
# HONG KONG MEDICAL FORUM '97

26th - 27th July 1997

Hong Kong Convention & Exhibition Centre

## PROGRAMME BOOK


Department of Medicine
The University of Hong Kong
Queen Mary Hospital

## *HONG KONG MEDICAL FORUM*

The Hong Kong Medical Forum is an annual event of the Department of Medicine of the University of Hong Kong at Queen Mary Hospital. It is a weekend postgraduate meeting held in July each year.

The Forum focuses on topics of current interests in the medical field and aims to bring a programme that will be of interest to general practitioners and to physicians who are in specialised care.

Each year distinguished overseas and local speakers are invitied to share with us the latest developments and results in their field of speciality. Participants are welcome to ask questions and share their experiences and knowledge with us during the discussion period.

This year the Forum focuses on gastroenterology, hepatology, neurology and nephrology. There will also be a joint session with the Hong Kong Surgical Forum on Saturday afternoon on the first two topics.

The Organizing Committee welcomes comments and suggestions from participants so we can better plan your future Forums.

## *ORGANIZING COMMITTEE*

| | |
|---|---|
| Chairman : | Prof. Ching-lung Lai |
| Co-chairman : | Prof. Mary Ip |
| Members : | Prof. Shiu-kum Lam |
| | Dr. Daniel T. M. Chan |
| | Dr. Shu-leong Ho |
| | Dr. Raymond T. F. Cheung |
| Co-ordinator : | Miss Denise Yu |

## CONTENT PAGE

# *JOINT MEDICAL / SURGICAL PROGRAMME*
# *26TH JULY 1997, SATURDAY*



| TIME | ACTIVITY | SPEAKER/LOCATION |
|---|---|---|
| **13:00 - 14:00** | **Registration** | Theatre Foyer, 2/F |
| **14:00 - 14:10** | **Opening Ceremony** | Theatre 1, 2/F |
| **14:10 - 15:50** | **Joint Medicine / Surgery Symposium: Gastroenterology & Hepatology**<br>Chairmen: S.T. Fan (H.K.) & S.K. Lam (H.K) | Theatre 1, 2/F |
| 14:10 - 14:30 | Brief Synopsis of Presentation on Klatskin's Tumors | C.A. Pellegrini (U.S.A.) |
| 14:30 - 14:50 | Indications for Liver Transplantation | W.C. Maddrey (U.S.A.) |
| 14:50 - 15:10 | Auxiliary Liver Transplantation for Fulminant Hepatic Failure | J. Belghiti (France) |
| 15:10 - 15:30 | Post-Liver Transplant Medical Complications | W.C. Maddrey (U.S.A.) |
| 15:30 - 15:50 | Discussion / Question Time | |
| **15:50 - 16:20** | **Coffee Break** | **Theatre Foyer, 2/F** |
| **16:20 - 17:00** | **Joint Medicine / Surgery Symposium: Gastroenterology & Hepatology**<br>Chairmen: W.M. Hui (H.K.) & F. Branicki (H.K.) | Theatre 1, 2/F |
| 16:20 - 16:40 | Helicobacter pylori - where do we stand now? | J.J. Misiewicz (U.K.) |
| 16:40 - 17:00 | Helicobacter pylori and Upper Gastrointestinal Surgery | K.M. Chu (H.K.) |
| **17:00 - 18:10** | **Plenary Lectures: Gastroenterology & Hepatology**<br>Chairman: C.L. Lai (H.K.) | Theatre 1, 2/F |
| 17:00 - 17:30 | Guidelines for the Eradication of Helicobactor pylori | J.J. Misiewicz (U.K.) |
| 17:30 - 18:00 | An Update on Viral Hepatitis | W.C. Maddrey (U.S.A.) |
| 18:00 - 18:10 | Discussion / Question Time | |
| **18:10** | **End** | |

# *PROGRAMME*
# *27TH JULY 1997, SUNDAY*

| TIME | ACTIVITY | SPEAKER/LOCATION |
|---|---|---|
| **10:00 - 10:30** | **Registration** | Theatre Foyer, 2/F |
| **10:30 - 11:30** | **Plenary Lectures: Neurology**<br>Chairman: S.L. Ho (H.K.) | Theatre 1, 2/F |
| 10:30 -11:00 | Thrombolysis for Acute Stroke | P.D. Lyden (U.S.A.) |
| 11:00 - 11:30 | Carotid Angioplasty and Stenting for Secordary Stroke Prevention | G.S. Roubin (U.S.A.) |
| **11:30 - 12:30** | **Symposium: Neurology**<br>Chairman: R.T. F. Cheung (H.K.) | Theatre 1, 2/F |
| 11:30 - 11:45 | Angioplasty and Stenting of Extracranial Cerebral Arteries for Prevention of Strokes | D.S.W. Ho (H.K.) |
| 11:45 - 12:00 | Acute Stroke Therapy in Hong Kong | R.T.F. Cheung (H.K.) |
| 12:00 - 12:15 | How to Run a Stroke Code | P.D. Lyden (U.S.A.) |
| 12:15 - 12:30 | Discussion / Question Time | |
| **12:30 - 14:00** | **Lunch Break** | |
| **14:00 - 15:25** | **Plenary Lectures: Nephrology**<br>Chairman: D.T.M. Chan (H.K.) | Theatre 1, 2/F |
| 14:00 - 14:40 | Diabetic Nephropathy: Natural History and Therapeutic Interventions | E.J. Lewis (U.S.A.) |
| 14:40 - 15:20 | Pathogenesis and Therapeutic Interventions in Progressive Renal Diseases | J.A. Breyer (U.S.A.) |
| 15:20 - 15:25 | Discussion / Question Time | |
| **15:25 - 16:30** | **Symposium: Nephrology**<br>Chairmen: W.K. Lo (H.K.) & F.K. Li (H.K.) | Theatre 1, 2/F |
| 15:25 - 15:45 | Management of Severe Lupus Nephritis | D.T.M. Chan (H.K.) |
| 15:45 - 16:05 | Immunotactoid Glomerulopathy | E.J. Lewis (U.S.A.) |
| 16:05 - 16:25 | Renal Transplantation: Local Issues | I.K.P. Cheng (H.K.) |
| 16:25 - 16:30 | Discussion / Question Time | |
| **16:30** | **End** | |

## *SPEAKERS*

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# Brief Synopsis of Presentation on Klatskin's Tumors
# by
# Carlos A. Pellegrini

Klatskin's tumors are usually located near the bifurcation of the hepatic ducts. They are scirrous, sclerotic lesions, usually not bulky and in the majority of patients, they cause a complete obstruction of the bile ducts. The most important characteristic of this tumor is its tendency to be locally invasive, causing liver failure and biliary infection rather than distant metastasis.

The mode of presentation is primarily by obstructive jaundice. The tumor is usually diagnosed by a combination of "painless jaundice", the ultrasonographic appearance of a shrunken or small gall bladder with dilated intrahepatic ducts, and the lack of gallstones or choledocholithiasis. A CT scan and MRI rarely show the lesion; in fact, when the lesion is clearly visible in either one of these modalities it is usually an advanced and unresectable tumor. Ultimately the diagnosis is made by ERCP in most patients in the western world. However, as useful as ERCP is in determining the presence of a proximal obstruction of the bile duct, the most important test is a cholangiographic image of the **proximal** portion of the bile ducts. A transhepatic cholangiogram is usually the only way to obtain this information, although forced injection of contrast through an ERCP may opacify the proximal ducts in some patients. The reason cholangiography of the proximal ducts is so important is that it is the main way to assess the extent of the tumor, and thus, to adequately plan the operation. Angiography can and has been used but it is usually not helpful. For example, patients may show occlusion of an artery or a branch of the portal vein and yet have a resectable tumor or, on the other hand, may have normal arterial and venous anatomy but have an unresectable lesion.

