GP Handbook

GI & Liver Disorders

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CONSTIPATION

Important Causes

- Dietary: Inadequate fluid and fibre intake
- Disease: Irritable bowel syndrome.
- Don't forget: CA colon
- Drugs: Aluminum-containing antacids, calcium supplements, iron supplements, opiates, antihypertensives (calcium-channel blockers, clonidine), anticholinergics (antidepressants, neuroleptics, antihistamines), some antiparkinsonian drugs, antispasmodics, oestrogen and progestins.

Evaluation

Infants and young adults usually need minimal work-up. Exceptions are suspected Hirschsprung's disease or chronic refractory constipation.

In adults the extent of evaluation depends on symptoms. A more detailed evaluation may be indicated if there is a history of severe straining, incomplete evacuation, or presence of anaemia. Blood in the stool (occult or frank) merits a work-up for colon cancer in older adults with constipation. In this case colonoscopy is preferred over barium enema because in colonoscopy,

- the patient feels less pain and discomfort (because of sedation)
- polypectomy and mucosal biopsy can be concomitantly performed
- visualization of the bowel lumen is better

Investigations: CBC, ESR, LFT, RFT, calcium, glucose, thyroid function tests, AXR, abdominal ultrasound, sigmoidoscopy/colonoscopy, and barium enema.

Management

Patient education

- Avoid irritant and combination laxatives (eg *Senokot, Bisacodyl*) in chronic constipation.
- Allow adequate time and a relaxed environment to have a bowel movement.
- Increase exercise.

Fluid and fibres

- Insoluble fibre is more important than soluble fibre in treating constipation.
- Insoluble fibre is found in grains and legumes.
- Commercial psyllium preparations (eg Metamucil, Normacol, Forlax) are useful long-term treatment, but those with laxative ingredients (eg Normacol-plus) should not be taken continuously for more than 4 weeks.
- Increase fluid intake to at least 8 glasses of water per day.

Stool softeners and lubricants

- Avoid products that combine stool softeners with irritant laxatives (eg Senokot) unless specifically indicated.
- An example of stool softener is docusate sodium.

Hyperosmotic preparations

- The mainstay of therapy for chronic constipation.
- Examples include non-absorbable sugars such as lactulose (Duphalac) or sorbitol.
- These agents work by increasing the water content of stools.
- The dosage of lactulose varies a lot among patients (5-50 mL in a single or divided doses), and has to be titrated accordingly.
- 70% sorbitol is less expensive and also effective.

Enemas and suppositories

- Initiate reflex evacuation by distending or irritating colon and rectum.
- A common enema is Fleet enemas.
- Bisacodyl and glycerin suppositories work as local irritants.

DIARRHOEA

Aetiology

Infections

- Bacterial: 33% of cases in developed countries; 50% in developing tropical and semi-tropical regions
- Viral: most of the domestic cases in developed countries; most of the enteric disease in infants (rotavirus is the commonest cause in children; there is often associated otitis media or URTI)
- Parasitic

Other causes

- Toddler diarrhoea (peas and carrots motions): intestinal hurry; settles with time
- Allergy (celiac disease; disaccharide, galactose, glucose, or lactose intolerance)
- Antibiotics (mild: disruption in the carbohydrate metabolism in the normal bowel flora; severe: *Clostridium difficile*-associated diarrhoea)

History

- Travelling – bacterial for most cases
- Antibiotic use
- Sporadic vs multiple cases: public health concern
- Incubation period
- Special notes on paediatric cases: it is normal for breast-fed babies to have liquid stools. Some cows milk feeds cause green stool which is of no clinical significance. Diarrhoea may be the first sign of a urinary tract infection.

Physical Examination

- Dehydration: tongue inspection, skin turgor and capillary refilling time
- Postural hypotension
- Temperature, pulse, respiratory rate
- Weight loss
- Skin rashes
- Lymphadenopathy
- Abdominal examination
- +/- rectal examination, stool routine +/- culture

Investigations

Most mild cases require no further evaluation than a clinical one; for moderate to severe or persistent diarrhoea; faecal leucocyte examination can be quite useful.

Stool culture in

- severe and/or persistent diarrhoea;
- febrile and/or dysenteric diseases;
- hamburger associated diarrhoea where *E coli* O157 H7 is endemic;
- faecal leucocyte positive cases.

Parasite examination in

- persistent diarrhoea;
- diarrhoea in homosexual male;
- regular contact with day-care centre inmates or other institutionalised patients.

