CONTROVERSIES AND INNOVATIONS IN GASTROENTEROLOGY*

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INTRODUCTION

This symposium covered a wide variety of topics which included some of the more controversial issues in the current practice of gastroenterology. Controversy was generated by discussion of the problem of resource allocation in the modern National Health Service (NHS) and a number of speakers returned to this theme throughout the meeting. Given that resources in terms of time and money are limited, therapeutic innovations which may only be applicable to a very small number of patients carry a high financial cost.

The debate over screening programmes for diseases of the gastrointestinal tract has been widened recently with the introduction of two pilot schemes of population screening for colorectal cancer. Much was made of the resource implications of such a project were it introduced nationally. Is it reasonable for the NHS to invest large sums of money on expensive therapies which may benefit only small numbers of individuals, while other initiatives with a potential impact on much greater numbers of people, such as screening for common malignancies, may be under-funded? The answer to this question concerned audience and speakers alike at the symposium.

One speaker reminded the audience that health care policy should be based on evidence gathered from a variety of sources, including properly conducted randomised controlled trials; however, it is designed to apply to populations and does not necessarily translate well when applied to the care of individual patients.

Session 1

GASTROINTESTINAL EMERGENCIES

Chairman: Dr Kelvin Palmer, Edinburgh

In 1933, Hardy and Bulmer[1] described acute severe colitis as a condition which carried a one year mortality of 75%. The introduction of treatment with corticosteroids in the 1950s helped to reduce this alarming mortality, which has been reduced still further by improvements in post-operative care.

Dr Simon Travis began the symposium by describing those features, clinical and genetic, which may be helpful in anticipating an attack of acute, severe colitis and predicting its outcome. Clinically, anatomically extensive disease is predictive of a severe attack. Genetic markers are less readily available but may be useful; for instance, patients who carry the HLA-DRB 10103 allele are more likely to require colectomy when compared to those who do not carry this allele. Thirty-five per cent of these patients also have extra-intestinal manifestations of their inflammatory bowel disease. Other features such as bloody diarrhoea, tachycardia and a raised ESR remain vital clinical indicators of a severe attack. Eighty-five per cent of patients who are producing more than eight stools per day after three days of intravenous steroid therapy will require a colectomy.

A variety of novel therapies, including cyclosporin A and heparin, have been advocated as a means of avoiding the need for surgery. The role of cyclosporin A is not clearly defined; its potential to 'rescue' patients from colectomy is at the price of quite profound immuno-suppression with a combination of corticosteroids, cyclosporin A and azathioprine. In those patients who do not respond to cyclosporin A, colectomy should not be delayed. The initial promising reports of the beneficial effects of unfractionated heparin in open studies have not been borne out by properly controlled trials.

The timing of surgery is vital and depends on the clinician's anticipation of the likely outcome of this attack. An early, frank discussion of this anticipated outcome and the possibility of surgery with the patient is very important. The wishes of the patient should always be borne in mind.

In the future, it may be possible to administer therapy which is more tailored to the needs of an individual as genetic markers will allow us to identify those patients at risk of a severe relapse and to predict those unlikely to respond to treatment with corticosteroids.

KEYPOINTS

- A severe attack can be anticipated from knowledge of disease extent or from genetic studies
- Bloody diarrhoea, tachycardia and elevated ESR indicate a severe attack and the need for close clinical monitoring
- Joint management by physicians and surgeons is advisable from an early stage

Dr Alexander Gimson concentrated on assessing the patient with acute liver failure. In spite of measures such as the introduction of 'blister' packs to limit the number of tablets sold to any individual, paracetamol remains the main cause of fulminant hepatic failure in the UK, accounting for over 50% of cases. Those who abuse alcohol are at highest risk of developing hepatic failure and of death following ingestion of even relatively modest amounts of paracetamol. Viral hepatitis and drug reactions account for a further 36% and seven per cent of cases respectively. Newer drugs such as ecstasy, anti-HIV drugs, flutamide and troglitazones are becoming an increasingly common cause

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of hepatic failure. It is noteworthy that in 16% of cases of fulminant hepatic failure, no cause can be identified.

