500 mL of 5% urografin in 24 or 12 h before scanning, when necessary, visualization of large intestine is achieved by introduced 600-900 mL of air through a Folly tube scanning methods: simple scan, object scan, enhanced scan.

RESULTS: 83 cases included 80 with cancer or tumor, 1 with hiatal hernia, 1 with small intestinal crohn's disease, 1 with pyloric obstruction. In the newer-lesions group, there were 20 cases, diagnostic accuracy was 90%, 2 cases were false diagnosed. In the post-operation reexamination group, there were 33 cases, 15 cases had been found recurrence and/or metastasis, including 6 cases distant organ metastases. Recurrence rate is 45.5%. In the definite diagnosis group, there were 30 cases 100% lesions could be displayed by CT, there were 10 cases carcinoma infiltrated into adjacent tissue and 2 cases carcinoma metastasized to distant organ. In the 80 cases, metastasis rate is 25%.

CONCLUSION: With well prepared examination, CT of esophagus and gastrointestinal tract can well display the lesions of tumor. It is also valuable to study other diseases of esophagus and gastrointestinal tract, *e.g.* crohn's disease, hiatal hernia. Re-examination patients with CT scan can be observed the change of disease and found early recurrence and/or metastasis. The plan of treatment thus can be corrected. Definite diagnosis patients with CT scan . It can be found whether lesion infiltrate into adjacent tissue or metastasize to distant organ, so the plan of treatment can be ascertained.

Key words: Gastrointestinal diseases/radiography; Esophageal diseases/radiography; X-ray computed tomography

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Evaluation of colorectal carcinoma screening with fecal monoclonal antibody

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Abstract

AIM: To evaluate the effect of colorectal carcinoma screening with fecal monoclonal antibody test (FMAT) in certain populations, through comparison with fecal occult blood test and questionnaire.

METHODS: Fecal samples of 11272 staff workers aged 19-89 years from Guangdong Provincial Post-telecommunication Bureau were tested by monoclonal antibody CMU15 which reacted with gastrointestinal cancer. 1010 positive cases and 217 randomly selected negative cases were examined by sigmoidoscopy or pancolonoscopy. In the same time, 647 fecal samples were tested by occult blood test (FOBT) from as control. In another group, 285

cases were selected for sigmoidoscopy based on questionnaires. The main contents included: (1) polyps history, (2) bloody or sticky fecal, (3) pain or mass at lower abdomen, (4) colorectal carcinoma in one or both of his parents, brothers or sisters, (5) age 50 years and over. People with at least one of the 5 conditions would be examined by sigmoidoscopy. The results were compared with each group.

RESULTS: In 1010 FMAT positive cases 6 carcinomas were detected (0.58%), 152 adenomas (15.0%), 143 other kinds of polyps (14.1%) and 5 ulcerative colitis (0.50%). In 217 negative cases no carcinoma was detected, only 12 adenomas, other kinds of polyps (5.4%). Only 50% carcinomas, 11.1% adenomas, 9.8% other polyps were positive by the test of FOBT. In questionable group no carcinomas, there were adenomas 23 (8.1%), other polyps 26 (9.1%).

CONCLUSION: It suggested that the test of fecal monoclonal antibody was very sensitive to colorectal carcinomas and adenomas and can be used for colorectal carcinoma screening.

Key words: Colorectal neoplasms/diagnosis; Antibody, monoclonal; Screening; Colonoscopy

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Yu SP, Zheng SJ, Zhou HY. Evaluation of colorectal carcinoma screening with fecal monoclonal antibody. *World J Gastroenterol* 1998; 4(Suppl2): 115
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Clinical characteristics of alcoholic liver disease

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Abstract

AIM: To study the clinical characteristics and noninvasive diagnostic evidences of the alcoholic liver disease (ALD).

METHODS: Hepatitis B and C virus markers (HV), ALT, AST/ALT ratio, γ -glutamyl transpeptidase (γ -GT), alkaline phosphatase (ALP), prothrombin time (PT), serum albumin (Alb), jaundice, ascites, coexistent fatty liver, cirrhosis and hepatocellular carcinoma, all the 12 clinical characteristics in 16 patients with liver disease who ingested more than 40 g alcohol a day for more than 10 years (heavy drinkers group) were compared with the ones in 22 patients with liver disease who never or seldom ingested alcohol (control group).

RESULTS: There were 4 (25%) patients with positive HV in the heavy drinkers group. All the patients in the control group were positive in serum HV. The patients with AST/ALT ratio > 1 and coexistent hepatocellular carcinoma were 13 (81.2%) and 2 (12.5%) and γ -GT was 374 ± 170 U/L in the heavy drinkers group. In the control group they were 10 (45.5%), 10(45.5%) and 116 ± 91 U/L, respectively ($P < 0.05$). The patients coexistent fatty liver in the heavy drinkers group were 4 (25%) which were more than 1 (4.5%) in the control group, but $P > 0.05$ in statistics. In the other 7 menifestations there were no significant differences between the two groups.

CONCLUSION: Ingestion of more than 40 g alcohol per d for more than 10 years, AST/ALT ratio > 1 , much elevated γ -GT, coexistent fatty liver and negative HV (some patients may coexist viral hepatitis) are parameters for ALD diagnosis. ALD less leads to hepatocellular carcinoma than viral liver damage.

Key words: Liver diseases, alcoholic/diagnosis; Liver diseases, alcoholic/therapy; Liver cirrhosis; Liver neoplasms

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Relationship between *Helicobacter pylori* infection and gastric cancer

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Abstract

AIM: The purpose of this study was to investigate the relationship between *Helicobacter pylori* (Hp) infection and gastric cancer.

METHODS: Hp in 4 antral bioptic specimens was examined by rapid urease test and serum anti-Hp IgG was screened by enzyme linked immunosorbent assay in 21 chronic superficial gastritis (CSG), 26 duodenal ulcer (DU) and 23 advanced gastric cancer patients

(AGC). Gastroscopy and historical examination were carried out in all patients.

RESULTS: Hp infection percent in CSG, DU and AGC was 52.4%, 88.5% and 78.3%, respectively. There was significant difference between CSG and DU about Hp infection ($P < 0.01$) and there was no difference between CSG and AGC about Hp infection ($P > 0.05$). Hp infection was higher in gastric adenocarcinoma than in gastric signet-ring cellular cancer ($P < 0.05$).

CONCLUSION: (1) There was no significant relationship between Hp and AGC. (2) But there was much more relation between Hp and gastric adenocarcinoma.

Key words: Stomach neoplasms/pathology; *Helicobacter pylori*; *Helicobacter* infed; *Helicobacter* infections; Gastritis

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Yu XE, Zhao AX, Wei DL, Du JZ. Relationship between *Helicobacter pylori* infection and gastric cancer. *World J Gastroenterol* 1998; 4(Suppl2): 117
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Study on the relationship between *Helicobacter pylori* infection and proliferative kinetics of gastric mucosa

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Abstract

AIM: To explore the relationship between *Helicobacter pylori* (Hp) and proliferative activities of gastric mucosa.

METHODS: The data from the 68 cases of chronic gastritis biopsy specimens. The Hp detected by histological methods (wathings-terry, w.s. Silver-staining and 0.25% Fuchsin Basic staining and PCR techniques. The proliferating cell nuclear antigen (PCNA), C-erb-B2 and p53 gene protein expressions were analysed immunochemically (ABC method) Sliver-binding nucleolar regions (AgNOR) were

counted.

RESULTS: The Hp positive were 30 cases and Hp negative were 38 cases. The I, II, III, IV degree positive expressions of PCNA were 5, 7, 4, 14 and 27, 11, 0, 0 in Hp positive and Hp negative respectively ($P < 0.05$). The AgNOR counts of the former significantly more than that of the later (3.44 ± 1.20 and 1.08 ± 0.08 , respectively) ($P < 0.05$). The C-erb-B2 expressions were negative in non-Hp infected mucosa, but the local positive expressions were found in 4 Hp infected mucosa. The p53 were negative in chronic gastritis whether Hp positive or negative.