Whenever possible this tumor should be resected; however, the plan for resection differs according to whether palliation or cure is in view. For palliation, i.e., for those in whom the tumor is found at operation to extend into the liver parenchyma further than was thought preoperatively, resection encompasses either a resection of the tumor alone, or a more extensive local "cave" resection with excision of the distal bile ducts, the tumor and the right and left hepatic ducts as high as needed, and a hepatic jejunostomy in a "Kasai" mode.

When the operation's intent is to cure, usually a right or left lobectomy should be performed with **the excision of** the tumor. This allows the surgeon to remove the tumor with a better margin on the side where the tumor extends the most. Since these tumors usually extend above the bifurcation of the portal vein into the caudate lobe, the caudate lobe should be removed in order to assure a resection for cure.

Another form of resection is total hepatectomy with transplantation. Survival curves for patients who this procedure are no different than those who have extensive resection of the tumor with a portion of the liver parenchyma. Since the latter is cheaper and better tolerated and does not require immunosuppression, it is usually the preferred mode of therapy.

Finally, since these lesions are radiosensitive, postoperative, or intraoperative and postoperative radiation therapy has been shown in some trials to enhance survival.

# Indications for Liver Transplantation
# by
# Willis C. Maddrey

Liver transplantation has been performed for almost all chronic end-stage liver diseases as well as for a number of congenital metabolic disorders and for fulminant hepatic failure. As a general guideline, patients with end-stage liver disease in whom there is an estimated life expectancy of one year or less are considered potential candidates. It is most important in deciding on candidacy to establish a diagnosis which is exact insofar as possible and to diligently search for other conditions which may impair the ability of the patient to do well with the transplantation. There has been a general trend toward recommendation of transplantation earlier in the disease process before complications, which in and of themselves are harmful and reduce the likelihood of success.

Major specific indications for liver transplantation in the adult are outlined in the Table. Areas of greatest controversy revolve around transplantation in patients who have hepatocellular carcinoma. In this situation many will proceed to transplantation if there is evidence that the tumor in the liver is small, singular and has shown no evidence of metastasis. There are studies which indicate that patients in whom small hepatocellular carcinomas are found as incidental findings at the time of transplantation do as well as patients in whom no cancer is found. An additional area of some controversy relates to the role for liver transplantation in patients who have alcohol-induced liver disease. Part of the issue relates to the possible recidivism by the patients who have alcohol-induced liver disease. Early concerns regarding these matters led to few patients in whom alcohol was the cause of the liver disease being transplanted. From followup studies, it is apparent that results of liver transplantation in the patient with alcohol-induced liver disease are similar to those in non-alcoholic recipients. Many centers require that the patient demonstrate evidence of abstinence for six months, have a stable home situation, and be enrolled in some acceptable form of treatment for chronic alcoholism.

A third area, in which there is continued controversy, relates to the role of liver transplantation in patients who have chronic hepatitis B infection. Prior to the availability of hyperimmune gammaglobulin, recurrence of hepatitis B was almost universal after liver transplantation often leading to rapid graph rejection. However current results with the use of hyperimmune gammaglobulin are making liver transplantation in patients with chronic B feasible.

**Major Indications for Liver Transplantation in Adults**

- Cholestatic Liver Diseases
  - Primary Biliary Cirrhosis
  - Primary Sclerosing Cholangitis
  - Drug-induced Cholestatic Liver Diseases
- Cirrhosis of Many Courses
  - Hepatitis B
  - Hepatitis C
  - Hepatitis non-A, non-B, non-C (cryptogenic)
  - Autoimmune Hepatitis
  - Alcohol-Induced Liver Disease
- Fulminant Hepatic Failure
  - Viral Hepatitis (A, B, D)
  - Drug/Toxic Etiologies
- Metabolic Diseases
  - Wilson's Disease
  - Alpha-1 Antitrypsin Deficiency
- Hepatic and Biliary Malignancies Confirmed To the Liver
- Rare Conditions: Sarcoidosis, Budd-Chiari

**Table: Patient Selection for Liver Transplantation**

- Accepted Indications for Liver Transplantation
  - Advanced chronic liver disease
  - Fulminant hepatic failure
  - Inherited metabolic liver disease
- Controversial Indications for Liver Transplantation
  - Alcoholic liver disease
  - Chronic hepatitis B
  - Unresectable hepatic malignancy
- No Alternative Form of Therapy Available
- No Absolute Contraindication to Liver Transplantation
- Willingness and Ability to Accept Liver Transplantation and Comply with Follow-up Care

# Auxiliary Liver Transplantation for Fulminant Hepatic Failure

by
Jacques Belghiti

Auxiliary liver transplantation (ALT) theoretically bridges the period of acute liver failure until the native liver (NL) recovers and immunosuppression can be discontinued. However, this attractive concept is burdened by technical problems and by the selection of candidates. We report our experience of ALT with special references to early and long term graft function in a prospective study including all patients who underwent emergency liver transplantation for acute liver failure from April 1993 to October 1995.

Patients: Thirty adults patients aged from 16 to 62 years with acute liver failure were candidates for emergency liver transplantation according to Clichy criteria. Causal disease was drug toxicity (n=10) including paracetamol in 3; hepatitis B (n=6); hepatitis A (n=2) and other (n=12). We decided to perform standard orthotopic liver transplantation (OLT) with total hepatectomy in 18 because of age>60 years (n=3), pre-existing chronic liver disease (n=4), haemodynamic instability (n=4), poor liver graft (n=2) and poor neurological status with immediate risk of cerebral herniation (n=5). Twelve patients underwent ALT using full liver graft in 4, left graft in 5 and right graft in 3. Seven patients died postoperatively including 5 after ALT; in the latter group, among the 4 who received full graft, 3 died of graft compression and vascular thrombosis; other deaths were respectively due to sepsis and severe rejection of ABO incompatible graft. With a follow up ranging from 6 to 36 months among the 7 surviving patients, graft was removed in 2 respectively after 1 and 7 months, immunosuppression was stopped in 3 respectively after 8, 9 and 27 months. Liver biopsy demonstrated the presence of mild fibrosis in 3 respectively after 6 and 9 months. Two patients with fulminant liver failure due to hepatitis B who received ALT and survived demonstrated the absence of hepatitis B infection.

Conclusion: After auxiliary liver transplantation for fulminant hepatitis, there is no predictive value of the extent nor the delay of sufficient regeneration of the native liver. The higher operative risk associated with ALT suggests that this procedure should use partial graft and not be indicated earlier than standard OLT. This procedure should be restricted to patients<50 years without haemodynamic instability and should be performed using good quality ABO compatible graft.

# Post-Liver Transplant Medical Complications
# by
# Willis C. Maddrey

Fortunately the development of effective immunosuppressive drugs has markedly reduced the risk of cellular rejection following liver transplantation. The immunosuppressive regimens vary from center to center with the most frequent choices: prednisone/cyclosporine; prednisone/cyclosporine/azathioprine; prednisone/FK506. Clinical results from these several regimens are similar. FK506 is a more powerful immunosuppressive agent than cyclosporine; however it is more neurotoxic and is associated with a higher incidence of development of diabetes.