Test for reducing sugars in suspected disaccharide, galactose, glucose, or lactose intolerance.

Management

General

- Adequate fluids and salt intake: water, rice water, oral rehydration salts…etc.
- Diet alteration congee in both adults and children – avoid milk products, spicy and fried foods.

Medical treatment

- Symptomatic treatment eg Loperax (Loperamide) cap 2 initially followed by 2 capsules after each loose stool (not to exceed 8 capsules per day for 2 days). Dhamotil (Diphenoxylate + Atropine) can be used instead of Loperax.
- Antiemetics may be useful if vomiting is severe.
- Antibiotics are rarely indicated unless the responsible organism is identified as being bacterial or amoebic. They are prescribed mostly for traveller's diarrhoea: a 3-day course of Ofloxacin or Trimethoprim + Sulphamethoxazole is effective especially when used with Loperax (Loperamide).
- Most patients require just a few doses of medications. There is really no need to give more than 8 doses. The patient should be warned against the possibility of constipation if they over-treat themselves with anti-diarrhoeals.

Diarrhoea in children

Management for mild gastroenteritis consists of daily weighing the child, stopping milk and solids, and substituting an oral rehydration mixture. In practice, if the child is well, salt is rarely needed. Milk is gradually reintroduced after 24-48 hours. Some children may temporarily need lactose-free milk (eg soya milk). If the child is breast-fed and is not severely ill, breast-feeding can be allowed to continue (to supply antibodies, and to maintain milk production). Suggested medications include Smecta, which is safe and useful; Colimix, Syr Dimenate and Progesic prn may be prescribed.

When to Refer?

- Severe cases: which may warrant IV fluid replacement.
- Chronic cases: for diagnosis and treatment.
- Cases where the diagnosis is unknown.
- Patients with complicated inflammatory bowel disease or who require sigmoidoscopy, colonoscopy or intestinal biopsy, or small bowel sampling.

FATTY LIVER

Classification

Fatty liver occurs where large vacuoles of triglyceride fat accumulate in liver cells via the process of steatosis. It is commonly associated with alcohol (Alcoholic Fatty Liver Disease, AFLD).

Non-alcoholic fatty liver disease (NAFLD), on the other hand, is mainly associated with metabolic syndrome but can also be due to other conditions that influence fat metabolism. Drugs including have also been implicated.

Morphologically it is difficult to distinguish AFLD from NAFLD and both show micro-vesicular and macro-vesicular fatty changes at different stages.

NAFLD

NAFLD is growing to be the most common chronic liver disease worldwide. It affects 15% of the Chinese population and up to 50% of obese people in North America. Long-term studies show that NAFLD is associated with increased risk of cardiovascular disease. Up to 50% will have progressive liver fibrosis. Although the majority cases of NAFLD run a benign course, 13% of NAFLD patients eventually die of liver complications including cirrhosis and liver cancer.

NAFLD is strongly associated with metabolic syndrome and T2DM, which is often under-diagnosed in these patients. DM and obesity increase the risk of steatohepatitis (severe fatty liver with inflammation) and liver fibrosis dramatically.

Causes of asymptomatic raised transaminases which need to be excluded

- Chronic viral hepatitis B and C
- Drug history: statins, ticlodipine, NSAID, ACEI, anti-TB drugs, amiodarone, methotrexate, diltiazem, glucocorticoids, tamoxifen
- Consumption of herbal supplements and tonics, surreptitious or otherwise
- Autoimmune hepatitis
- Wilson's disease

Diagnosis

Most patients with fatty liver are asymptomatic and the condition is usually discovered incidentally because of abnormal liver function tests or hepatomegaly noted in unrelated medical condition. Elevated liver biochemistry is found in 50% of patients with simple fatty liver. The serum SGPT level usually is greater than the SGOT level in NAFLD and the opposite in AFLD. The rise in liver enzymes is usually mild, < 4x ULN for transaminases.

Ultrasonography reveals a "bright" liver with increased echogenicity. A fatty liver has lower density than spleen on CT scan and fat appears bright in T1 weighted MRI.

Fibroscan (please refer to the chapter "Chronic Hepatitis B") is a non-invasive method to assess liver fibrosis. It involves transient elastography that measures the stiffness of the liver. The machine however cannot perform well in patients with thick subcutaneous fat.