CONCLUSION: The proliferative kinetics of Hp infected gastric mucosa increased, that may be one of the risk factors of gastric carcinogenesis

Key words: Helicobacter infection; *Helicobacter pylori*; Gastric mucosa/pathology

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Zhu YH, Wang YR, Sun JJ, Zhu CL, Wu X, Lu B. Study on the relationship between *Helicobacter pylori* infection and proliferative kinetics of gastric mucosa. *World J Gastroenterol* 1998; 4(Suppl2): 118 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/118.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.118>

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Investigation of serum anti-HpIgG and stomach mucosa *Helicobacter pylori* at Tibetan altitude

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Abstract

AIM: To determine the effects of measuring serum anti-HpIgG in high altitude Hp infection.

METHODS: The serum anti-HpIgG was measured by a ELISA and the stomach mucosa Hp was investigated in MB staining. The results were compared.

RESULTS: Of 542 healthing donors, both 198 serum anti-HpIgG and 187 stomach mucosa Hp were positive; compared with these 398 serum anti-HpIgG and 402 stomach mucosa Hp were positive in the stomach disease group. The differences of two group were not significant ($P > 0.05$) and the false positive/negative was a little.

CONCLUSION: These results suggest that a synergistic measurement of both serum anti-HpIgG and stomach mucosa Hp were important steps in determining of high altitude Hp infection.

Key words: Gastric mucosa/microbiology; *Helicobacter pylori*/immunology; IGG/analysis

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Fu XY, Xu ZC. Investigation of serum anti-HpIgG and stomach mucosa *Helicobacter pylori* at Tibetan altitude. *World J Gastroenterol* 1998; 4(Suppl2): 119 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/119.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.119>

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Expression of antral somatostatin mRNA in duodenal ulcer disease complicated with antral gastritis associated with *Helicobacter pylori*

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Abstract

AIM: To explore the gene expression of antral somatostatin mRNA in duodenal ulcer disease complicated with antral gastritis associated with *Helicobacter pylori*.

METHODS: Twenty-six patients with active duodenal ulcer (all cases *Helicobacter pylori* are positive), antral biopsy showed moderate or severe gastritis. Twenty-four non-ulcer control subjects (6 *Helicobacter pylori* positive) antral biopsy showed mild gastritis. *Helicobacter pylori* were examined by rapid urease test, giemsa stain and Hp specific IgG (ELISA), at least two of them are positive. The diagnosis of antral gastritis was accordant with the criterion of "quantitative diagnosis of chronic gastritis". The contents of somatostatin in antral mucosa were determined by means of radioimmunoassay. The counts of D-cells were investigated by means of immunohistochemistry. The expression of SS mRNA was measured by northern blot and slot-blot analysis.

RESULTS: (1) In twenty-six patients with active duodenal ulcers, the contents of somatostatin in antral mucosa tissues ($266.37 \pm$

56.25 pg/mg wet weight) were significantly decreased compared with those in twenty-four non-ulcer control subjects (335.48 ± 110.22 pg/mg wet weight) ($P < 0.01$). According to antral mucosa biopsy, giemsa stain and SS radioimmunoassay, we found that the SS contents of antral mucosa had close relation to infected Hp quantity and the degree of antral gastritis. The more the Hp quantity and the more severe the degree of antral gastritis, the lower the SS contents. (2) The counts of D-cells in duodenal ulcer group ($36.28 \pm 13.34/\text{mm}^2$) were remarkably decreased compared with those in non-ulcer control group ($58.96 \pm 41.75/\text{mm}^2$) ($P < 0.05$). The counts of D cells have close relation Hp quantity in antral mucosa and the degree of antral gastritis. Owing to almost all duodenal ulcer diseases are complicated with moderate or severe antral gastritis associated with Hp, therefore D cell counts are obviously decreased. (3) Somatostatin mRNA levels were significantly lower in active duodenal ulcer (0.52 ± 0.11 densitometer unit) than in non-ulcer control subjects (3.26 ± 0.87 densitometer unit) ($P < 0.01$). This showed that at the level of gene transcription, owing to the affection of antral gastritis associated with Hp, the synthetic function of SS had decreased.

CONCLUSION: *Helicobacter pylori* infection has close relation to duodenal ulcer occurrence. *Helicobacter pylori* infection can lead to antral gastritis. Owing to the influence of antral gastritis associated with *Helicobacter pylori*, antral D-cells in patients with duodenal ulcer not only showed decrease in quantity but also decrease in function of synthesis.

Key words: Duodenal ulcer; Gastritis; *Helicobacter pylori*; somatostatin; RNA, messenger

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Zheng CQ, Fu WQ, Li YQ, Sun SY, Zhou Z. Expression of antral somatostatin mRNA in duodenal ulcer disease complicated with antral gastritis associated with *Helicobacter pylori*. *World J Gastroenterol* 1998; 4(Suppl2): 120 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/120.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.120>

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Analysis of Hp infection detection in 150 cases by ^{14}C -UBT

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Abstract

AIM: To study the sensitivity, specificity and clinical utility of ^{14}C urea breathing test of *Helicobacter pylori* infection.

METHODS: All the 150 cases (40 cases of chronic gastritis, 30 cases of gastric ulcer, 50 cases of duodenal ulcer, 20 cases of gastric carcinoma 8 cases of polypous gastritis, 2 cases of portal hypertensive gastropathy) were examined by fibrogastroscope and confirmed by biopsy pathology, 15 cases of duodenal ulcer and 5 cases of gastric ulcer were treated with

PPI tetratherapy for 1 mo, then a comparison between the pretreatment and posttreatment was made, ^{14}C -urea was calculated by scintillator.

RESULTS: (1) The Hp infection rates of chronic gastritis duodenal ulcer and gastric ulcer and gastric carcinoma had no difference in statistics with the method of ^{14}C -UBT. (2) There was no difference of ^{14}C -UBT radioactivity value between chronic gastritis and duodenal ulcer, (3) Chronic gastritis accompanied with gastric mucosal erosion atrophy and entero-metaplasia was significantly higher than simple chronic gastritis ($t < 0.05$). (4) After one-month bactericidal treatment the bactericidal rate reached 100%.

CONCLUSION: ^{14}C -UBT is a sensitive, high effective and specific method for Hp detection.

Key words: Helicobacter infection/diagnosis; Gastritis; Stomach ulcer; Duodenal ulcer; Stomach neoplasms

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Zheng YG, Liu DP, Fu BY. Analysis of Hp infection detection in 150 cases by ^{14}C UBT. *World J Gastroenterol* 1998; 4(Suppl2): 121 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/121.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.121>

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Gastrointestinal tract complications in severe acute pancreatitis

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Abstract

AIM: To evaluate clinically the gastrointestinal (GI) tract complications of severe acute pancreatitis and discuss management to the complications.

METHODS: Sixty-five cases with acute pancreatitis admitted to our hospital during past two years (Jan.1996 to Feb.1998) were analysed. The group consisted of 56 male patients and 19 females with average age of 48.3 (28-76). The recorded mean Ranson-s score was 2.73 (0-7).

RESULTS: Seven cases developed severe paralytic ileus, in

six of them their symptom subsided gradually with a group of treatments including GI tract aspiration, sufficient oxygen supply, use of glucocorticoid supplement of albumin, selective digestive decontamination (SDD) and cathartica L. therapy especially the use of Chinese medicine, rhubarb. Four patients developed serious duodenal adynamic ileus leading to a long term gastric aspiration. Gastroduodenal or gastrojejunal feeding is an appropriate method to help patients to overcome the high risk period when adynamic duodenum is detected, Pancreatitis-induced intestinal necrosis and intestinal fistula developed in 3 cases, Total mortality rate in our group is 6.1% (4/65).

CONCLUSION: Gastrointestinal tract is frequently involved in severe acute pancreatitis. Synthetical treatment, espacially, gastroduodenal or gastrojejunal aspiration and feeding and SDD is helpful to the group of patients.