The advent of Orthotopic Liver Transplantation (OLT) has helped reduce the high mortality associated with fulminant hepatic failure, but patients must be selected carefully for transplantation. The presence of certain clinical features, including the underlying aetiology of hepatic failure, is known to influence survival. For example, in paracetamol poisoning a pH <7·3, or the presence of cerebral oedema and renal failure in combination, carries a 96% mortality. The combination of a prothrombin time (PT) over 100 seconds, along with a serum creatinine greater than 300μmol/L and advanced encephalopathy, carries a 67% mortality. The mortality of non-paracetamol induced hepatic failure exceeds 90% in the presence of any three of the following: age under ten years or over 40 years; PT over 50 seconds; bilirubin over 300μmol/L; or time from onset of jaundice to onset of encephalopathy of more than seven days.

KEYPOINTS

Indications for referral to transplant centre.

Paracetamol induced hepatic failure

Days 1–2	Day 3	Days 4–6
pH <7·3	Hepatic encephalopathy	Hepatic encephalopathy
Serum creatinine >250μmol/L	Serum creatinine >250μmol/L	Serum creatinine >350μmol/L
PT* >50 seconds	PT >60 seconds	Rising PT

Non-paracetamol induced hepatic failure

- Presence of hepatic encephalopathy (any grade)
- PT >30 seconds
- Presence of renal failure (serum creatinine >150μmol/L)

* PT: prothrombin time

A number of prognostic indices have been compiled using these criteria to allow clinicians to readily identify and intervene in those patients who would almost certainly die without OLT. When OLT is performed in patients with fulminant hepatic failure who satisfy these clinical criteria, the survival is in the order of 75%.

Peptic ulceration accounts for over 50% of cases of upper gastro-intestinal bleeding. Dr Peter Fairclough outlined some of the advances in management over the past 20 years. The initial assessment of patients has been improved by the introduction of clinically validated risk scores such as that described by Rockall *et al*.[2] Risk stratification enables the clinician to administer appropriate treatment to those with significant bleeds and arrange safe, early discharge for less serious cases.

Drug therapy plays a limited role in the management of peptic ulcer bleeding. The anti-fibrinolytic drug, tranexamic acid and acid suppression with H2 receptor antagonists and with proton pump inhibitors have all been shown to be modestly superior to placebo. They may be of some benefit in those situations where endoscopy is not readily available, but are not acceptable as an alternative to endoscopy.

In the developed world, endoscopy is central to the treatment of peptic ulcer bleeding as it allows prompt diagnosis of the source of bleeding in the majority of cases. In addition, the endoscopic appearance of an ulcer crater, whether clean-based or with evidence of a vessel or actively bleeding at the time of endoscopy, gives important prognostic information about the risks of re-bleeding and mortality when incorporated into the full Rockall score.

A variety of treatments may also be applied directly to the bleeding ulcer via the endoscope to achieve haemostasis. These fall broadly into the categories of injection therapies (using adrenaline, sclerosant solutions or tissue glue) and thermal therapies (such as heater probes, electrocautery or laser therapy). A combination of both thermal and injection therapy is likely to give the best results. Endoscopic therapy reduces re-bleeding rates, the need for surgery and, ultimately, mortality.

As peptic ulceration is on the decline in the Western world, perhaps as a consequence of better hygiene and declining rates of *Helicobacter pylori* carriage, the challenge for the future is to prevent iatrogenic ulceration. In the US, the number of deaths as a consequence of gastro-intestinal complications of non-steroidal anti-inflammatory drugs (NSAIDs) is only marginally less than the number of deaths due to leukaemia. Enteric coating and rectal administration of NSAIDs do not protect against ulceration, but increasing awareness of the potential hazards of NSAIDs, co-prescription of 'gastro-protective' agents and the use of selective cyclo-oxygenase-2 (COX-2) NSAIDs may be of greater benefit.

Session 2

DIFFICULT PROBLEMS IN GASTROENTEROLOGY

Chairman: Professor David Webb, Edinburgh

The presence of ascites in patients with hepatic cirrhosis carries a very poor prognosis with a mortality of 50% at two years. In addition, during the first year from onset of ascites, patients have an 18% risk of developing the hepato-renal syndrome (HRS). The survival of patients with established HRS is less than 10% at ten weeks.[3] Ascites develops as a consequence of portal hypertension, and particularly of sinusoidal hypertension. Lymph production is increased to the extent that the capacity for its transport in the thoracic duct is exceeded. This is then further diluted by free water from the splanchnic bed.