Histological diagnosis by liver biopsy is sought when assessment of severity is indicated. Although major complications from liver biopsy is rare, the procedure requires hospitalization and may cause

discomfort and anxiety inpatients. Serum markers to predict liver fibrosis in NAFLD patients have been validated with reasonable accuracy.

Management

- LIFE-STYLE MODIFICATION: weight reduction and regular exercise.
- Bariatric surgery can improve liver condition dramatically in NAFLD patients with co-existing morbid obesity.
- Metformin has been shown to reduce the level of liver aminotransferase in NAFLD patients. Pioglitazone (Avandia), a thiazolidinedione, also improved the metabolic profile and histologic features of NAFLD patients

GASTRO-OESOPHAGEAL REFLUX DISEASE

Gastro-oesophageal reflux disease (GERD) is characterized by symptoms of heartburn, acid (+/- bile) reflux, and delayed oesophageal clearance. Atypical symptoms include chest pain, asthma, hoarseness and chronic cough. Rarely gastric hypersecretion is also implicated.

Rates of GERD vary from 2% in some Asian countries to 20% in the USA. Risk factors include hiatus hernia, obesity, old age and male gender.

Investigations

- **OGD**: there seems to be poor correlation between symptoms and endoscopic evidence of oesophagitis (20% of patients with oesophagitis are symptom free; 30% of symptomatic patients have non-erosive reflux disease, aka NERD)
- 24-hour pH monitoring and oesophageal manometry are rarely indicated
- **The Proton-pump Inhibitor (PPI) test: empirical use of PPI has been shown to be specific and sensitive in diagnosing GERD in patients with non-cardiac chest pain**

Management

Lifestyle modification

- Stop smoking and avoid alcohol
- Loose weight
- Raise head of bed

Drug Treatment

- Life-long therapy often required (usually with half the treatment dosages)
- **PPI** is now considered both the first-line and the most cost-effective treatment – it should be taken 30 minutes before breakfast (for once-daily dosing), and 30 minutes before breakfast and dinner for twice-daily dosing.
- **Pro-kinetic drugs**: medications that promote gastric emptying (eg Motilium); they are best taken 30-45 min before meals
- Itopride, a new pro-kinetic dopamine D2 antagonist with acetylcholinesterase effects, may prove to be an effective alternative in the future.

Surgical Intervention

Patients with persistent and severe symptoms refractory to medical treatment should be referred, and surgery is most effective for the patient with a defective lower esophageal sphincter (LES). The surgical procedure is called fundoplication, which involves constructing a new "valve" between the esophagus and the stomach by wrapping the fundus around the lowest port of the esophagus. In general, more than 90% of patients who undergo fundoplication have no reflux after surgery. Nowadays about 95% of all cases can be performed laparoscopically.

HELICOBACTOR PYLORI INFECTION

H pylori infection is associated with duodenal ulcer, gastric ulcer, gastric cancer, gastric MALT (mucosa-associated lymphoid tissue) lymphoma, non-ulcer dyspepsia, and other extra-GI diseases. The mode of *H pylori* infection is still unknown.

Prevalence

- About 50% of the Hong Kong population
- Increase with age
- Decrease with improvement in socio-economic condition

Diagnosis

Invasive tests: endoscopic antral biopsy sample is needed

- Rapid urease test: eg CLO test, PyloriTek...etc. A colour change (yellow to red) indicates positive infection. CLO tests should be read at 24 hours, while PyloriTek can give a diagnosis within an hour.
- Histology
- Culture: A special transport medium is needed. It is difficult to grow *H pylori* successfully. The test is not commonly available, but is the only test that allows assessment of antibiotics sensitivity.

Non-invasive tests: OGD not required

- Urea breath test (carbon-13): suitable for both pre- and post-treatment diagnosis. Non-radioactive, good for children and pregnant women. Accuracy 95%.
- Stool antigen test: measures antigen, not antibody. Suitable for both pre- and post-treatment assessment.
- Blood tests (serum or whole blood): assessing antibody levels. Validity in Hong Kong to be confirmed. Not to be used in post-treatment patient as changes in antibody levels occur over a prolonged period of time.

Choice of tests

- Does the patient require an OGD? [yes -> invasive tests; no -> non-invasive tests]
- First time test or post-treatment? If post-treatment, wait for 4 weeks after stopping all drugs. Breath test, histology and culture are best choices.
- Blood tests or any other antibody tests must NOT be used for post-treatment.
- Test results affected by recent (usually 2-4 weeks) intake of proton-pump inhibitors, antibiotics, and bismuth compounds.