Key words: Pancreatitis/complications; Gastrointestinal diseases/diagnosis; Gastrointestinal diseases/therapy

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Shu ZJ, Li WQ, Wang XB, Wang ZM, Wang SH, Wang L, Du JX, Li JS. Gastrointestinal tract complications in severe acute pancreatitis. *World J Gastroenterol* 1998; 4(Suppl2): 122 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/122.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.122>

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Study on the therapeutic effect of all-trans retinoic acid and malotilate on CCl₄-induced hepatic fibrosis of rats

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Abstract

METHODS: The effect of all-trans retinoic acid and malotilate on CCl₄-induced hepatic fibrosis of rats was investigated, using colchicine as control, Immunohistochemical stain of I, III, IV, V collagen and

desmin, computer imaging analysis and electronic microscopy were applied to study the effect.

RESULTS: All-trans retinoic acid and malotilate had mild effect of fibrolysis, compared to colchicine. Additionally, CCl₄-induced fibrosis of rats had restored to some degree without treatment.

Key words: Liver cirrhosis/drug therapy; Retinoic acid/therapeutic use; Malotilate/therapeutic use

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Yin F, Yao SK, Li ZH, Shi HC. Study on the therapeutic effect of all-trans retinoic acid and malotilate on CCl₄-induced hepatic fibrosis of rats. *World J Gastroenterol* 1998; 4(Suppl2): 123 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/123.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.123>

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Effect of needling points of lower extremities of foot Yangming meridian on area of gastric antrum with ultrasonography B observation

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Abstract

AIM: To clarify the relationship between the foot Yangming meridian and gastric movement.

METHODS: Six points: Futu, Liangqiu, Zusanli, Shangjuxu, Chongyang and Neiting, of lower extremities of foot Yangming meridian were selected as needling points in 90 volunteers of 6 groups (15 cases/ each group). The control point was positioned 1 cm place near points. Ultrasonography B was used to observe the figure of gastric movement in 3 min prior to needling and 3 min

during needling. 180 figures were trapped and processed by using computer. The area of gastric antrum was calculated with cumulating areas method.

RESULTS: Needling zusanli, Shangjuxu, Chongyang and Neiting prints of lower extremities of foot Yangming meridian have significant effect on area of gastric antrum. $P < 0.01$, compared with prior to needling point. The diameter between upper and lower of gastric antrum was significantly increased after needling Zusanli and Chongyang ($P < 0.01$). The only point to enhance the diameter of anterior and posterior of gastric antrum was Zusanli.

CONCLUSION: Needling points of lower extremities of foot Yangming meridian have specific and significant effect on function of gastric movement.

Key words: Stomach/ultrasonography; Foot yangming meridian; Acupuncture

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Chang XR, Yan J, Yi SX, Lin YP, Yang RD, Huang BQ. Effect of needling points of lower extremities of foot Yangming meridian on area of gastric antrum with ultrasonography B observation. *World J Gastroenterol* 1998; 4(Suppl2): 124 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/124.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.124>

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Distribution of esophageal and cardiac carcinoma and precancerous of 2238

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Abstract

AIM: To master the distribution of the carcinoma of the esophagus and precancerous and research the regulation of the lesion.

METHODS: According to the 5 grade criterion of the esophagus and pre-ventriculus of cytology. We made a widely health examination in high risk area Yangcheng county, Shanxi Province to dweller whose age is older than 35 years.

RESULTS: 2238 patients were examined by cytology, of them, 27 (1.21%) were early stage carcinoma of the esophagus, 6 (0.26%) were esophageal precancerous; 27 (1.21%) were early stage of carcinoma of the cardia of the stomach, 3 (0.13%) were cardiac precancerous, total incidence rate is 2.82%, male to female is 1.74:1.51 (2.28%) were esophageal dysplasia II, 226 (10.09%) were esophageal dysplasia I, 10 (0.45%) were cardiac dysplasia II, 108 (4.83%) were cardiac dysplasia I. Male to female is 1.94:1, the peak age is 40-60 years, 50-60 years respectively.

CONCLUSION: To research the distribution of the carcinoma of the esophagus, the carcinoma of the cardia of the stomach and precancerous by cytology can offer science proof for the preventive treatment.

Key words: Esophageal neoplasms; Stomach neoplasms; Precancerous condition

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He LJ, Wu M. Distribution of esophageal and cardiac carcinoma and precancerous of 2238. *World J Gastroenterol* 1998; 4(Suppl2): 125 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/125.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.125>

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Human cytomegalovirus infection in rat alimentary canal

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Abstract

AIM: We investigated the role of infection by HCMV AD169 strain in gastroenteropathy.

METHODS: Forty rats were divided into three groups at random: twenty of viral inoculation, ten of inactive virus control, ten of normal control. HCMV AD169 strain was injected into caudal venous as 104TCID₅₀. Animals were killed and dissected in 50 d. Their gastric, enteric and hepatic tissues were observed by pathological methods and HCMV antigen was detected by immunohistochemistry *in situ*. Virus extracted from liver were recovered in HEL, then pathogenic cell was manifested by electron microscope and its supernate was

determined by ELISA for HCMV antigen.

RESULTS: The tissues from two groups of control animals were normal. Seven of viral inoculated animals died and pathological alternatives were observed that focal gastroenteric mucous membrane degenerated and necrosed, even deeper into smooth muscle layer and lymphocytes infiltrated around the focus, hepatomegaly or hepatatrophy with hyperemia, hemorrhage and necrosis, compensational hyperplasia emerged round the focus. HCMV located in gastroenteric mucous membrane cell, hepatocyte, cholangiolar epithelial cell. Virus extracted from rats died of inoculation was recovered in HEL. Cytopathic effects appeared in 12 d, groups of viral particulates were found in nucleus of pathogenic hepatocyte by electron microscope and HCMV antigen was determined from its supernate by ELISA.

CONCLUSION: HCMV can infect gastroenteric mucous membrane cell and hepatocyte with serious pathological damage exhibited as degeneration, necrosis and lymphocyte infiltration.

Key words: Cytomegalovirus infection; Gastric mucosa/pathology; Intestinal mucosa/pathology

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Meng H, Wang J, Liu JH, Shi YY, Liu HB, Wu HL, Guo JL. HCMV infection in rat alimentary canal. *World J Gastroenterol* 1998; 4(Suppl2): 126 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/126.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.126>

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Analysis on clinical features of hepatic encephalopathy of 108 cases

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Abstract

AIM: We reviewed and analysed clinical features of hepatic encephalopathy of 108 cases.

METHODS: One hundred and eight patients in this group were confirmed diagnosis as hepatic encephalopathy with 83 male, 25 female, age range of 16-81 years old and hepatocirrhosis course of 2-11 years. Of them 87 cases (80.6 %) were hepatocirrhosis resulted from hepatitis, 17 cases (15.7%) were alcoholic cirrhosis and 4 cases (3.7%) were congestive cirrhosis. 16 cases of all patients were performed splenectomy before. Of disease causes inducing hepatic encephalopathy infection was in the first place, accounting for 46.7%, hemorrhage of upper digestive tract was the second, accounting for 24.1% and the others were azotemia high-protein diet

letting our ascites and so on.

RESULTS: This paper indicates that the mortality of hepatocirrhosis resulted from hepatitis is 94.3%, that of alcoholic cirrhosis is 35.3%, and after comparing the mortalities of the two groups and processing the data statistically, we find the difference is very significant, $P < 0.01$, which indicates that because of different encephalopathy are different, so we should concentrate our efforts on treatment.

The main predisposing cause of hepatic encephalopathy in this group is infection, but data from home and abroad indicate that it is hemorrhage of upper digestive tract. We think that this can be related to the measures of lowering portal venous pressure, protecting gastric mucosa, supplementing Vitamin K at the early stage and increasing the concentration of plasma albumin and so on. The true cause remains to be studied further.

CONCLUSION: There is no specific treatments for hepatic encephalopathy so far and its mortality is very high, so the prevention is very important. It is the best way out to avoid all predisposing causes, keep close watch over patient's condition confirm diagnoses at the early stage and treat patients efficiently without delay.