Hepatic cirrhosis is associated with a number of haemo-dynamic changes, all of which contribute to peripheral arterial vasodilatation. This in turn triggers a cascade of homeostatic mechanisms, including activation of the sympathetic nervous system, the renin-angiotensin-aldosterone system and non-osmotic release of vasopressin. The result is an increase in cardiac output, increased arterial (and renal) vascular resistance and retention of free water and sodium. The precise cause of the initial vasodilatation remains unclear, but many possible vasoactive substances, including nitric oxide (NO), have been implicated.

The established therapeutic options for ascites begin with conservative treatments such as bed rest, dietary sodium restriction and inducing natriuresis with combinations of diuretics including spironolactone, frusemide and even metolazone. Experimental interest is presently focused on agents such as Niravolin, which promotes the excretion of free water and hence avoids the problems of hyponatraemia seen with diuretic therapy. When patients are diuretic resistant or diuretic intractable, the clinician must consider invasive or 'extra-corporeal' treatments. Repeated abdominal paracentesis with intravenous fluid expansion is an effective therapy but can be uncomfortable for the patient and carries a risk of bacterial peritonitis. Attempts to reduce sinusoidal pressure by Transjugular Intrahepatic PortoSystemic Shunting (TIPSS) have had mixed results; TIPSS is only effective in around two-thirds of patients with ascites. In controlled trials comparing paracentesis with TIPSS, patients with advanced cirrhosis (Child's Grade C) treated with TIPSS had a higher mortality. Since the presence of ascites reflects very poor hepatic function, Orthotopic Liver Transplantation (OLT) would appear to be a logical treatment and is very effective in those patients who are suitable for transplantation.

KEYPOINTS

- Ascites reflects decompensated liver disease and carries a poor prognosis
- Conservative therapy with bed rest, sodium restriction and diuretics may be tried in the first instance
- 'Extracorporeal' treatments such as paracentesis, TIPSS or OLT may be required in refractory ascites
- Patients with refractory ascites and advanced cirrhosis (Child's Grade C) are better treated by repeated paracentesis than by TIPSS

Gastroenterologists are becoming increasingly aware of bone disease in patients with inflammatory bowel disease and coeliac disease. The World Health Organisation defines osteoporosis as a bone density which is more than 2·5 standard deviations below peak bone mass. The risk of a fracture at all sites doubles with each standard deviation decrease in bone density.

The scale of the problem is hard to define since different methods and definitions are used in many studies, which makes comparisons difficult. Undoubtedly, the prevalence of osteoporosis is greater than in the 'normal' population.

The use of corticosteroids, malnutrition, hypogonadism and a general lack of physical activity due to malaise all contribute to decreased peak bone mass and increased bone loss in patients with inflammatory bowel disease. The inflammatory process itself may also play a role via the effects of pro-inflammatory cytokines such as interleukin-1 (IL-1) and tumour necrosis factor-α (TNF-α).

In a study of 845 patients, Vestergaard[4] found a 2·5-fold increase in the relative risk of fracture in females with Crohn's disease. No increased risk was seen in ulcerative colitis. Klaus *et al*.[5] describe a high incidence of vertebral deformities in patients with Crohn's disease. Twenty-five out of 128 patients had more than one deformity but only four were symptomatic.

Treatment should begin with general measures such as minimising the use of corticosteroids, advocating plenty of exercise and avoiding alcohol and smoking. Malnutrition should be corrected and hormone replacement therapy (HRT) given if there is evidence of hypogonadism. Calcium supplements may be of some benefit. A number of specific drug therapies have been used. The evidence for any beneficial effect of calcium and vitamin D supplements is patchy. Hormone replacement therapy may help to reduce bone loss in post menopausal women. Alendronate has been shown to increase the bone mineral density of the lumbar spine in patients with Crohn's disease, but the effectiveness of bisphosphonates is still largely unproven in patients with inflammatory bowel disease. Concerns exist about their toxicity to the oesophagus and their low bioavailability (<1% at best) which may be further lowered in inflammatory bowel disease.

Corticosteroid-induced osteoporosis is a major concern for clinicians and patients. A recent study by Van Staa *et al*.[6] showed that patients taking between 2·5 and 7·5 mg of prednisolone per day, doses previously thought to be relatively safe, were at increased risk of fracture. There is no evidence that the use of calcium and vitamin D supplements can prevent the development of osteoporosis in steroid treated patients. A number of important questions remain unanswered, including the risks to patients who require frequent short courses of steroids or those patients who require long-term parenteral nutrition.