It is useful to group medical and surgical complications into categories based on the usual time of appearance:

**Early Complications**
**(3 days to 3 weeks after liver transplantation)**

- Cellular Rejection
- Hepatic Artery Thrombosis
- Portal Vein Thrombosis

**Complications Encountered Between 3 Weeks and 3 Months**

- Biliary Tract Obstruction/Bile Leak upon Choledochal Tube Removal
- Cellular Rejection
- Viral Hepatitis (HBV, HCV, CMV)

**Complications Encountered After 3 Months**

- Hypertension- Drug-Induced (Cyclosporine/FK506)
- Nephrotoxicity - Drug-Induced (Cyclosporine/FK506/Antivirals/Antibiotics/NSAIDS)
- Osteoporosis - exacerbated by prednisone
- Diabetes Mellitus
- Lymphoproliferative Syndromes (B cells) - correlates with intensity of immunosuppression
- Recurrence of Initial Disease (HBV, HCV, PBC (rare); Alcohol-Induced Liver Disease)

**Infections in Liver Transplant Patient Post-Surgery**

**1. First Month**

a. Infections in Recipient Prior to Transplant (eg hepatitis, tuberculosis)
b. Infection Transmitted with Graft (eg hepatitis, HIV, candida)
c. Infection Secondary to Technical Complications (pneumonia, liver abscess, biliary sepsis, around infection)

**2. 1-6 Months**

a. Viral Infection (eg CMV, EB, hepatitis B. hepatitis C)
b. Opportunistic Infections (eg Pneumocystis, Listeria, Nocardia)

**3. Greater than 6 Months**

a. Progressive CMV, EB, hepatitis B. hepatitis C
b. Increase in Community Acquired Infections
c. Opportunistic Infections (especially in patients who have required considerable immunosuppressors, eg Cryptococcus, Listeria, Pneumocystis)

**Reference:** Maddrey, W.C. and Sorrell, M.F.
Transplantation of the Liver. Second Edition
Appleton & Lange, Norwalk, CT
1995

# Helicobacter pylori - Where Do We Stand Now?

by
J.J. Misiewicz

The discovery of Helicobacter pylori (Hp) has profoundly revolutionised our understanding of diseases of the foregut and has opened up new possibilities for treatment and cure. It is now accepted that Hp is one of the commonest infections affecting humans, and the main cause of chronic gastritis, which underlies many of the conditions affecting the stomach and the duodenum. Hp has a world-wide distribution, its prevalence being strongly related to the socio-economic status of the given community. The route of transmission is still uncertain, but faeco-oral. and oro-gastric routes are strong contenders. Hp is acquired mostly in childhood and persists for most of the individual's lifetime, despite marked humoral and tissue immune responses to the organism. Gastric mucosa forms the obligatory habitat for Hp, which resides below the adherent layer of gastric mucus. Strong expression of urease by Hp affects its survival, toxicity and forms a basis for diagnostic tests, Pathogenic (CagA expressing) and non-pathogenic strains of Hp have been characterised - there are a strong asscolations between CagA +ve strains and diseases attributable to Hp, e.g. duodenal (DU) and gastric (GU) ulcer, MALT Iymphoma, atrophic gastritis and gastric cancer.

Hp antral gastritis results in decreased somatostatin release leading to hypergastrinaemia, acid hypersecretion, consequent gastric metaplasia in the duodenal bulb and increased risk of DU. Corpusitis leads to gastric atrophy, hypoacidity and increased risk of GU, or of gastric cancer. All of these changes can be reversed by the eradication of Hp.

The diagnosis of Hp infection can be made using non-invasive serological tests that can be done in the doctors office; these tests are also good for epidemiology, but not for monitoring the results of treatment. The $^{13}C$ urea breath test is the best non-invasive diagnostic modality. Invasive tests need endoscopy and depend on detection of urease activity in a biopsy, on histology, or on culture. The latter provides a gold standard and an opportunity to determine the sensitivity of Hp to antimicrobials.

Eradication of Hp is the aim of treatment and is best achieved with triple therapy, comprising a proton pump inhibitor (PPI) and two of a macrolide, an imidazole or amoxycillin. Eradication incidence approaching 90% on a ITT analysis is attainable. Quadruple therapy (triple + bismuth) is best kept for triple therapy failures. Most estimates of efficacy are based on twice daily dosage given for one week. Treatment failure is caused mainly by microbial resistance (most commonly to metronidazole), or by poor compliance. Various management guidelines have been developed . In general, Hp eradication is strongly recommended For non-NSAID related DU and GU and for MALT Lymphoma. Indications for NSAID-related ulcers, for functional dyspepsia and in the presence of long term PPI treatment for GORD are disputed. The next main treatment advance could be the development of a vaccine for Hp. This would be essential for large scale eradication policies in areas with high incidence of gastric cancer.

# Helicobacter pylori and Upper Gastrointestinal Surgery

by
Kent-man Chu

The discovery of Helicobacter pylori (*H pylori*) by Warren and Marshall in 1983 is one of the most exciting advances in gastroenterology this century. The infection has been linked to acute and chronic gastritis, duodenal and gastric ulcer diseases, gastric adenocarcinoma, and gastric non-Hodgkin's Lymphoma of mucosa-associated lymphoid tissue (MALT).

Before the era of *H pylori*, surgery was the mainstay of therapy for patient with peptic ulcer disease that is resistant to conventional medical therapy. The number of elective and emergency operations for peptic ulcer disease has decreased in the past decade owing to the availability of various potent ulcer healing drugs. Such medications, however, have to be taken continuously to avoid recurrence. Patients with recurrent ulcer disease despite treatment with ulcer healing drugs were used to be candidates for surgery. In the late 80s and early 90s, when *H pylori* was not generally accepted as a cause of peptic ulcer disease, revolution in laparoscopic surgical techniques had stimulated a lot of interest in laparoscopic acid-reduction surgery. Nowadays, eradication of *H pylori* appears to provide a relapse-free outcome and elective surgery is seldom required.

Nonetheless, there remains a definite group of patients with peptic ulcer disease who are indicated for surgery.
In an elective setting for patients who are:

1. *H pylori* negative with recurrent gastric or duodenal ulceration
2. *H pylori* positive with recurrent ulceration who could not tolerate eradication treatment or have multiple failures in eradication treatment
3. *H pylori* negative with recurrent ulceration after previous incomplete acid-reduction surgery (thoracoscopic vagotomy)
4. having stomal ulceration after previous partial gastrectomy (thoracoscopic vagotomy) having pyloric stenosis failing conservative management (laparoscopic vagotomy and gastrojejunostomy).

In an emergency setting for patients with:

1. perforated peptic ulcer
2. bleeding peptic ulcer with failed therapeutic endoscopic intervention.

Our recent study on 143 patients with past history of perforated peptic ulcer revealed that the recurrence of symptoms and ulcer in such patients were significantly related to *H pylori* infection. This finding supports the use of omental patch repair as the sole treatment rather than the additional performance of acid-reduction surgery.

Surgery remains the mainstay of treatment for gastric carcinoma, lymphoma, and stromal tumour. *H pylori* eradication is indicated for patients with low grade gastric MALT lymphoma. Successful *H pylori* eradication could result in 60 to 80% complete tumour regression.

# Guidelines for the Eradication of Helicobacter pylori
## by
## J.J. Misiewicz

Treatment of Helicobacter pylori (Hp) has radically changed the management of many conditions affecting the proximal gastrointestinal tract. Eradication of Hp from the foregut constitutes a cure for Hp associated chronic duodenal ulcer (DU) and chronic benign gastric ulcer (GU). Successful eradication of Hp in the non NSAID associated ulcer is followed by healing of the ulcer crater and reversal of gastric hypersecretion in the DU patient, and by healing of the ulcer and remission of gastritis in the GU patient. Low grade mucosa associated lymphoid tissue lymphoma (MALT) is Hp dependent and eradication of Hp is followed by remission of most tumours.