Key words: Hepatic encephalopathy/diagnosis; Hepatic encephalopathy/therapy; Liver cirrhosis/complications; Hepatitis/Complications

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Gu SQ, Li LY, Li Z, He D. Analysis on clinical features of hepatic encephalopathy of 108 cases. *World J Gastroenterol* 1998; 4(Suppl2): 127 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/127.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.127>

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Clinical analysis of 36 cases of hepatopulmonary syndrome

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Abstract

AIM: To analyse the causes and pathogenesis of Hepatopulmonary Syndrome (HPS) in patients with liver cirrhosis.

METHODS: Femoral artery blood samples of 102 cases with liver cirrhosis were taken right after their admission to the hospital to detect the PaO₂ and SaO₂.

RESULTS: PaO₂ and SaO₂ in patients with HPS were markedly lower than that without HPS ($P < 0.01$); PaO₂ and SaO₂ in patients with a liver function of child C were markedly lower than that of child A

($P < 0.01$); HPS incidence in patients with liver function of child C was markedly higher than that with child A ($P < 0.01$); The average PaO₂ and SaO₂ in patients with pylephlebotasis (> 1.4 in diameter) were markedly lower than that without pylephlebotasis ($P < 0.01$); HPS incidence in patients with pylephlebotasis was markedly higher than that without pylephlebotasis ($P < 0.001$); PaO₂ and SaO₂ in patients with cutaneous spider nevi were markedly lower than that without cutaneous spider nevi ($P < 0.05$); HPS incidence in patients with cutaneous spider nevi was markedly higher than that without cutaneous spider nevi ($P < 0.001$).

CONCLUSION: HPS might occur in any stage of patients with liver cirrhosis. The more severely the liver function was damaged, the more chances there were to suffer from HPS, and the more severe the symptoms would be.

Key words: Liver cirrhosis; Lung diseases/physiopathology; Lung diseases/diagnosis; Syndrome

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Wei H, Wang YX. Clinical analysis of 36 cases of hepatopulmonary syndrome. *World J Gastroenterol* 1998; 4(Suppl2): 128 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/128.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.128>

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Poorly differentiated gastric neoplasm immunohistochemical analysis and significance

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Abstract

AIM: To distinguish poorly differentiated epithelial from none
epithelial gastric neoplasm of using a group of antibodies.

METHODS: Appropriate, special immunohistochemical chief
antibody were chosen including cytokeratin (broad-spectrum CK),
LCA (CD45), Vimentin, CEA and NSE. Forty-three cases of poorly
differentiated neoplasm were analyzed by immunohistochemically

assay under microscope.

RESULTS: Thirty-nine (90%) of 43 cases of poorly differentiated
gastric neoplasm were CK positive, 2 (5%) LCA (CD45) positive,
1(2%) Vimentin positive 2%, 31 (72%) CEA positive, 16 (57%) NSE
positive (1 case had No cell > 50 %).

CONCLUSION: It is most efficacious to choose a group of
appropriat sensitive immunohistochemical antibodies to distinguish
epithelial from nonepithelial ingredient of gastric neoplasm. Its
operation is very simple, and specificity is high which can de widely
used in pathologic diagnosis.

Key words: Stomach neoplasms/pathology; Stomach neoplasms/
diagnosis; Immunohistochemistry

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Relation between HBsAg/IgM circulating immune complex and hepatic injury

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Abstract

AIM: To observe the relation between HBsAg/IgM circulating immune complex (CIC) and hepatic injury.

METHODS: Serum HBsAg/IgM CIC were measured by capture-ELISA, Alanine aminotransferase (ALT) were detected in 31 symptomless subjects with HBsAg-positive, 60 patients with acute Hepatitis B, 78 with chronic active Hepatitis B, 18 with severe Hepatitis B, 49 with hepatic cirrhosis caused by Hepatitis B respectively.

RESULTS: The results showed that the positive rates of HBsAg/IgM CIC in various Hepatitis B were arranged from high to low in order

of hepatic cirrhosis > severe Hepatitis > chronic Hepatitis > acute Hepatitis > symptomless HBsAg positive subjects. Among 236 cases with various Hepatitis B, 132 cases had abnormal level ALT and the HBsAg/IgM CIC positive rate was 50.0% (66/132), and 104 cases with normal ALT, the HBsAg/IgM CIC positive rate was 32.7% (24/104). There was significant difference between the two groups ($P < 0.01$). Based on clinical type, the positive rates of HBsAg/IgM CIC were 3.2% (1/31) in 31 symptomless HBsAg-positive persons; 33.3% (4/12) in patients with acute hepatitis and normal ALT, 37.5% (18/48) in patients with acute hepatitis and abnormal ALT ($P > 0.05$); 43.8% (14/32) in patients with chronic-hepatitis and normal ALT, 50.0% (23/46) in chronic-hepatitis and abnormal ALT ($P > 0.05$), 16.7% (1/6) in patients with severe-hepatitis and normal ALT, 75.0% (9/12) in patients with severe hepatitis with abnormal ALT ($P < 0.05$); 60.9% (14/23) in patients with hepatic cirrhosis and normal ALT, 61.5% (16/26) in patients with hepatic cirrhosis and abnormal ALT ($P > 0.05$) respectively.

CONCLUSION: The positive rates of HBsAg/IgM CIC are closely related to hepatic injury.

Key words: Hepatitis B; IgM; Antigen-antibody complex; Hepatitis B; Hepatitis B surface antigens

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Exploration on treatment of chronic superficial gastritis and gastric precancerosis with integrated Chinese and Western medicine

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Abstract

AIM: Gentamicin and Bi agent (trilogy) were used to eradicate Hp, KANGWEIHUAATANG of Chinese traditional Medication was used to enhance physiological function of gastric mucosa, to improve gastric mucosal circulation, to reinforce blood flow and to make atrophied intestinal metaplastic cell reversion. They stop developing from gastric precancerosis to gastric carcinoma.

METHODS: Fifty gastritis patients with Hp(+), intestinal metaplasia and partial atrophy were confirmed diagnosis by gastroscopy and pathological bacteriology examination. They were treated with amoxioillin 0.75 g three times every day; gentamicin 80000 unit three times every day; Lizhuchangle diluent 110 mg four times every day. Continuous 3 wk is a course of treatment. Kang wei hua tang of Chinese traditional medication were made by the author himself (*radix codonopsis*, *radix astragali*, *herba-taraxaci*, *rhizoma pinelliae*, *aspongopus*, *rhizoma corydalis*, *fructus amomi*, *radix cynanchi paniculati*, *lasiophaera seu calvatia*, *herba hedyotis diffusae*). A dosage was divided in to two times to be decocted and taken orally

every day, 250 cc-300 cc every time. Continuous 4 wk is a course of treatment. Reexamination was undergone after a month of the end of treatment.

RESULTS: Fifty cases with Hp(+) concomitant intestinal metaplasia and sixteen cases with partial atrophy gastritis have been reexamined after all courses of treatment. There were forty-three cases with Hp reversing negation and twenty-six cases with disappearance of treatment intestinal metaplasia, among which there were sixteen cases with intestinal metaplasia linking atrophy, atrophy disappear in fifteen cases.

CONCLUSION: Trilogy therapy was employed to eradicate Hp, Chinese traditional medicine kang wei hua tang blocked the development from gastric precancer to gastric carcinoma, and promoted the reversion of gastric precancer. In fifty cases treated, elimination rate of Hp was 86%, elimination rate of intestinal metaplasia was 52%, among which there were sixteen cases of intestinal metaplasia linking atrophy, fifteen cases of them showed disappearance of atrophy, cure rate 94%. It demonstrated certain effect that trilogy therapy combined with Chinese traditional medicine kang wei hua tang treated gastritis and pre-cancerous lesion, and demands further investigation.

Key words: Gastritis/therapy; Stomach neoplasms/therapy; Drugs, chinese herbal; CTM-WM therapy

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Study of histopathological typing of chronic atrophic gastritis

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Abstract

AIM: One hundred and eighty-four cases of chronic atrophic gastritis (CAG) with gastric mucosa biopsy specimen have been studied. Documents that put forward the criterion of the diagnosis of the CAG have been consulted. According to the degree of glandular atrophy, hyperplasia, expansion, metaplasia and epithelial dysplasia, the nature and amount of mucus, and the number of inflammatory invasive cells, CAG can be divided into four type: the simple types, the hyperplasia type, the metaplasia type and the dysplasia type.