Professor Guido Tytgat delivered the Davidson Lecture on the subject of gastro-oesophageal reflux disease (GORD) and its consequences. Gastro-oesophageal reflux disease is a common problem affecting up to one in five individuals in the UK. Contrary to previous opinion, the incidence of GORD in the UK has remained stable, affecting 21% of the population in 1976 and 16% in 1999. Endoscopic assessment of GORD can be misleading as 50% of patients will have no endoscopic abnormality. The most reliable and reproducible endoscopic classification of oesophagitis is the Los Angeles classification described by Lundell[7] in 1999 which eliminates unreliable 'minor changes' at endoscopy. The most severe endoscopic grades are usually seen in older, overweight, male patients who are negative for *Helicobacter pylori* and who tend to have severe symptoms.

KEYPOINTS

- Osteoporosis is common in patients with inflammatory bowel disease
- General preventative therapeutic measures include minimising use of corticosteroids, increasing exercise, decreasing smoking and alcohol intake and the correction of malnutrition and hypogonadism
- Specific therapies include HRT (for postmenopausal women) and bisphosphonates
- Primary prevention should be considered in older, poorly nourished patients or those taking more than 15 mg of prednisolone for three months or more
- Secondary prevention should target those patients with a DEXA T-score <1·5 or who have already suffered a low impact fracture

The importance of lifestyle advice has been played down in recent years, but such advice can do little harm and should be given in association with any other therapeutic measure.

Studies using oesophageal manometry have shown increased frequency of transient lower oesophageal sphincter relaxations (TLOSRs) in patients who complain of GORD. Conventional prokinetic drugs such as cisapride have no effect on TLOSRs and have been withdrawn due to their cardiac side-effects. However, a fruitful area of recent research has been the role of gamma aminobutyric acid (GABA) as a neurotransmitter for the lower oesophageal sphincter (LOS). Molecules similar to baclofen can activate the GABA-B receptor and reduce the frequency of both TLOSRs and reflux episodes. These properties may form the basis of future therapies for GORD.

Acid suppression has conventionally been the mainstay of treatment of GORD. A step down approach to treatment beginning with proton pump inhibitor (PPI) drugs to control symptoms is better for the patient, and probably more cost effective. H2 receptor antagonists may be of some benefit but tachyphylaxis soon develops. The timing of doses of PPI is important; once daily doses should be given before breakfast or, if twice daily dosing is necessary, the second dose should be given before the evening meal. Nocturnal acid breakthrough can still occur in spite of twice daily dosing. The addition of an H2 receptor antagonist before bedtime may give some additional benefit.

Surgery provides an alternative for those patients who gain no benefit from or are intolerant of medical therapy. Surgical repair of a hiatus hernia may be of benefit as it brings the LOS back into anatomical proximity to the crura of the diaphragm in a situation which is analogous to the anal sphincter mechanism. However, the results of anti-reflux surgery are less predictable than those of medical therapy, with post-operative dysphagia being the most common problem.

KEYPOINTS

- GORD is a common problem, affecting one in five people in the UK
- GABA was identified as a neurotransmitter for the lower oesophageal sphincter
- Baclofen, which activates GABA-B receptor, reduces reflux episodes
- Timing of doses of PPI is important
- Patients taking PPI who experience nocturnal breakthrough reflux may benefit from the addition of an H2 receptor antagonist
- Results of surgery are less predictable than drug therapy

Session 3

EXAMINING THE GI TRACT

Chairman: Dr William Ruddell, Falkirk

In the early days of gastroenterology, very limited information in terms of imaging was available regarding the anatomy of the gastrointestinal tract and its associated organs. The advent of flexible endoscopy changed that, but now newer technology in the form of powerful cross-sectional imaging techniques is changing the way we acquire the information we require to make management decisions.

Professor William R. Lees treated the audience to a display of the latest advances in imaging of the intestine and biliary tree. Considerable improvements in both hardware and computer software have facilitated the rapid acquisition of images by magnetic resonance imaging (MRI), allowing high quality imaging of the pancreas and biliary tree. This is particularly helpful in staging cholangiocarcinomas and in defining the complications of acute pancreatitis such as phlegmon or pseudocyst.