Treatment

It is important to confirm diagnosis before treatment.

Who needs to be treated?

- Active or past history of DU and GU and *H pylori* +ve - definite benefit

- Prolonged NSAID therapy, dyspepsia, post-resection of early gastric cancer, and gastric MALT lymphoma - may have benefit

First-line treatment

Despite use of the currently most effective treatment regimes, approximately 10% of patients will fail to achieve eradication of their infection. Because re-treatment is always difficult, choosing the best available first-line treatment regime still represent the best strategy.

- PPI in standard dose bd x 1/52
- Clarithromycin 500mg bd x 1/52
- Amoxicillin 1gm bd x 1/52

Second-line treatment

The choice of second-line treatment depends on which treatment approach was used initially, because re-treatment with the same regime is not recommended. If a clarithromycin-based regime was used initially, a metronidazole-based regime should be used next, and vice versa.

- PPI in standard dose bd x 2/52
- Metronidazole 500mg bd x 2/52
- Bismuth subcitrate 120mg qid x 2/52
- Tetracycline 500mg qid x 2/52

OR

- PPI in standard dose bd x 1/52
- Amoxicillin 1gm bd x 1/52
- Bismuth subcitrate 120mg qid x 1/52
- Tetracycline 500mg qid x 1/52

OR

- Rabeprazole 20mg bd x 10/7
- Amoxicillin 1gm bd x 10/7
- Levofloxacin 500mg qd x 10/7

Further failures should probably managed by specialists, but the following regimes seem to offer an encouraging opportunity for eradication:

- PPI in standard dose bd x 1/52
- Levofloxacin 500mg qd x 1/52
- Rifabutin 300mg qd x 1/52

Local data on eradication rates

- Losec + Klacid +Amoxyl : 92%
- Losec + Klacid + Flagyl : 70%
- Takepron + Klacid + Flagyl : 87%
- Pylorid + Klacid +Flagyl : 92%

Eradication rates are affected by antibiotic resistance. In Hong Kong, metronidazole resistance is ~50%, and clarithromycin resistance ~10%. Double resistance is ~7%.

Other Important Points

- Non-ulcer dyspepsia: symptoms may not respond to H pylori eradication.
- Symptoms recur after *H pylori* eradication: one should look for ulcer relapse, re-infection of *H pylori*, GERD, IBS.
- Not all patients with pain or dyspepsia are infected by *H pylori*.
- Not all H pylori carriers will benefit from *H pylori* eradication.

- Treating asymptomatic *H pylori* carriers: no proven benefits.

IRRITABLE BOWEL SYNDROME (IBS)

Irritable bowel syndrome (IBS) is a functional GI disorder characterized by abdominal pain and altered bowel habits in the absence of specific and unique organic pathology. The syndrome has been referred to spastic, irritable, and nervous colon.

Although markedly different among countries, the prevalence of IBS is estimated at 10-20% and the incidence 1-2% per year. Of people with IBS, approximately 10-20% seek medical care. Both men and women are affected.

Pathophysiology

Traditional theories regarding pathophysiology may be visualized as a 3-part complex of:

- Altered GI motility
- Visceral hyperalgesia
- Psychopathology

Serotonin is now known to be a key mediator of GI motility and visceral sensitivity.

Recently, microscopic inflammation has been documented in some patients. This concept is groundbreaking in that IBS had previously been considered to have no demonstrable pathologic alterations.

Clinical Features & Diagnosis

IBS is a diagnosis of exclusion. No specific motility or structural correlates have been consistently demonstrated, and so IBS remains a clinically defined illness. The Manning Criteria, although historically important (1978), are both insensitive (58%) and nonspecific (74%).

The Rome Criteria of IBS

The Rome diagnostic criteria presume the absence of a structural or biochemical explanation for the symptoms. In patients with no alarm symptoms*, they have a positive predictive value of ~98%. The Rome III Criteria (2006) require that patients must have the following continuous or recurrent symptoms for at least 6 months and be currently active for 3 months:

(1) Abdominal pain or discomfort characterized by at least 2 out of the following:
- Relieved by defecation
- Associated with a change in stool frequency
- Associated with a change in stool consistency

(2) Supporting symptoms include the following:
- Altered stool frequency (> 3 bowel movements/day or < 3 /week)
- Altered stool form (too hard or too loose)
- Altered stool passage (straining, urgency, or feeling of incomplete evacuation)
- Mucorrhoea
- Abdominal bloating or subjective distention