METHODS: Of the 184 CGA cases 113 were male and 71 female. They were divided into five age-groups: (a) ≤ 40 , 40, 41-50, 51-60, 61-70, ≥ 71 . Tissues were fixed in 10% neutral buffered formalin, routinely processed through serial concentrations of ethanol and embedded in paraffin.

RESULTS: The simple type: glandular atrophy shows that in the mild cases atrophy formed 1/3 of the intrinsic glands and in severe cases atrophy formed 2/3 of the intrinsic glands. The size of the gland becomes smaller and its number becomes less and hyperplasia of epithelial cells in mild. There is a tiny simple glandular expansion but no metaplasia can be seen. The invasion of chronic inflammatory cells may be either mild or severe. There is no apparent change in the nature of the mucus but there is a decrease of the neutral mucus. The hyperplasia type: glandular atrophy accompanies glandular hyperplasia. Intrinsic gland displays a glandular concentration. No gland of metaplasia and dysplasia can be seen. The invasion of chronic inflammatory cells may be either mild or severe. There is no change in the nature of mucus, Neutral mucus decreases in atrophic glands but increases in hyperplasia glands. The metaplasia type: the outstanding characteristics of this

type is metaplasia (including intestinal metaplasia, colonal metaplasia and pseudopyloric metaplasia) except meagre mucosa and glandular atrophy. It may or may not be accompanied with epithelial dysplasia. The invasion of chronic inflammatory cells may be mild or severe. The nature of mucus may be changed to mucus of salivary acid and/or mucus of sulphuric acid, and there is a reduction in neutral mucus. The dysplasia type: mucosa meagre and glandular atrophy become severe. More than 2/3 of the intrinsic glands become glandular atrophy. The glandular atrophy forms compensatory hyperplasia and the back-back or the common wall, Dysplastic glandular hyperplasia and dysplastic glandular expansion usually appear, Cystic glandular or adenomatous dysplasia mentioned in our former study also appears. There is a heavy invasion of inflammatory cells and most of them are lymphocytes. The nature of mucus may be salivary acid and/or sulphuric acid, with reduced neutral mucus. It may be accompanied by mild metaplasia.

CONCLUSION: The results indicate that the rate of CAG malignant change depends mainly on the change of histopathology. Most cases of the simple type affect people over sixty. It is comparatively stable in morphology and may be regarded as a degeneration with age in inflammatory changes. It is only a change in quantity in regard to glandular atrophy, diminished function and reduction of mucus secretion. The majority of the hyperplasia type are people at forty to sixty years old. The pathological changes are mainly a change in quantity. Relief of symptoms or cure can be achieved after aggressive treatment. The metaplasia type increases with age, especially among those who are over 70 years old. The mucus secretion has not only quantitative changes but also qualitative changes. A long-term follow-up may be conducted due to its dissipative difficulty and tendency of aggravation in pathological change. CAG of the dysplasia type is mostly developed from the other types mentioned above. Glandular atrophy forms compensatory hyperplasia and dysplasia. There is a light positive reaction on the monoclonal antibodies of gastric cancer. A close follow-up should be conducted because its rate of malignant change is 5.6%.

Key words: Gastritis, atrophic/pathology; Gastritis, a trophic/diagnosis; Gastric mucosa/pathology; Chronic diseases

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Effect of jianpiyiwei capsule on gastric secretory function, mucosal hexosamines and malonic dialdehyde concentrations in chronic atrophic gastritis in rats

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Abstract

AIM: To study the therapeutic mechanism of Jianpiyiwei capsule (JPYW) on chronic atrophic gastritis (CAG) in rats.

METHODS: The model of CAG was established in male wistar rats by synthetical method: a metallic spring was inserted into gastric pylorus sphincter. I week after operation, 50-60 °C hot paste which contains 15% NaCl were given twice a week orally for 15 wk, then 10 normal and 11 CAG model rats were killed and sampled to study: (1) The volume of gastric juice, (2) Gastric acidity and total output of gastric acid, (3) Activity of pepsin and its total output, (4) Mucosal hexosamines and malonic dialdehyde (MDA) concentrations. The other CAG rats were treated with JPYW 1.5 g/kg/d or 4.5 g/kg/d, weimeisu (WMS) 0.6 g/kg/d, or distilled water (DW) respectively ($n = 10$ each group). After 12 wk, all the rats were killed and detected as above.

RESULTS: The volume and acidity of gastric juice, activity of pepsin,

total output of acid and pepsin, mucosal hexosamines and MDA concentrations were 1.17 ± 0.29 mL/2h, 48.54 ± 16.95 mEq/L, 0.519 ± 0.115 unit/mL, 27.63 ± 8.07 μ Eq/h, 0.291 ± 0.058 unit/h, 4.82 ± 0.74 μ g/mg, tissue and 37.41 ± 4.91 μ mol/100mg, tissue in model group whereas 2.08 ± 0.19 , 96.80 ± 18.20 , 0.843 ± 0.143 , 100.11 ± 17.63 , 0.873 ± 0.139 , 6.85 ± 1.14 and 24.90 ± 2.48 in normal group, which were significantly different ($P < 0.01$). After 12 wk treatment, JPYW increased the volume and acidity of gastric juice, activity of pepsin, total output of acid and pepsin significantly (2.12 ± 0.86 , 96.10 ± 30.91 , 0.780 ± 0.168 , 95.84 ± 31.05 , and 0.779 ± 0.169 respectively in 4.5 g/kg group) as compared with DW group (1.37 ± 0.51 , 50.20 ± 16.47 , 0.515 ± 0.142 , 32.89 ± 11.73 and 0.327 ± 0.082 respectively) ($P < 0.05$ or $P < 0.01$). Furthermore, it decreased mucosal MDA concentration obviously (27.09 ± 3.98 in 4.5 g/kg group and 41.87 ± 4.27 in DW group) ($P < 0.01$). Although the hexosamines concentration was increased mildly (5.62 ± 0.93 in 4.5 g/kg group), it made no statistical difference to DW group (4.90 ± 0.84) ($P > 0.05$). WMS also had influence on above-mentioned indices, but was not as marked as JPYW 4.5 g/kg/d group, especially in total output of acid (56.54 ± 12.25) and pepsin (0.585 ± 0.100) and mucosal MDA concentration (31.43 ± 5.02) (comparing to 4.5 g/kg group, $P < 0.05$ or $P < 0.01$).

CONCLUSION: Improving the secretory function of gastric juice and preventing gastric mucosa from the injury of free radical may be one of the therapeutic mechanism of JPYW on chronic atrophic gastritis.

Key words: Gastritis, atrophic/therapy; Jianpiyiwei capsule; Hexosamines; Malonic dialdehyde; Disease models, animal

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Frequent inactivation of *p16* and *p15* expression in human esophageal squamous cell carcinoma detected by RT-PCR

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Abstract

AIM: The cyclin-dependent kinase inhibitors *p16* and *p15* play important roles in the regulation of the cell cycle, and have been found to have tumor suppressor roles in a variety types of cancer. It has been shown that *p16* aberrant methylation and *p15* homozygous deletions were frequently involved in human esophageal squamous cell carcinoma (ESCC). The present study was to examine the impact of such molecular alterations on the expression of these genes.

METHODS: The mRNA level of both genes was measured in 21 frozen ESCC specimens using semi-quantitative RT-PCR.