Like ultrasound, MRI is a dynamic technique and the results obtained depend on the interaction between radiologist and patient. Administration of intravenous secretin stimulates pancreatic secretion which distends the duodenum and acts as a contrast medium. The volume of pancreatic juice in the small bowel can be calculated, giving some measure of pancreatic function.

Multislice computed tomography (CT) represents the single most important advance in cross-sectional imaging. The addition of extra rows of detectors within the scanner allows for increased speed of scanning and gives finer definition of structures. Huge amounts of anatomical data are generated. Software advances mean that images can be reconfigured in a variety of different planes to resemble a barium follow-through or enema (CT pneumocolon), or allow a luminal, virtual endoscopic view of the intestine. Views are not restricted to these conventional images but can also be used to show details of lesions within the mesentery or intestinal wall. In comparisons with conventional barium studies, CT pneumocolon is better tolerated by patients and provides more information. Patients are exposed to less radiation than during a barium enema, and, at the Middlesex Hospital at least, the procedure is cheaper than a colonoscopy. The development of faecal 'tagging' techniques may obviate the need for bowel preparation altogether.

A good economic argument can be made for using this technology for colorectal cancer screening. To screen those aged 50–65 every five years in a population of 500,000 would require four scanners performing 30–40 scans per day. This would generate 3,000 extra colonoscopies per year. The estimated cost per year of life saved is £2,000.

Dr Brian Saunders made the case for colonoscopy, a more conventional and widely available form of colonic imaging. Colonoscopy is now accepted as the investigation of choice for suspected colonic disease, offering both diagnosis and potential therapy in a single procedure.

Demand for colonoscopy is increasing steadily. Data from St Mark's Hospital, Harrow show that 4,000 procedures were performed last year, twice the number performed in 1998. If the national pilot programmes for population screening for colonic cancer by use of faecal

occult blood testing are adopted nationwide, some 77,000 extra procedures per annum are likely to be generated.

The British Society of Gastroenterology National Audit of colonoscopy suggests that training in colonoscopy could be greatly improved. Concern was expressed particularly over the number of trainees who perform colonoscopy under minimal or no supervision. The manner in which colonoscopy is taught may need to change, moving more towards the establishment of regional centres with special responsibility for training. More use should be made of emerging technology such as colonoscopic simulators and tri-split video assessment to pass on both the knowledge and hand skills required for safe, effective colonoscopic practice.

Dr Ian Penman presented a balanced view on the importance of endoscopic surveillance of Barrett's oesophagus, a complication of chronic GORD. The incidence of adenocarcinoma of the oesophagus is on the increase in Europe, nowhere more so than in the UK,[8, 9] and columnar metaplasia of the distal oesophagus or Barrett's oesophagus has been suggested as a major risk factor for this malignancy. However, as stated earlier in the Davidson Lecture, the incidence of malignant transformation in Barrett's oesophagus may have been exaggerated in the past. Post mortem studies[10] suggest that Barrett's oesophagus may be present in up to 1% of the adult population, so only one case in 20 is being diagnosed endoscopically at present. Most patients with a Barrett's oesophagus (in excess of 95%) will die of other causes. Barrett's associated malignancy is commonest in older white males, particularly those who are smokers or have long segments of metaplasia.[11] Patients with complications such as a Barrett's ulcer or stricture are also at increased risk.

KEY POINTS

- Incidence of adenocarcinoma of the distal oesophagus is rising, particularly in the UK
- The risk of malignant transformation of Barrett's oesophagus is between one in 200 and one in 250 patient years
- In terms of cost benefit, five yearly endoscopic surveillance compares favourably with cardiac transplantation, but is five times more expensive than screening for colonic cancer

Endoscopic screening of Barrett's oesophagus should only be undertaken in those who have histological evidence of specialised intestinal metaplasia and who are fit to undergo oesophago-gastrectomy should it be required. However, the screening process is prone to many problems. The interpretation of dysplasia in biopsies is subjective and observer-dependent. The metaplasia dysplasia adenocarcinoma sequence is less well defined than in the colon and not every patient with low-grade dysplasia will go on to develop high-grade dysplasia or adenocarcinoma. Cost utility analysis data from the US suggest that a screening endoscopy every five years would cost $98,000 for each quality adjusted life year saved, comparing favourably with such interventions as cardiac transplantation, but five times more expensive than breast or colon cancer screening.[12]

In a world of limitless resources there would be no question over whether to survey patients with Barrett's oesophagus. However, in the real world in which every day 17 people die because of Barrett's associated cancer, while 137 die because of colorectal cancer, one must be mindful of how our limited resources are allocated.