**Alarm symptoms (NOT typical of IBS)*

- *Pain interfering with sleep*
- *Diarrhoea interfering with sleep*
- *Constipation causing faecal impaction*
- *Blood in stool (visible or occult)*
- *General symptoms like anorexia, weight loss, fever*
- *Anaemia*
- *First symptoms after 40 years of age*
- *Family history of GI cancers, coeliace disease and inflammatory bowel disease*

To sum up the picture, IBS can be clinically identified by recurrent or chronic symptoms of:-

- **Abdominal pain, usually lower**
- **Disturbed bowel movements**
- **Abdominal distention**

Investigations

According to specific information provided in the history and physical findings, and understanding that upper GI conditions like gastritis commonly coexist, the following tests are useful:-

- Blood tests: CBP, ESR, LFT, RFT, amylase, FBS, lipid profile, TFT
- Urine and stool tests: routine and culture
- X-rays: CXR, KUB
- Ultrasound: whole abdomen
- Endoscopy: OGD and colonoscopy

Treatment

General principles

- Successful management relies on a strong patient-physician relationship.
- Reassure the patient that the absence of an organic pathology indicates a normal life expectancy.
- Emphasize the expected chronicity of symptoms with periodic exacerbations.
- Teach the patient to acknowledge stressors and to use avoidance techniques.
- Consider mood disorder as one of the possible underlying or associated conditions.

Diet

- Fibre supplementation may improve symptoms of constipation and diarrhea. Individualize the treatment because some patients experience exacerbated bloating and distention with high-fiber diets.
- Judicious water intake in patients experiencing constipation is recommended.
- Food that commonly trigger/worsen symptoms: diary products, chocolate, alcohol, caffeine, fatty food, soda and other food stuff that contains or generate gas

Medical treatment

- Symptomatic: analgesics, antispasmodics, antidiarrhoeals, prokinetics, bulk-forming laxatives, stool softeners, mood regulators, analgesics, hypnotics
- In patients with symptoms refractory to the above, SSRI and SNRI have been tried with variable results.
- Zelmac (tegaserod maleate), a selective partial agonist of the serotonin-4 (5HT4) receptor and possesses GI prokinetic activity, has been removed from markets since

March 2007 because of cardiovascular safety concerns.

CHRONIC HEPATITIS B

Chronic infection of the hepatitis B virus : the persistence of HBsAg positivity for > 6/12.

Chronic hepatitis B (CHB) is diagnosed in patients with elevated HBV DNA levels and elevated SGPT levels or necroinflammation on liver biopsy.

Hepatitis A superinfection in patients with CHB is associated with increased morbidity, and early vaccination should be considered in patients with chronic liver disease.

Natural History of CHB

(1) Immune tolerant
Infected infants first enter this phase, and after many years the following phase when their hepatitis becomes active

(2) IMMUNE CLEARANCE
Infected adolescents and adults immediately enter this phase (HBeAg positive chronic hepatitis B)

(3) Non-replicative
Inactive HBsAg carrier

(4) REACTIVATION
HBeAg-negative chronic hepatitis B

Treatment is recommended for patients in the **immune clearance** and **reactivation** phases. SGPT criteria used for determining the indications for therapy should be based on the revised upper limit of normal (ie 19 U/L in women and 30 U/L in men). Traditionally a more than 2 fold increase (ie >2xULN) is taken a major criterion of instituting treatment. A local study however, revealed that the risk of long-term complications was increased at even >0.5xULN.

Liver Biopsy

- More sensitive and accurate than ALT as an indicator of liver disease
- Establishes baseline hepatitis activity and fibrosis stage prior to initiation of therapy
- Excludes other causes of liver disease
- Predicts the likely response to antiviral treatment and evaluates therapeutic effects

Transient Elastography (Fibroscan®)

Transient elastography (TE) is a novel non-invasive, rapid and reproducible method to quantify hepatic fibrosis by measuring liver stiffness. It can be easily performed at the bedside or in the outpatient clinic with immediate results.

TE cannot replace liver biopsy. It should be employed as a screening and monitoring tool in management of a wide variety of hepatic conditions that could result in cirrhosis. Local studies are underway to confirm its usefulness in evaluation and treatment of chronic hepatitis B infection.

Examination Process

A mechanical pulse is generated at the skin surface, which is propagated through the liver. The velocity of the wave, which is measured by ultrasound, is directly correlated to stiffness of the liver, which in turn reflects the degree of fibrosis, ie the stiffer the liver the greater the degree of fibrosis.