These major advances in therapy depend on successful eradication of Hp from the foregut. Because of its habitat beneath the adherent mucus layer and rapid development of resistance to antibiotics, treatment of Hp demands the concurrent use of several antimicrobial agents. The complexity of the regimens has led to the development of various national and international guidelines for treatment . The Maastricht guidelines evolved in collaboration between European specialists and primary care physicians recommend one week triple therapy regimens based on twice daily dosage with a PPI combined with a combination of two agents selected from amoxycillin, a macrolide or an imidazole. The choice of macrolide or imidazole is governed by the estimated likelihood of microbial resistance. Quadruple therapy, which adds bismuth to the triple regimen, is probably best reserved for triple therapy failures. Bacterial resistance and poor compliance are the most important factors leading to unsuccessful treatment.

With good compliance and Hp strains that are sensitive to the antimicrobial agents used, one week, PPI - base triple regimens therapies can deliver eradication rates in the region of 80 to 90% after 7 days of treatment.

# An Update on Viral Hepatitis
## by
## Willis C. Maddrey

There are five major viruses (hepatitis A-E) which cause acute hepatitis. Many other viruses including EB, herpes simplex, cytomegalovirus, dengue, and yellow fever also lead to hepatic inflammation. A recently described virus, HGV, is found in many patients who have viral hepatitis; however this agent has not been proven to independently cause hepatitis.

Serologic diagnosis of the specific virus causing hepatitis in an individual patient has simplified exact diagnosis. The natural histories of the illnesses caused by the major viruses differs considerably: Hepatitis B and hepatitis E are transmitted by fecal-oral routes. Both cause acute disease which is usually self-limited. No treatment beyond symptomatic support is indicated. There is an effective vaccine to prevent hepatitis A. A variant of hepatitis A may be present with prolonged cholestasis simulating obstructive jaundice and may require a short course of corticosteroid therapy. Hepatitis E seems more likely to cause fulminant disease and death in pregnant women.

Hepatitis B is a major worldwide health problem. Acute infection leads to chronic hepatitis B infection in >90% of neonates who acquire the disease from an infected mother and in 1-7% of adults who acquire the disease from sexual contact or exposure to infected blood. Chronic hepatitis B is a leading cause of chronic hepatitis, cirrhos is and hepatocellular carcinoma. There are effective vaccines to prevent acquisition of hepatitis B and universal vaccination programs may lead to eradication of hepatitis B. In some patients with chronic hepatitis B. the use of interferon and lamivudine therapies have proven successful in eradicating the virus. Hepatitis D is an RNA virus which is unable to independently replicate and has an absolute requirements for the presence of HBV to cause infection. Hepatitis D is a more serious disease when it occurs as a superinfection in a chronic carrier of HBV than when hepatitis D occurs as a co-infection with HBV. Therefore, prevention of hepatitis B by vaccine also prevents hepatitis D.

Hepatitis C is the leading cause of chronic hepatitis, cirrhosis and hepatocellular carcinoma in the United States. > 75 % of patients who develop acute hepatitis C progress to chronic disease. No vaccine is available. Interferon therapy, supplemented with ribavirin, is proving effective in eradicating HCV in some patients. Treatment response depends on the genotype of hepatitis C, viral load, duration of infection, and presence of cirrhosis.

| | HAV | HBV | HCV | HDV | HEV |
|---|---|---|---|---|---|
| **Genome** | RNA | DNA | ANA | RNA | RNA |
| **Incubation (days)** | 15-45 | 30-180 | 15-150 | 30-180 | 15-60 |
| **Transmission** | Fecal/Oral | Blood<br>Semen/Saliva<br>Maternal-Fetal | Blood | Blood | Fecal/Orai |
| **Serologic Diagnosis** | IgM anti-HAV | HbsAg | Anti-HCV | IgM Anti-HDV | IgM Anti HEV |
| **Progress to Chronic Hepatitis** | No | Yes | Yes | Yes | No |
| **Prevention** | Vaccine | Vaccine Available | None Available | | None |

# Thrombolysis for Acute Stroke
# by
# Patrick D. Lyden

**Learning Objectives**

1. Define and describe 5 types of stroke, including clinical presentation, examination findings, radiographic findings, prognosis and currently available treatment.
2. Understand the ischemic penumbra and its implications for therapeutic intervention.
3. List the major steps in cerebral resuscitation after ischemic stroke.
4. Describe the use of thromobolytic therapy for stroke, including appropriate patient selection.

**Summary**

Stroke is a common and devastating disorder, afflicting 500,000 new patients each year and costing more than $12 billion in 1989. New developments in our basic understanding of stroke pathophysiology stimulated a revolution in our approach to stroke. We now know that it is possible to prevent up to 50% of all strokes. This development arose out of clinical trials of surgery for carotid artery stenosis, and trials of antiplatelet therapy for stroke prevention. It is possible to predict with a reasonable degree of certainty which patients are at highest risk for stroke, and to then target preventative therapy. Laboratory studies have shown that the window of opportunity for stroke treatment is probably a few hours long, challenging the traditional teaching that stroke deficit was irreversible after a few minutes. Thrombolytic therapy has proven to be safe and effective in animal models; clinical trials have established that intravenous tPA is safe and highly effective for acute stroke victims. A larger European trial showed that tPA given in the first 6 hours after stroke was very effective, but only if certain "high risk" patients are excluded. The NINDS tPA Stroke Study showed that if patients are treated within 3 hours of symptom onset that long term outcome was dramatically improved. Laboratory studies suggest that the excitotoxic neurotransmitter, glutamate, plays a key role in mediating stroke induced brain damage, and further, that antagonists of glutamate are potent neuroprotectants. The key to delivering these and any future stroke intervention is the development of a triage system similar to the Code Blue or Trauma Code. At UCSD we have developed the Code Stroke, now in place in San Diego Country, to demonstrate the feasibility of rapid patient identification, triage, and transport. In the future this system will allow widespread application of new, effective therapy for acute stroke.

**Talk Outline**

**Introduction**

1. Stroke is a common disease
2. There are several common stroke risk factors
3. There are 4 types of ischemic stroke
4. Current management is no better than chicken soup

**Recent Research Progress**

1. The ischemic penumbra
2. An ischemic temporal window
3. Laboratory studies of thrombolysis

**Thrombolytic Therapy**

1. Pilot Studies
2. ECASS
3. The NINDS Study
4. Current Practice and FDA Approval

**Building a Stroke Emergency Response System**

1. It all begins with 911
2. Paramedic protocols
3. Base station radio/pager/hotline protocols
4. Training pre-hospital personnel
5. The stroke "code" team
   - First responders in the emergency department
   - The role of the neurologist
   - The role of the stroke nurse
6. Streamlining patient flow in the hospital
7. A brain resuscitation unit

## How to Run A Stroke Code

1. Basic Life Support
2. The history is critical
3. Quick examination
4. Prioritize tests
5. Rule out concomitant disorders
   - Myocardial infarction
   - Hypoglycemia
   - Intoxication
   - Seizure
   - Old event made apparent by a new disease
   - Cerebral hemorrhage

## Future Directions

1. Find effective thrombolysis protocols
2. Develop neuroprotection
3. Determine if reperfusion is a problem and if so, treatment
4. Develop triage/EMS protocols
5. Improve public awareness of stroke warning signs