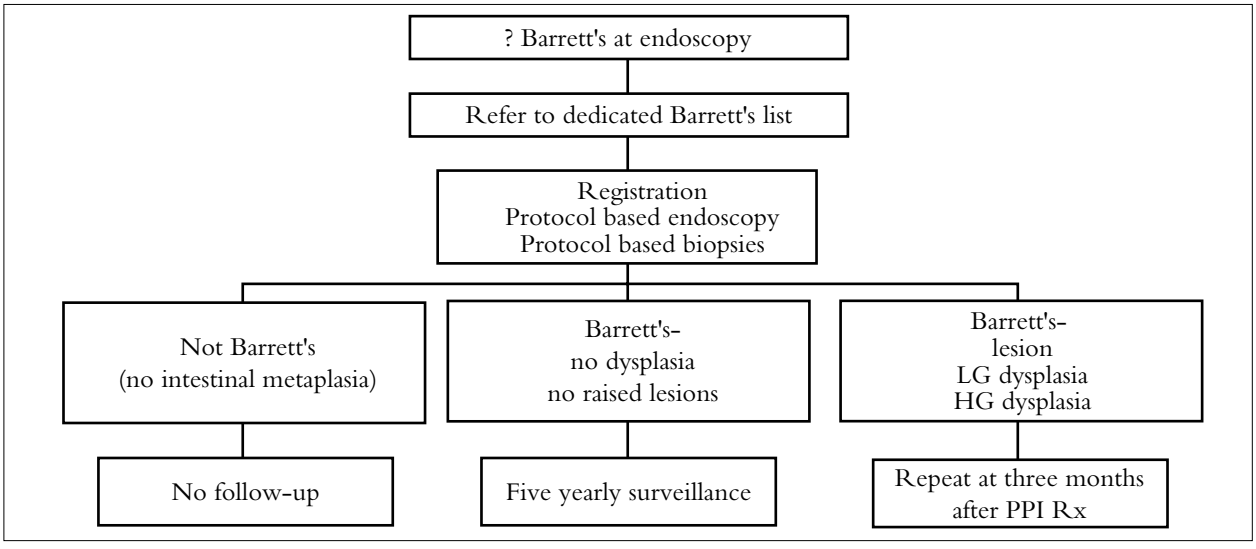

FIGURE 1
Suggested algorithm for management of Barrett's oesophagus: Edinburgh practice.

Session 4

EXPENSIVE THERAPIES – ARE THEY JUSTIFIED?

Chairman: Professor El-Omar, Aberdeen

Rationing of resources is a reality in every sphere of life. As basic science continues to unravel some of the molecular pathways of common diseases, ever more sophisticated investigations and refined therapies appear, but all this comes at a considerable price. Increasingly, such therapies are becoming commonly used in inflammatory bowel disease, viral hepatitis and in the field of organ transplantation. Can these expensive therapies be justified for the few when resources are limited? Does the end result justify such expenditure? These questions were addressed in the final session of the day.

Professor Stefan Schreiber postulated that within a susceptible host, the development of inflammatory bowel diseases may be viewed as the consequence of abnormal interactions between a dysfunctional intestinal mucosal barrier and the contents of the intestinal lumen, e.g. dietary components or bacteria. Such interactions may stimulate the release of a variety of pro-inflammatory cytokines including IL-1β, IL-12, IL-8 and TNF-α.

TNF-α is over-expressed in patients with inflammatory bowel disease, and those with higher serum levels of this cytokine are at greater risk of relapse. Activation of the nuclear factor κB (NFκB) by bacterial lipopolysaccharide (LPS) initiates transcription of inflammation genes and production of TNF-α. Conventional therapies such as 5-aminosalicylic acid drugs and corticosteroids work by inhibiting this pathway, but attention has been focused on improving results and reducing long-term side-effects by more specific blockade.