Limitations
These include failure in around 5% of cases. The degree of fibrosis may be over-estimated in patients with SGPT higher than 2xULN. TE should not be used on the following patients:

- with ascites
- who are pregnant
- under the age of 18 years
- with a BMI >30

FDA-Approved Therapies

- Interferon alfa-2a (1991) – replaced by peginterferon alfa-2a (2005)
- Antiviral agents: lamivudine (1998), adefovir (2002), entecavir (2005), telbivudine (2006).

Overall, interferon and peginterferon (one-year therapy) leads to sustained virological response. The advantage of interferon is that it only requires a finite period of therapy with no risk of drug resistance. The main disadvantages are that there are more complications associated with its use. Patients indicated for interferon therapy should be referred to a specialist centre, eg the university hepatic units.

Antiviral agents are oral form of treatment. They all provide effective suppression of HBV DNA and are associated with less side effects. Treatment choices are largely influenced by long-term efficacy, safety, resistance, clinical status and cost.

Long-term safety data show that lamivudine (Zeffix) treatment for up to 6 years has an excellent safety profile in patients with HBeAg-positive compensated liver disease.

The primary goal of any of the above therapy is long-term suppression of serum HBV DNA, which will likely reduce progression to cirrhosis and hepatocellular carcinoma (HCC).

When to Start Rx?

According to the 2008 APASL (Asian Pacific Association for the Study of the Liver) guidelines, the patient should have their blood tested for HBeAg and HBV DNA when their SGPT level is elevated to >2xULN.

- If HBeAg-positive: start Rx when HBV DNA levels are >20,000 IU/mL

- If HBeAg-negative: start Rx when HBV DNA levels are >2,000 IU/mL

Those with compensated cirrhosis with HBV DNA levels >2000 IU/mL should be treated, as should all decompensated cirrhosis. Interferon-based therapies are only recommended in compensated cirrhosis in the absence of hepatitis flares.

During therapy, LFT, HBeAg and HBV DNA should be monitored every 3/12.

Patients being considered for perinterferon alfa-2a therapy should have their HBV genotype tested: genotype B responds somewhat better than genotype C (both common in Asia).

When to Stop Rx?

- HBeAg positive patients: when HBeAg seroconversion with undetectable HBV DNA has been documented on 2 occasions >6/12 apart

- HBeAg negative patients: NOT clear, but can be considered if undetectable HBV DNA has been documented on 3 occasions 6/12 apart

After the end of therapy, levels of SGPT and HBV DNA should be monitored monthly for the first 3/12 to detect early relapse, and then every 3-6/12.

Drug Resistance

Definition: Rebound in serum HBV DNA levels with increased SGPT levels or worsening histology

Long-term resistance rates

- High with lamivudine (70% at 5 years)
- Intermediate with telbivudine (20% in HBeAg-positive and 10% HBeAg-negative patients at 2 years)
- Low with adefovir (30% in 5 years)
- Very low with entecavir (1% after 4 years in the absence of prior lamivudine resistance, BUT 40% after 4 years in the presence of prior lamivudine resistance)
- Non-existent with interferon or peginterferon

Lamivudine resistance

Emergence of virological resistance increases from 5% in the first year to up to 70% by the 5th year, but this can be managed by the addition of adefovir (Hepsera). Predictors for the emergence of resistance to lamivudine include higher baseline HBV-DNA (>9 logs) and the female gender.

Antiviral drug resistance should be managed in a specialist centre. A useful technique in combating drug resistance is long-term "add-on" treatment – eg adding adefovir on top of (NOT replacing) lamivudine.

It has been shown that although lamivudine-resistant mutations had reduced the benefits from lamivudine therapy, the outcome of these patients had still been better than untreated patients.

CHB in Pregnancy

- Pregnancy does not generally alter the clinical course of CHB.
- CHB infection is not usually associated with an increased risk of congenital malformation, stillbirth, abortion or retardation.
- Interferon is contraindicated in pregnancy.
- US FDA classifies lamivudine, adefovir and entecavir as Category C drugs.
- In pregnant women with a high viral load, lamivudine administered from week 32 of gestation to week 4 postpartum, followed by hepatitis B vaccination and hepatitis B immunoglobulin (HBIG) given to the infant, significantly reduced the risk of vertical transmission compared with HBV vaccination plus HBIG alone.
- No overall increase in prevalence of congenital anomalies has been detected with the use of lamivudine during pregnancy.