RESULTS: Nineteen cases were observed at a low basal level

of *p16* expression (0.11 ± 0.07 , expression units normalized by housekeeping glyceraldehyde-3-phosphate dehydrogenase gene as internal standard) in the normal epithelia adjacent to the cancer tissue. Among the 19 cases, only 5 showed a significant elevation of *p16* expression (> 3.2 folds) in the tumor, whereas the remaining 14 showed either a slight increase (1-2 folds), or decreased *p16* expression compared to normal, whereas 11 had only a slight increase (1-2 folds) or a decrease in tumor. In the 5 cases where *p15* was already activated (> 0.5) in the adjacent normal epithelium, 4 of them had similar or a slightly lower expression level, but one had a great decrease in *p15* expression ($< 1\%$ of the normal level). For intact *p16* and *p15* genes, which encode cell cycle regulators, significant increase of their expression is expected in the cancer cells as a response to accelerated cellular proliferation. However, in our samples, significant activation was only seen in 7 cases for *p16* gene and 9 cases for *p15* gene. Fourteen cases for *p16* (70%) and 12 cases (57%) for *p15* either maintained low basal levels or had decreased expression levels in tumor, respectively, which indicate suppression or inactivation of the genes. No correlation between *p16* and *p15* expression was observed in our frozen samples.

CONCLUSION: The present findings indicate that distinct and independent mechanisms are involved in the inactivation of *p15* and *p16* genes in ESCC.

Key words: Esophageal neoplasms; Carcinoma, squamous cell; *p16* gene; *p15* gene; Gene expression

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Multiplex PCR-SSCP: A highly effective and efficient method of mutation detection and analysis

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Abstract

AIM: The method of PCR-SSCP we used previously for P53 mutation detection could only analyze one exon at a time. In addition, DNA extraction from microdissection samples is tedious and produces small amounts of DNA for analysis. To increase the efficiency of mutation detection and analysis while conserving the amount of DNA used, multiplex PCR, to amplify four exons simultaneously, and applied to human esophageal cancer samples for P53 mutation detection in this study.

METHODS: Multiplex PCR involves three successive PCR amplifications: (1) two sequence-specific primers are used, one containing a universal tail at its 5'-end, (2) the universal tail from the first round and another nested sequence-specific primers containing another universal tail at its 5'-end are used, (3) the two

distinct universal tails from the first and second rounds are used. We analyzed exons 5 to 8 of the *p53* gene in 8 paraffin-embed dedhuman esophageal squamous cell carcinoma specimens from Linzhou (Linxian, originally), Henan, China. Several different running and labeling conditions were tried in the multiplex PCR-SSCP to determine the most efficient and the highest mutation-detecting conditions. Direct sequencing was followed to get sequence of shift bands in four exons.

RESULTS: After numerous trials, it was demonstrated that internal labeling of primers and a running condition of 50 watts for 4-5 h produced the most reliable and reproducible results. From the 8 samples analyzed, 4 out of 8 (50%) possessed shift bands, with 3 out of these 4 (75%) having multiple shift bands, amounting to a total of 9 shift bands overall. This mutation rate of 50% is consistent with published results. Sequencing analysis revealed 7 confirmed mutations, while 2 bands have been confirmed as garbage bands. The multiple P53 mutations at different exons detected in a single sample demonstrate the benefits of multiplex PCR-SSCP.

CONCLUSION: Our result suggest that multiplex PCR-SSCP is a highly effective and efficient method of mutation detection and analysis and that internal labeling of primers and a running condition of 50 watts for 4.5 h produced the most reliable and reproducible results.

Key words: Esophageal neoplasms; *p53* gene; Mutation; DNA; Polymerase chain reaction

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***p53* immunostaining positive cells correlated positively with S phase cells as measured by BrdU in the esophageal precancerous lesions from the subjects at high incidence area for esophageal cancer in northern China**

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Abstract

AIM: To characterize the S phase cell distribution as measured by BrdU in esophageal precancerous lesions and to correlate the changes of *p53* protein accumulation with S phase cell proliferation for further understanding the mechanism of *p53* protein accumulation in esophageal carcinogenesis.

METHODS: One hundred and nine symptom free subjects from Henan were examined with endoscopy and histopathologically. The biopsies from the esophagi were incubated with BrdU for 1 h and then fixed with 85% ethanol, embedded in paraffin and cut at 5 μ m for H&E staining and immunohistochemistry (ABC). Quantitative analysis was performed by recording the positive immunostaining cells for *p53* and BrdU per mm² of the tissue section.

RESULTS: Histopathologically, 53 subjects were found with normal esophageal epithelia, 46 with basal cell hyperplasia and 10 with dysplasia. In tense nuclear immunostaining for *p53* and BrdU was observed in the normal and different severity of esophageal lesions. Quantitative analysis showed that the positive immunostaining cells for *p53* was low in normal (70 ± 31 , mean $\pm s$), and increased in basal cell hyperplasia (91 ± 82 , mean $\pm s$), and dramatically increased in dysplasia (402 ± 48 , mean $\pm s$) ($P < 0.05$). On the other hand, BrdU positive cell number increased with disease progressing and was a little lower than that of *p53* in normal and basal cell hyperplasia, but much lower in dysplasia (402 vs 98). *p53* immunostaining positive cells correlated positively with S phase cells as measured by BrdU with the epithelia progressing from normal to basal cell hyperplasia and to dysplasia ($P < 0.05$).

CONCLUSION: BrdU is a valuable biomarker to measure cell proliferation of esophageal biopsy. *p53* immunostaining positive cells correlated positively with S phase cells as measured by BrdU during the disease progressing, which can be explained by the loss of normal *p53* function due to mutation.

Key words: Esophageal neoplasms; *p53* protein; Precancerous condition; BrdU

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Zhou Q, Wang LD, Gao SS, Li YX, Zhao X, Wang LX. *p53* immunostaining positive cells correlated positively with S phase cells as measured by BrdU in the esophageal precancerous lesions from the subjects at high incidence area for esophageal cancer in northern China. *World J Gastroenterol* 1998; 4(Suppl2): 136 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/136.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.136>

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Expression of hMSH2 in human esophageal cancer from patients in a high incidence area in Henan, China

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Abstract

AIM: DNA repair enzymes are important in maintaining genomic stability by limiting the rate of mutation. The genetic alteration of mismatch repair genes (*e.g.*, hMSH2) has been identified in association with the development of hereditary nonpolyposis colorectal cancer. The present study was undertaken to investigate a possible role of hMSH2 alteration in causing esophageal cancer in a high-risk population from Henan, China.

METHODS: Twenty-two cases of human esophageal squamous cell carcinoma from a high incidence area for esophageal cancer in Henan were analyzed immunohistochemically (ABC) for the expression hMSH2 repair enzyme.

RESULTS: The hMSH2 protein was detected in all 22 esophageal

cancers and non-cancerous squamous epithelia. The hMSH2-positive cancer cells were mainly distributed in the peripheral cell layers of the well-differentiated cancer nests. In carcinoma *in situ* and poorly differentiated cancers, more than 90% of cancer cells showed positive immunostaining for hMSH2. Positive immunostaining was detected throughout the proliferation compartments of basal cell hyperplasia and dysplasia lesions. In the morphologically-normal squamous cell epithelia, hMSH2-positive cells were mainly located in the parabasal cell layers, while only "scattered" positive cells were observed in the basal cell layer. The staining intensity remained constant from the cancers to the non-cancerous epithelia. The hMSH2 immunostaining patterns coincided with those observed for the proliferation cell nuclear antigen (PCNA), with the exception that promitotic and mitotic cells lacked hMSH2 immunostaining.

CONCLUSION: The present findings indicate that the occurrence of hMSH2 protein expression is associated with the cell cycles and related to PCNA expression, implying that the hMSH2 protein is expressed as a guardian in DNA-synthesizing cells. Assuming the immunodetected protein is normal hMSH2 enzyme, our results further suggest that hMSH2 alteration is not a frequent event among this high cancer risk population in Henan, China.

Key words: Esophageal neoplasms; hMSH2; Colorectal neoplasms; DNA repair enzymes; Proliferation cell nuclear antigen

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Alteration of *p19* mRNA expression in esophageal cancer tissue from patients at high incidence area in northern China

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Abstract

AIM: The INK4a tumor suppressor gene locus on human chromosome 9 *p21* encodes two unrelated proteins: *p16* INK4a, a specific inhibitor of the cyclin D-dependent kinases CDK4 and CDK6, and *p19ARF*, an alternative reading frame protein which can also induce cell cycle arrest in G1/S and G2/M transition. Inactivation of *p16INK4* is a frequent event in various human tumors; mice lacking *p19ARF* develop tumors early in life. The specific aim for this study was to investigate the possible role of *p19ARF* and its relationship with other tumor suppressor gene *p53* and *p21* in esophageal carcinogenesis.