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# Angioplasty and Stenting of Extracranial Cerebral Arteries for Prevention of Strokes

by

David S.W. Ho

Extracranial cerebral artery thrombosis and artery-to-artery embolization have been reported to account for 30% of all strokes. For patients with warning symptoms and those with good functional recovery, surgical endarterectomy has been shown to reduce the risk of recurrent strokes, which is often debilitating and associated with a high mortality. Many patients, however, are not suitable surgical candidates due to underlying medical disease or unsuitable anatomy. From January 96 to April 97, 16 patients (12 male, 4 female) underwent 17 novel percutaneous revascularization procedures to 17 extracranial cerebral vessels. The indication was transient ischemic attacks (TIA) or stroke (n=12), and vertebro-basilar ischemia (VBI) or subclavian steal syndrome (n=5). Mean age was 63 ± 15 years. The patients were unsuitable for surgery due to anatomical reasons (n=12), underlying medical conditions (n=9), or significant disease in the contralateral vessel (n=6). The target lesions included the internal carotid artery (n=9), vertebral artery (n=2), and subclavian artery (n=6). A single stent was deployed in each lesion. Mean stenosis was reduced from 92 ± 5% to 0 ± 0%. Clinical success (defined as procedural success without any in-hospital complications) was achieved in 16/17 procedures (94%). There were no mortality, myocardial infarction or need for surgery. One patient presenting with TIA suffered left hemiparesis due to distal embolization. Following rehabilitation, this patient was independent in daily living with only mild left upper limb weakness. All patients were discharged home with a median hospital stay of 2 days post-procedure. At a mean follow-up of 6.8 ± 4.2 months, there were no stroke or TIA. For patients with carotid disease, in addition to this early procedural success and clinical success in prevention of further TIA's or stroke, 3 patients reported improvement in motor function and 2 reported improvement in higher centre function. For patients with VBI and subclavian steal syndrome, all reported resolution of arm claudication and dizziness. We conclude that percutaneous angioplasty and stenting to the extracranial cerebral arteries was associated with a high procedural success rate. Preliminary results suggest that this procedure is effective in reducing recurrent FIA or stroke. Besides reduction in stroke risk, a pleasant surprise was improvements in motor and higher centre function with reversal of perfusion deficit in some patients.

# Acute Stroke Therapy in Hong Kong
## by
## Raymond T.F. Cheung

Stroke is a syndrome of rapidly developing clinical signs of focal or global disturbance in cerebral or visual functions due to non-traumatic vascular causes, with symptoms lasting 24 hours or longer or rapidly leading to death. Transient ischaemic attack (TIA) is similar to ischaemic stroke but lasts less than 24 hours; this arbitrary time limit should be shortened since effective acute interventions are available in ischaemic stroke. When compared to the Caucasian figures, intracerebral haemorrhages are more common (30-35%) and ischaemic stroke are less common (60-65%) in Hong Kong.

At Queen Mary Hospital, management of stroke begins with an accurate diagnosis and classification of stroke types from history, physical examination, and investigations. When beds are available, patients are admitted to our acute stroke unit and managed by neurologists. Initial evaluation is to assess vital signs, confirm the diagnosis of stroke, make a diagnosis of acute ischaemic stroke, provide clues on the most likely aetiology, and screen for early complications. Computed tomography (CT) of the brain effectively excludes intracranial haemorrhage and brain tumor. Pertinent personal and clinical information is collected in a standard form which will generate the Hong Kong Island Stroke Databank. General management at the acute stage comprises of regular neuro-observation, attention to vital signs and potential complications, and ensuring adequate tissue oxygenation. When increased intracranial pressure is suspected, osmotherapy and/or hyperventilation are initiated. Anticonvulsants are prescribed to prevent recurrent seizures. Infection is treated vigorously, and elevated brain temperature is lowered. Good nursing care, early physiotherapy, cautious feeding, and adequate nutrition are provided.

Intravenous treatment with recombinant tissue plasminogen activator (rt-PA) within 3 hours of onset has been shown by a North American Study to improve the functional outcomes in highly selected patients with ischaemic stroke; there was also a non-significant trend of reduction in mortality. Nevertheless, intravenous rt-PA treatment carries a 6% risk of symptomatic intracerebral haemorrhage, and 60% of those who bled died within 6 weeks. The benefit was equivocal in another study when stroke patients were recruited within 6 hours of onset. Intravenous streptokinase is ineffective in acute ischaemic stroke. A pilot safety study will be conducted in Queen Mary Hospital to see if the risk of symptomatic intracerebral haemorrhage is higher in Hong Kong Chinese and whether local intra-arterial thrombolysis is safer and equally effective.

Subcutaneous low-molecular-weight heparin (nadroparin) is effective in preventing deep vein thrombosis and pulmonary embolism and improving the outcome in acute ischaemic stroke of all types. In the nadroparin stroke study, the treatment time window was 48 hours, and the therapy was remarkably safe without any increase in bleeding complications. While further clinical trials are underway to confirm the beneficial effects of subcutaneous low-molecular-weight heparin in ischaemic stroke, this treatment is now offered to all eligible stroke patients admitted to Queen Mary Hospital.

In summary, ischaemic stroke is treatable at the acute stage and brain attack is the preferred term. The arbitrary time limit of 24 hours in TIA is obsolete, and the management of TIA is similar to that of acute ischaemic stroke. At Queen Mary Hospital, we routinely consider subcutaneous nadroparin in our stroke patients. The role of intravenous or intraarterial rt-PA will be explored in a pilot study. Otherwise our management emphasises on prevention and treatment of neurological and systemic complications.

# How to Run a Stroke Code
# by
# Patrick D. Lyden

The stroke code should be activated by an Emergency Department nurse or physician who suspects that a patient may be having a stroke. The number one priority for the stroke team is to respond immediately to the Department. Prior to their arrival, Department staff should begin the stroke code protocol. this process is facilitated by standing orders that can be initiated by Department nursing staff without MD authorization.

The first order of business is to establish the time of onset of the stroke. This is critical because some therapies cannot be given beyond a certain time window. For example, thrombolysis for stroke must begin within 3 hours of the stroke beginning. Next, a brief but thorough examination must be done to assure that there are focal nurologic findings consistent with the diagnosis of acute stroke. This is not the time for a detailed mental status assessment or prolonged sensory battery. The purpose, at this point, is to confirm the presence of focal findings and perform enough examination to guess at the location of the occluded artery.

Next a laboratory panel must be sent in order to search for conditions that mimic stroke, such as hypoglycemia, or that may confound therapy, such as a prolonged prothrombin time. the full list of tests is included in the standard orders. Then, a 12 lead EKG must be done to rule out a simultaneous myocardial infarction, which is present in about 5% of all stroke patients. Finally, the patients must be taken to radiology for a brain CT scan to rule out hemorrhage.

It must be recognized that time is critical and the above sequence must be amended as needed to maintain speed. For example, if the CT scanner is ready for the patient, but the EKG has not been done, it would be better to go the scanner and get the EKG upon returning from CT.

Blood pressure must be below 185/110 prior to thrombolysis. A gentl anti-hypertensive, such as labetolol, may be used but if this fails then the patient must not receive thrombolysis. After thrombolysis, however, aggressive therapy must be used, if needed, to keep the pressure below those limits.

The patient should be admitted to an observation area where frequent vital signs and neuro checks can be performed. Discharge planning should begin on admission, as most patients will be ready for transfer to rehabilitation within 3 to 5 days.

# Diabetic Nephropathy: Natural History and Therapeutic Interventions

by
Edmund J. Lewis

Diabetic nephropathy is the single most common cause of renal failure in the United States, currently accounting for over one third of the patients enrolled in the end stage renal disease program. At current rates of increase, patients with diabetes will account for 50% of all end-stage renal diseased (ESRD) patients in the United States. The development of diabetic nephropathy greatly decreases the survival in patients with diabetes. Patients with insulin-dependent diabetes develop diabetic nephropathy in a particular time frame, on average 17 years, plus or minus 6 years, after the onset of their diabetes. It is rare for the Type I diabetic patient to develop proteinuria before 10 or more years duration of diabetes. It is also uncommon for them to do so for the first time after having diabetes for over 25 years without this complication. 40% of patients with Type I diabetes develop diabetic nephropathy. There is familial clustering of diabetic nephropathy. The epidemiologic data and the presence of familial clustering suggest the possibility of a genetic susceptibility to the development of diabetic nephropathy.