Anti-TNF-α antibodies have been used to great effect in patients with Crohn's disease. Dramatic improvements have been seen with mucosal healing of colonic disease and closure of fistulae. Its great cost has meant it has been reserved for those patients refractory to other therapies, but even in this difficult group 33% achieve full remission and 60% experience some improvement. The effects are relatively short lived, and following a single intravenous infusion remission rates fall off from 88% at one week to 21% by eight weeks post treatment. Remission rates can be maintained by repeated administration, but even then after the fourth treatment effectiveness begins to wane. This is likely due to production of neutralising antibodies by the host. Concerns have been raised over the long-term safety of such profound suppression of host immunity, especially the potential increased risk of lymphoproliferative disorders and malignancies. These fears do not seem to be justified but chest infections and even tuberculosis have been reported as complications resulting from this treatment. Other novel therapies include IL-10 which was effective in a placebo-controlled trial but was most effective in those patients with the most active disease. β-interferon also showed some promise but again proved useful only in certain sub-groups.

The future is bright with a host of new molecules to target, including IL-12 and IL-1 receptor antagonist as well as new molecules to block other cytokines such as IL-18.

These therapies are effective but undeniably expensive; they do not work universally in all patients, being effective only in sub-groups, and have considerable potential for side-effects. Genetic probes should allow easier identification of the sub-groups that would benefit from them in the future. Patients with mutations of the gene coding for the tumour necrosis factor receptor-II have been shown to respond poorly to treatment with anti-TNF-α.

Dr David Mutimer reminded the audience that anti-inflammatory biological molecules have been used in the treatment of viral hepatitis for many years. The original description of the use of α-interferon for treatment of what was then known as non-A, non-B viral hepatitis was published by Hoofnagle in 1986.[13] Monotherapy with α-interferon reduced serum levels of transaminases but many patients relapsed when treatment was stopped. A sustained response to treatment is now defined as normal transaminase levels and no Hepatitis C virus (HCV) RNA detectable by polymerase chain reaction.

A meta-analysis of 25 trials performed using monotherapy with α-interferon favoured treatment overall, but it was noted that responses were better when higher doses of interferon were given, and worse when the studies contained large numbers of cirrhotic patients.

The HCV genotype is an important determinant of response. Interferon can eradicate the virus in the majority of those with genotype 2 or 3 (who make up 50% of those with HCV in the UK) and in 50% of those with genotype 1. Even in the absence of a virological cure, treatment can improve overall survival, slow the fibrotic process, reduce progression of cirrhotic patients from Child's Grade A to Grade B and reduce the risk of development of hepatocellular carcinoma.

Using ribavirin in combination with α-interferon can improve the sustained response rate but will also increase the side-effect profile of antiviral therapy. It is important to tailor the doses of both interferon and ribavirin to an individual patient according to their weight in order to achieve the best chance of effective therapy.

Mr Stephen Pollard brought the symposium to a close with an overview on small bowel transplantation. Early experience of this procedure in the 1960s was disappointing due to a combination of difficulties controlling rejection and the need to operate on very frail, nutritionally compromised patients in the days before safe, effective parenteral nutrition. The first successful procedure, a combined liver and small bowel transplant, was performed in 1990.[14] The advent of the immunosuppressive drug tacrolimus allowed for better control of rejection.

KEYPOINTS

- Combination therapy of HCV with α-interferon and ribavirin is effective
- Virological cure is possible in most cases of genotype 2 and 3 (50% of those in UK) and in 50% of genotype 1
- Even in the absence of a virological cure, α-interferon therapy slows progression of fibrosis and cirrhosis and improves survival in HCV

In the UK, small bowel transplantation is viewed as the final option for patients with intestinal failure. Since survival post-transplant is still worse than survival on long-term parenteral nutrition, parenteral nutrition remains the treatment of choice. Fourteen cases have been performed

in the UK to date, against a background of 350 patients worldwide. It was originally estimated that nationwide there may be between 50 and 60 individuals who required long-term parenteral nutrition per annum, and assumed that half of these may require transplantation. However, partly due to considerable variation in the use of home parenteral nutrition across the UK, only three cases are performed annually.

Multiple episodes of acute rejection are common and tolerance to the graft takes a long time to develop. Another major problem is that of post-transplant lympho-proliferative disorder (PTLD), a condition driven by infection with Epstein-Barr virus. The five year survival of small bowel transplantation stands currently at 40%, but this is better than other organ transplant programmes at a similar stage in their development.

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