METHODS: RT-PCR was used to measure the expression of *p19A*

RF, *p53* and *p21* in 19 pairs of frozen normal esophageal and tumor samples. The cycle number for each pair of primers was fine-tuned to limit the amplification to a linear range. PCR products were then resolved on 2% agarose gel. The density and area of each band was measured using image-pro-plus 1.3 software. The relative expression level of each gene in tumor and normal was calculated using the housekeeping gene GAPDH as an internal control.

RESULTS: In the total of 19 tumor samples, 8(42) had at least a 3-fold decrease in *p19ARF* but with no decrease in *p53* expression, 5(26%) had significantly decreased expression of *p53* but had normal expression of *p19ARF*, only two samples (11%) had decreased level in both *p19ARF* and *p53* expression. The results suggest a negative correlation between the alterations of these two genes in the esophageal tumor. The relative expression level of *p21* in *p19ARF* negative sample (0.78 ± 0.16) is about half of that in *p19ARF* positive samples (1.63 ± 0.22).

CONCLUSION: Our results support the hypothesis that *p19* inactivation contributes to esophageal tumor progression and follows the same pathway as *p53* and *p21*.

Key words: Esophageal neoplasms; Chromosome 9 *p19*; *p53* gene; *p21* gene; mRNA

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Blood clot as a DNA source for studying genetic polymorphism of human carcinogen-metabolizing enzymes

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Abstract

AIM: Genetic polymorphism of human carcinogen-metabolizing enzymes such as cytochromes p450 (CYP) and glutathione S-transferases (GST), may cause alterations of enzyme activity and affect an individuals ability to metabolize environmental carcinogens. In cancer epidemiological and interventional studies, serum from cancer patients and non-cancer subjects are often discarded. The present study was undertaken to investigate the possibility of using blood clots as a DNA source for PCR-based genetic polymorphism

analysis on carcinogen- metabolizing enzymes.

METHODS: Twenty blood samples were obtained from healthy subjects in Henan, China. The blood clots were stored in -80 °C prior to use. PCR-based identification was performed in comparison to the use of purified DNA.

RESULTS: The DNA yield from 4 clot samples ranged from 13 to 96 µg/mL clots. Successful polymorphism analysis of CYP2E1 (Pst 1, Rsa 1, and Dra 1), GSTM1, and GSTT1 was demonstrated for all 20 samples examined. The concordance rate of PCR-based identification was 100% for direct use of clot lysate in comparison to the use of purified DNA.

CONCLUSION: We conclude that the blood clot is a valuable DNA source for genetic polymorphism analysis. Concerning with the existing cancer epidemiological studies, this convenient DNA source provides a good opportunity to determine the relationship between genetic polymorphism and cancer susceptibility.

Key words: Cytochromes p450; Glutathione S-transferase; Genetic polymorphism; DNA; Carcinogen metabolizing enzymes

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Detection of angiogenic growth factors in patients with precancerous and cancerous lesions of esophagus from high-risk area in Henan, China

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Abstract

AIM: Angiogenesis, the formation of new blood vessels, is regarded as an indispensable prerequisite for tumor growth. Tumor cells are considered to produce angiogenic factor(s), and in some cases these factors are secreted at high levels to be detected easily in the peripheral blood. Circulating angiogenic and proliferative cytokines may be markers of tumor aggressiveness and of metastatic potential. The present study was undertaken to better understand the impact of angiogenic growth factors in esophageal carcinogenesis.

METHODS: The serum level of vascular endothelial growth factor

(VEGF), basic fibroblast growth factor (FGF2), Interleukin-6 (IL-6) and HER-2 was determined with Elisa method. The blood samples were obtained from 263 cases with normal esophagus, 93 with basal cell hyperplasia, 19 with dysplasia and 103 with esophageal cancer.

RESULTS: VEGF, FGF2, and IL-6 were detected in 74.1%, 19.4% and 12.2% of normal subjects compared with 96.1% ($P < 0.01$), 94.6% ($P < 0.01$), and 86.5% ($P < 0.01$) of cancer patients. Though the mean VEGF values was lower in the cancer patients (234 vs 156 pg/mL, $P < 0.01$), the mean FGF2 and IL-6 were higher in cancer patients (12 and 60 pg/mL vs 7 and 3 pg/mL, $P < 0.01$ respectively). HER-2 was frequently detectable in the sera of cancer patients (98% normal vs 67.5% cancer, $P < 0.01$) but the average levels were similar (38.5 vs 34.0 Hne/mL). Patients with dysplastic and hyperplastic esophageal lesions had normal or low levels of all angiogenesis peptides.

CONCLUSION: The present findings suggest that serum FGF2 and IL-6 detectability may serve as a marker of esophageal carcinogenesis.

Key words: Esophageal neoplasms; Angiogenic growth factors; Precancerous condition

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Yue WB, Wang LD, Ding I. Detection of angiogenic growth factors in patients with precancerous and cancerous lesions of esophagus from high-risk area in Henan, China. *World J Gastroenterol* 1998; 4(Suppl2): 140 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/140.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.140>

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Relation between *p16* expression and biological behavior of gastric carcinoma

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Abstract

AIM: To discuss the relationship between *p16* expression and biological behavior of gastric carcinoma.

METHODS: Immunohistochemical methods were used in this study to detect *p16* expression of gastric carcinoma and normal gastric tissues.

RESULTS: The expression levels of P16 protein in normal gastric tissue and gastric carcinoma were separately 100.0% (12/12) and 39.2% (20/51). There was significant difference ($P < 0.001$). The positive rate of P16 protein expression was not related to the differentiation and the cancerous infiltration degree of gastric carcinoma ($P > 0.05$). In the cases with or without lymphnode metastasis, the positive rate of p16 protein was 25.8% (8/31) and 60.0% (12/20), there was significant difference ($P < 0.00$).

CONCLUSION: The defect expression of P16 protein was correlated with occurrence and lymphnode metastasis of gastric carcinoma. Determination of P16 Protein expression may be useful in diagnosis and predicting prognosis of gastric carcinoma.

Key words: Stomach neoplasms; *p16* gene; Lymphatic metastasis; Immunohistochemistry

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Zhang L, Fu HM, Jin SZ, Zhou CG. Relation between *p16* expression and biological behavior of gastric carcinoma. *World J Gastroenterol* 1998; 4(Suppl2): 141 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/141.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.141>

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Experimental and clinical study on interventional therapy with sclerotic complex agents for hepatic cysts

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Abstract

AIM: To study the action of sclerotic complex agents (SCA) on the gallbladder wall of hybrid rabbits and its therapeutic effect in hepatic cysts.

METHODS: The SCA combined with tetracycline and dexamethasone was injected into the gallbladder of rabbits and its action on the gallbladder wall was compared with normal saline and absolute ethylalcohol. The therapeutic effects of SCA and absolute ethylalcohol in hepatic cysts were observed.

RESULTS: There was no abnormal change in the tissue of gallbladder in normal saline group. But in absolute ethylalcohol

group, a large amount of oozing liquid and blood appeared, the absorption process was slow, and the fibrous tissue had scarce proliferation. In SCA group, there was less oozing liquid, no blood in the gallbladder and the absorption was active, fibrous tissue grew obviously. In clinical practice SCA possesses much advantage in the treatment of hepatic cysts, by which the cysts closed quickly, the exudates reduced from early stimulation, and no relapse occurred. The third, sixth, twelfth and twenty-fourth mo cure rate were 58.5%, 92.5%, 96.2%, 98.1%; but in the control group were 3.6%, 33.9%, 66.1% and 85.7%, respectively. The difference was significance ($P < 0.05-0.01$). After twenty-four month no relapse occurred in the SCA group, but 5 cases relapsed in control group ($P < 0.05$).