The natural history of diabetic nephropathy in patients with Type I diabetes has been well described. In newly diagnosed diabetics, functional changes occur in the kidney in virtually all patients, these include: glomerular hyperfiltration, increases in urinary albumin excretion, and increases in renal size. Renal size and urinary albumin excretion appear to decrease with the control of blood sugar. Early glomerular hyperfiltration has been reported to predict a later onset of proteinuria and declining renal function. Patients with newly diagnosed diabetes have a normal renal biopsy. Within 1-1/2 to 2 years, however, develop morphologic changes which include glomerular basement membrane thickening , mesangial expansion, hyaline arteriolosis and glomerulosclerosis. Glomerular basement membrane thickening is a sensitive indicator for the presence of diabetes and mesangial expansion is associated with declining renal function. Microalbuminuria can appear after 5 years duration of diabetes. Patients with microalbuminuria will have routine urine dipsticks negative for protein and normal urinary protein excretion in 24 hour urine collections. However, sensitive radioimmune assays for urinary albumin excretion reveal that elevated urinary albumin excretion rates of 30 to 300 milligrams per 24 hours. Of the patients with microalbuminuria, 80-90% will progress to proteinuria and declining renal function. The current recommendations are to test patients with Type I diabetes for microalbuminuria yearly after 5 years duration of diabetes. If the patients have elevated urinary albumin excretion rates, the test should be repeated three times over four to six months to confirm persistent microalbuminuria. Transient causes of microalbuminuria should be ruled out.

Systemic hypertension may also be an important predictor of the development of diabetic nephropathy in some patients. Once proteinuria develops, renal function inevitably declines with 50% of patients reaching ESRD in seven to 10 years. Survival for patients for Type I diabetes who reach ESRD is poor. Living-Related donor during transplant has the best overall survival amongst the renal replacement therapies available. Therapeutic interventions to slow the rate of decline of renal function in patients with Type I diabetes and diabetic nephropathy include glycemic control, control of systemic blood pressure, reducing protein intake in the diet and the inhibition of the renin-angiotensin system.

# Pathogenesis and Therapeutic Interventions in Progressive Renal Diseases
by
Julia A. Breyer

The population of end-state renal disease patients is growing world-wide. Diabetes is the most common cause of end-stage renal disease in the United States. Loss of renal function in patients with kidney disease is superimposed on the normal loss of renal function that occurs with age > 40 y/o. In many forms of kidney disease a linear rate of decline of renal function has been demonstrated. Factors that have been identified that contribute to progressive renal disease include: hypertension, both systemic and glomerular; proteinuria; cholesteral; dyslipidemia; high-protein diets; immunologic factors and toxins; and morphological factors.

**Systemic Hypertension**

Systemic hypertension can lead to a maladaptive glomerular response with afferent arteriolar dilatation. In experimental modes of chronic renal failure, the control of blood pressure can lead to decreased mean arterial and glomerular capillary pressures. Multiple studies in humans with diabetic and non-diabetic renal disease suggests the control of systemic blood pressure will slow the rate of decline of renal function. In addition, specific anti-hypertensive agents have been demonstrated to ameliorate renal diseases. In animal models, angiotensin converting enzyme (ACE) inhibition leads to decreased glomerular structure and function. In humans with Type I diabetes and diabetic nephropathy, ACE inhibitions has been demonstrated to dramatically decrease the rate of decline of renal function. Preliminarily, ACE inhibitions has also been demonstrated to slow rate of decline of renal function in people with other forms of kidney disease.

**Proteinuria**

Proteinuria has also been demonstrated in both humans and animals to be a marker for a more rapid rate of decline in renal function. It has been postulated that proteinuria in and of itself causes further damage to the kidney. Reduction of proteinuria appears to predict the effect of interventions on long-term renal function in human studies.

**Lipid Lowering Agents**

Lipid lowering agents reduce glomerular injury in multiple animal models of kidney disease. There are many mechanisms of lipid injury to the glomerulus. Lipid-lowering agents have been demonstrated to slow the rate of decline of renal function in studies in small numbers of humans.

**Blood Sugar Controls**

Poor blood sugar control in patients or animals with diabetes has been associated with a more rapid decline of renal function in both animal and humans. Better glycemic control as been demonstrated to have a clear benefit to glycemic control in preventing the development of diabetic kidney disease in patients with Type I diabetes.

**Protein**

In multiple animals models high protein diets have been shown to accelerate the rate of decline in renal function. In human studies with patients with diabetes, low protein diets have been demonstrated to slow the rate of decline of renal function. In patients with non-diabetic kidney disease, however, it has not yet been conclusively demonstrated that there is any benefit to low protein diets.

**Injuries/Toxins**

Immunological injuries are clearly present in multiple animal models of renal disease. Immosuppression is effective therapy for multiple forms of human renal disease. Toxins can cause acute renal failure and potentially alter the course of renal disease. These toxins include intravenous contrast dyes and non-steriodal anti-inflammatory agents.

**Morphologic Features**

Morphologic features seen on renal biopsy have been associated with more rapid progression of renal disease. A variety of factors have been demonstrated in experimental models to influence the progression of renal disease. Some of these have been confirmed to be factors that can be altered in human renal disease to slow the rate of decline of renal function.

# Management of Severe Lupus Nephritis
## by
## Daniel T.M. Chan

The prognosis of patients with diffuse proliferative lupus nephritis has improved over the last few decades, due to advances in immunosuppressive therapy and better management of complications related to disease or therapy. Early diagnosis followed by prompt and effective therapy are essential to minimise renal damage during the acute phase, which has significant implications on long-term renal survival. Renal biopsy is important to determine the type of renal involvement, and assess the severity as well as reversibility of renal lesions. In this regard, severe focal proliferative or diffuse proliferative lupus nephritis warrant more intensive immunosupppressive therapy than pure lupus membranous nephropathy.

Therapeutic intervention for severe lupus nephritis comprise heavy immunosuppression to control the acute inflammatory lesion, and prolonged low dose immunosuppressive medication to maintain patients in remission with minimal drug-related side-effects. The addition of a cytotoxic agent to corticosteroids has proven benefit both in the treatment of acute disease and the prevention of relapse. Nevertheless, the choice of cytotoxic agents and the route of administration remain controversial. Popular options include intravenous or oral cyclophosphamide, and azathioprine. The choice of cytotoxic agents should take into account possible complications that can result from their immunosuppressive or pharmacologic properties, such as infection, haemorrhagic cystitis, bladder carcinoma, malignant predisposition, and gonadal toxicity. The latter is of particular relevance since the disease often affects young females. Newer forms of therapy such as cyclosporin and methotrexate have given favorable results in some instances. Although plasmapheresis has not been shown to confer additional benefit when added to a regimenPf prednisolone and oral cyclophosphamide, its use in patients with severe disease has continued, which is attributable in part to its relative lack of side-effects. Intravenous immunoglobulin can induce transient improvement in some patients, especially when there is concomitant infection when heavy immunosuppression may be risky, but may also lead to disease exacerbation.

Heterogeneity in disease manifestations, the critical influence of the timing of treatment, and individual variations in therapeutic response present as difficulties for conducting clinical studies and obstacles to definitive conclusions and recommendations on therapy. Optimalmanagement needs to take into consideration individual circumstances. Early mortality in patients with severe lupus nephritis has decreased, and is mostly related to infection or other disease complications such as cerebral lupus. As the short-term outcome improves, increasing attention is required to minimize long-term vascular and metabolic complications.

# Immunotactoid Glomerulopathy
## by
## Edmund J. Lewis

Immunotactoid glomerulopathy is a term which has been coined to indicate the presence of a pathologic lesion which is characterised by the ultrastructural presence of glomerular deposits of microfibrils or microtubules which are extracellular, nonbranching, and without periodicity. These organized ultrastructural changes are Congo-red negative and contain immunoglobulins. Immunotactoid glomerulopathy is a primary process and is not associated with evidence of a systemic process. Hence, the lesion can be distinguished from similar histopathologic changes which might be associated with diseases where paraproteins or cryoglobulins or immune complexes may be involved. To date, almost 100 patients have been reported to have this lesion. There is no gender relationship. On the average all of the patients are 45 years +/- 15, all have had proteinuria, 2/3 of them being nephrotic. Hematuria has been noted in 2/3 of patients, as has hypertension. At the time of diagnosis renal insufficiency is present in 49%. The crystal-like structure of the abnormal deposit associated with this lesion suggests molecular uniformity. However, immunoglobulins associated with these deposits are polyclonal. The pathogenic process leading to the production of these fibrils is not known. Clinically the progression to renal failure is progressive with about 50% of patients reaching renal failure over approximately a seven year period. No response to steroid, cytotoxic, or plasmapheresis therapy has been reported. Four patients have received renal transplants, with recurrence reported in 2 cases. The importance of recognising this lesion resides in the fact that the differential diagnosis of the ultrastructural abnormality involves ruling out several disease entities which are potentially treatable. Hence it is important that this lesion and other lesions which can be included in the general category of "fibrillary glomerulopathies", be precisely identified.

# Renal Transplantation: Local Issues
## by
## Ignatius K.P. Cheng

Renal transplantation is the preferred treatment modality for patients suffering from end stage renal disease (ESRD). Recent advances in the development of immunosuppressive treatment including the discovery of Cyclosporin and more recently of FK506 and Mycophenolate Mofetil have greatly increased graft survival while improved prevention, monitoring and treatment of post-transplant infective, metabolic and other complications have signficantly prolonged patient survival. In Hong Kong, the clinical result of renal transplantation compares favourably with that of the West. Indeed, the 10 year graft survivals for related and cadaveric transplants of 86.2% and 67.7% are appreciably higher them the corresponding figures in Caucasian populations which suggests that an enhancing "race" effect may exist for Chinese. Despite its excellent clinical outcome, renal transplantation currently can be offered only to a limited number of ESRD patients in Hong Kong because of severe organ shortage. This is in part due to traditional Chinese cultural beliefs and in part due to inadequate knowledge on organ donation among the medical professionals and the public. As a result, living related transplantation was the predominant type of transplant performed in the territory till 1990. Increased educational efforts and the appointment of transplant co-ordinators in public hospitals in 1987 has resulted in a modest improvement in cadaveric donor recruitment so that cadaveric transplants now account for two thirds of transplants done locally. However, the figure of 5 donors per million population is till considerably lower than that in the West. The lack of organ donors has resulted in many patients going to underdeveloped neighbouring countries for transplantation. This has created special problems for clinicians in Hong Kong and has prompted the introduction of the Human Organ Transplant Ordinance and the formation of the Human Organ Transplant Board. Another unique medical problem facing transplant physicians in Hong Kong is the high incidence of hepatitis B carrier state among our normal and ESRD populations. The scarcity of donors has prompted us to use kidneys from HBV positive donors. Our experience shows that pretransplant passive or active immunisation of HBV negative recipients of HBV positive kidneys is able to protect them from becoming a carrier or from developing active chronic liver disease following transplantation. Our experience also shows that HBV carriers have a significant higher liver related mortality following transplantation when compared to HCV carriers or noncarriers. Preliminary experience shows that the use of new antiviral drugs against HBV e.g. Lamividine may reduce the liver related mortality and morbidity in these patients.

# *ACKNOWLEDGMENT*

The Organizing Committee would like to extend their gratitude to the following sponsors for their support and generous contribution to the Hong Kong Medical Forum '97 :-

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Last but not least, we would like to thank all speakers, chairmen and delegates for their participation and contribution.

## *NOTES*

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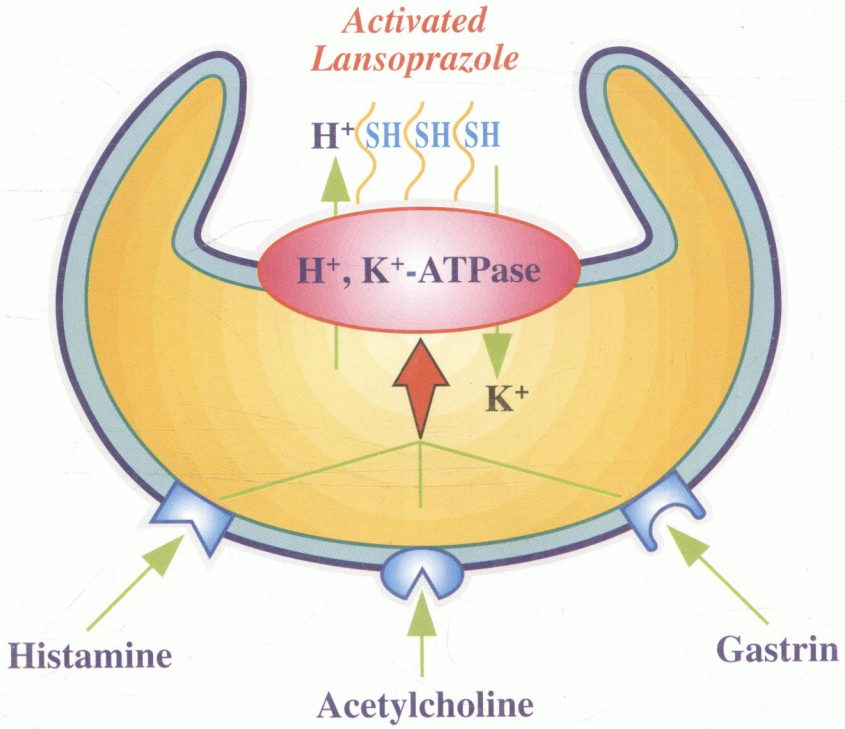


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For the maintenance of healing of erosive esophagitis, in the United States the recommended adult oral dose is 15mg once daily (FDA Approved, April 8, 1996). Controlled studies have not been conducted beyond 12 months.

For the maintenance of healing of duodenal ulcer, the recommended adult oral dose is 15mg once daily. (Approved February 96 in UK & April 96 in France).

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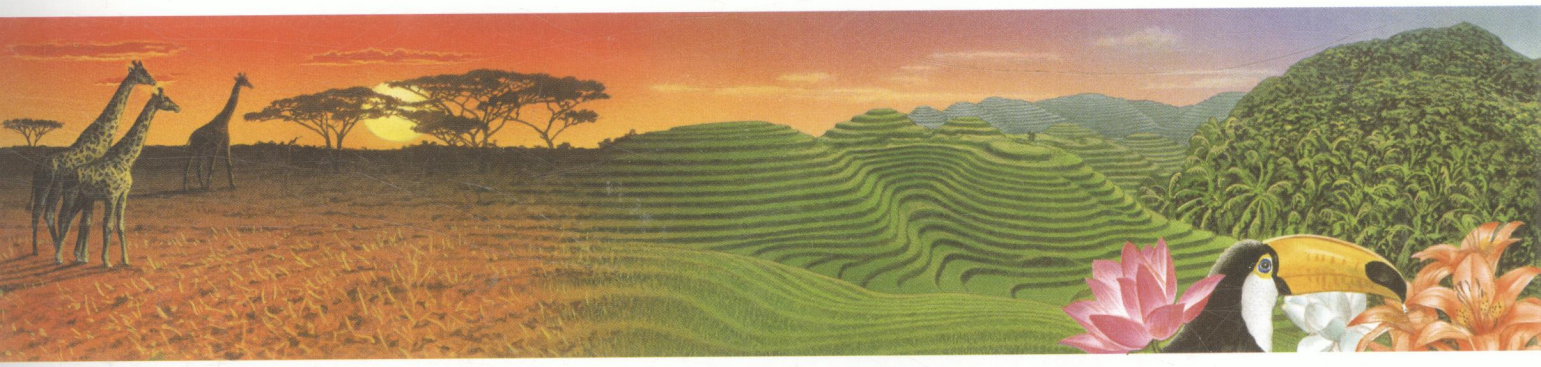