CONCLUSION: The sclerotic agents should be used in sequence, *i.e.* a high concentration was administered to reduce and destroy the epithelium of the cysts and to promote fibrous tissue proliferation and then the remaining drug was to stimulate epithelium to absorb the exudates. SCA was proved to be an ideal and effective method for treating hepatic cysts clinically.

Key words: Liver diseases/therapy; Cysts/therapy; Sclerotic agent/therapeutic effect

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An SZ, Yao XX, Cui DL. Experimental and clinical study on interventional therapy with sclerotic complex agents for hepatic cysts. *World J Gastroenterol* 1998; 4(Suppl2): 142 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/142.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.142>

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Novel cDNA fragment associated with gastric cancer drug resistance was screened out from a library by monoclonal antibody MGr1

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Abstract

AIM: To prepare gastric cancer MDR associated monoclonal antibody MGr1, and to screen tumor drug resistance cell epitope library with MGr1, the refer to obtain novel cDNA fragment associated with tumor MDR.

METHODS: By hybridoma technique, gastric cancer MDR associated monoclonal antibody MGr1 was prepared using gastric cancer MDR cell strain SGC79 01/VCR as immunogen. Tumor drug resistance cell epitope library was screened and rescreened by using MGr1 as a probe. The cDNA fragment brought by the positive recombinant was sequenced forward and backward, then, homology analysis was undertaken within GenBank. *In situ* hybridization and Northern blot determined the expressing level of positive cDNA fragment in several types of tissues and cells.

RESULTS: 26 clones of hybridoma whose supernatant had the ability to bind SGC7901/VCR were obtained from 3268 clones after 21 times cell fusing. And one monoclonal antibody of interest, which was named MGr1, was selected out by immunohistochemistry and

MDR reversal test of monoclonal antibody. The staining results showed that MGr1 stained much more on SGC7901/VCR than on SGC79 01. MGr1 could enhance the cytotoxicity of 5-Fu and ADR on SGC7901/VCR. And was tern blot showed that the M_r of MGr1 was about 80000-110000, which could not be recognized by Pgp or MRP antibody. Therefor MGr1 could be regarded as gastric cancer MDR associated monoclonal antibody. About library screening, five bacterial clones showed having affinity to MGr1, and one clone ws confirmed to bring the positive recombinant after being screened repeatedly. The cDNA fragment brought by the positive recombinant, which was named MGr1-Ag, had 310 bp and showed no homology with other genes in GeneBank. Results of *in situ* hybridization suggested that, the normal tissues of liver, esophagus, stomach, colon did not express the MGr1-Ag. Results of Northern blot suggested that the Mgr1-Ag was expressed in SGC7901, SGC7901/VCR, EC109 and HCC7402. The expressing level of MGr1-Ag was very high in SGC7901/VCR, but low in EC109 and eve n low in SGC7901 and HCC7402.

CONCLUSION: Gastric cancer MDR associated monoclonal antibody MGr1 was successfully prepared; A novel cDNA fragment associated with gastric cancer MDR, MGr1-Ag, was obtained by screening tumor drug resistance cell epitope library with MGr1.

Key words: Stomach neoplasms; Autibody, monoclonal; Multidrugs resistance; Gene library

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Fan DM, Xiao B, Shi YQ, Ming-Feng, Qiao TD, Chen BJ, Chen Z. Novel cDNA fragment associated with gastric cancer drug resistance was screened out from a library by monoclonal antibody MGr1. *World J Gastroenterol* 1998; 4(Suppl2): 143 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v4/iSuppl2/143.htm> DOI: <http://dx.doi.org/10.3748/wjg.v4.iSuppl2.143>

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Gastric cancer screening in 16 villages of Zhuanghe region: AS high risk area of stomach cancer in China

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Abstract

AIM: To accomplish the comprehensive prevention for high risk population of stomach cancer, a gastroduodenal screening was carried out in 16 villages of Zhuanghe region, a high risk area of stomach cancer in China.

METHODS: The screened subjects were those aged over 35 years with family histories of stomach cancer. The methods include clinical

epidemiology investigation, double-contrast X-ray, serum associated index analysis, gastroscopic biopsy and histopathologic examinations were adopted in the screening.

RESULTS: Out of the 3303 subjects who were examined, 82% were found with gastric disorders. Thirty-two (1.06%) patients with gastric cancer were detected and 18 (56.25%) were in early stage. Up to now the patients with gastric cancer have already accepted early treatment successively. Aside from gastric cancer, several other gastric lesions were also detected, including dysplasia, metaplasia, atrophic gastritis, superficial gastritis, erosive gastritis, ulcer, etc. All these laid a solid basis for further treatment. The screening also showed that 93.97% local residents consume salted pork and more than 60% gastric mucosa of the local residents indicated *H. pylori* infection.

CONCLUSION: Gastric diseases, *H. pylori* infection and salted pork consumption are very common in Zhuanghe region. These are very dangerous factors for gastric cancer, and comprehensive preventive measures should be taken.

Key words: Stomach neoplasms/epidemiology; Stomach neoplasms/etiology; Mass screening; Risk factors

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Clinical research on Changqing decoction for colonoscopy preparation

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Abstract

AIM: To study a satisfying traditional Chinese remedy for the intestinal tract.

METHODS: 55 healthy male pilots without any digestive symptom or any acute or chronic disease of other systems were divided into two groups at random, 30 of them in the Changqing decoction group and 25 in mannitol group as control. 203 patients were divided into

three groups at random, 86 of them in the Changqing decoction group, 59 in a senna group and 58 in mannitol group as control groups. By colonoscopy, the effects of Changqing decoction, senna and mannitol on the whole large intestinal tract, preparation time, after taking medicines, the first time to pass feces, the frequency of passing stool, and the side-effects were studied.

RESULTS: The cleaning effect of the Changqing decoction is much better than that of senna or mannitol, including in the healthy groups or in the patient groups ($P < 0.01$) and the side effects are less than those in two control group ($P < 0.01$). After taking medicines, there are no significant difference among all groups for the first time and the frequency to pass stool.

CONCLUSION: These findings indicate that the cleaning effect of the Changqing decoction is exact, cheap and has less side effects. It is worthy of further studying and recommending.

Key words: Digestive system diseases; Drugs, Chinese herbal; Colonoscopy

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Screening of *Helicobacter pylori* infection in 16 villages of high risk population of gastric cancer

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Abstract

AIM: To study the status of *Helicobacter pylori* (Hp) infection in Zhuanghe area and to analyse the relationship between gastric diseases, gastric cancer and Hp infection respectively.

METHODS: A total of 3033 people in 16 villages at the high risk area of gastric cancer were screened by X-ray examination and serum pepsinogen determination. Endoscopy and biopsy were further performed in 1779 cases of them. The histologic changes and status of Hp infection were observed by HE and MB staining. PCR method was also used to detect Hp.

RESULTS: The total detection rates of Hp infection were 60.8%. In the group of age 30-59 is the highest; In the male group it was

higher than in the femal group. In the mountainous areas group (64.4%) it was higher than in the coastal areas group (56.7%), and in the group of gastric antrum (36.2%) it was higher than in the group of gastric angles (32.6%) and gastric body (31.2%) ($P < 0.01$). The detection rates of Hp infection in patients with gastric mucosa erosion, gastric ulcer, moderate and severe superficial gastritis and atrophic gastritis was 90.6%, 87.0%, 79.8%, 75.3% respectively, which were higher than that mild superficial gastritis 6.8% ($P < 0.01$). Comparing to that in normal in gastric mucosa (0%), the detection rates in dysplasia (80.0%), and intestinal metaplasia (77.7%) were significantly higher ($P < 0.01$).

CONCLUSION: Hp infection rates in residents of Zhuanghe city was positively related to morbidity of gastric mucosa erosion, gastric ulcer, moderate and severe superficial gastritis, atrophic gastritis and gastric cancer. In Zhuanghe, the incidence of gastric cancer is high and there is high prevalence of Hp infection.

Key words: Stomach neoplasms/epidemiology; Stomach neoplasms/etiology; *Helicobacter* infections; Mass screening

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