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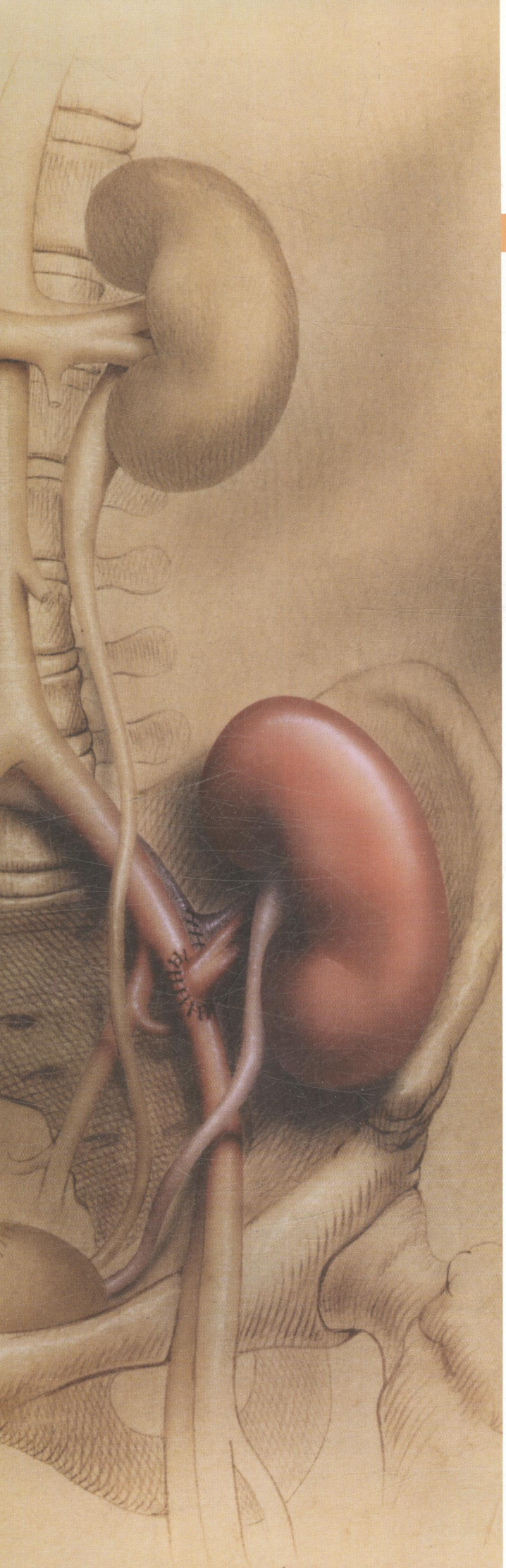

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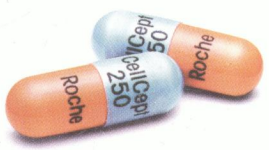



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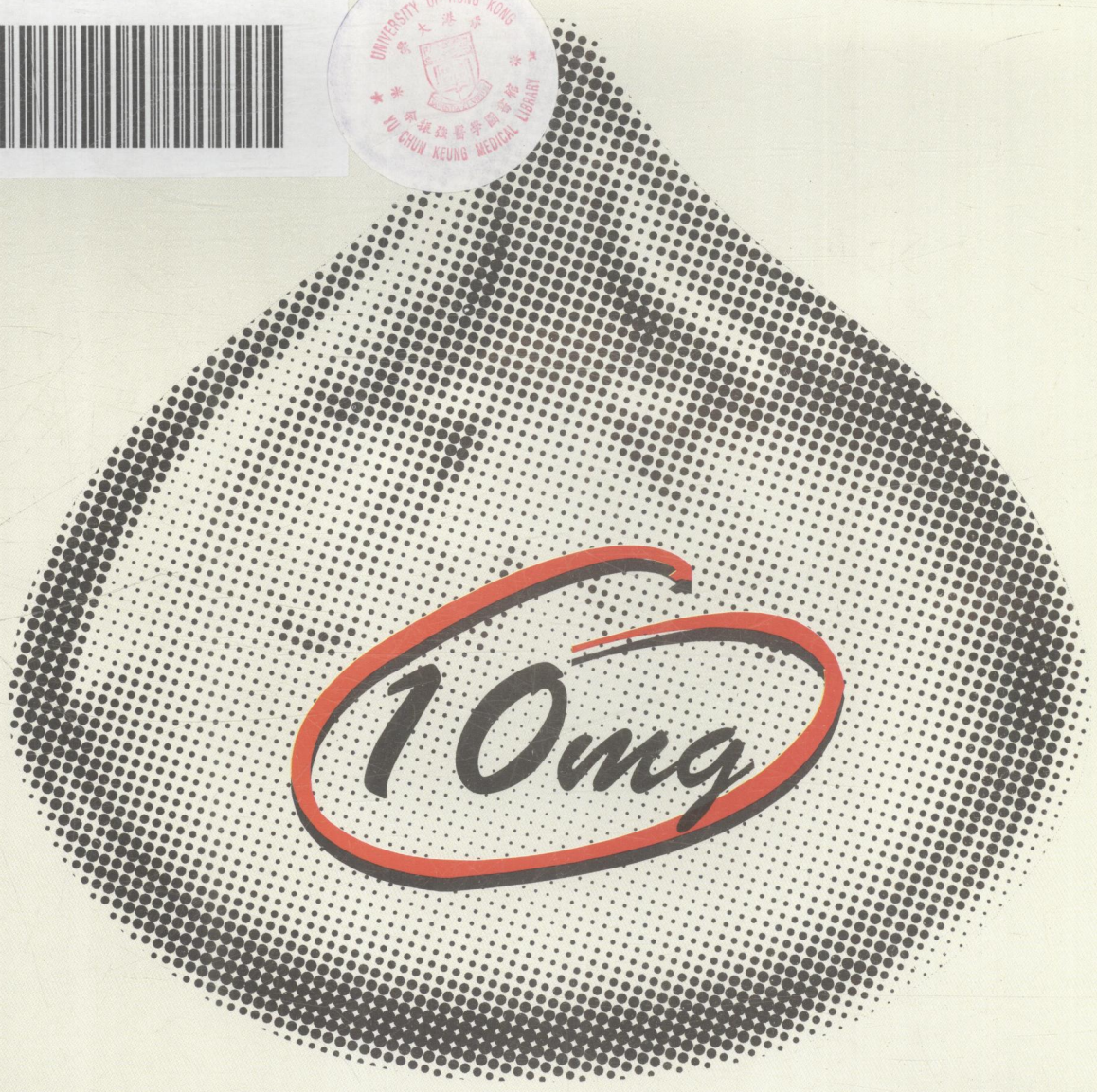
P.O. Box 98593 Tsim Sha Tsui Post Office, Hong Kong.
Tel: 2723 2832 Fax: 2723 7820

# Losec®

(omeprazole-Astra)






*A new strength for mild acid-related disease and for maintenance treatment*

ASTRA

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