

Liver

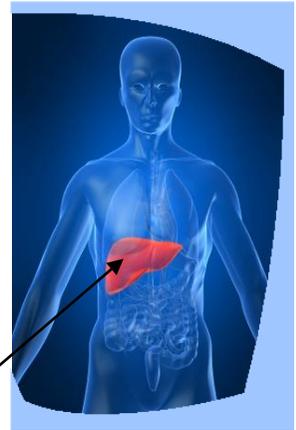
F.O.C.U.S

Factual, Open, Current, Useful, Straightforward

Welcome to the first edition of *Liver Focus!* Published twice yearly, it will **INFORM** you about the research taking place into liver disease at the Centre for Liver Research and the National Institute for Health Research Biomedical Research Unit in Birmingham. It provides **UPDATES** on the progress of studies and **HIGHLIGHTS** other work and activities that have been taking place. This newsletter promises to cut through the medical jargon and provide you with useful information in plain English.

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The Liver

Your liver: the facts

- It is the second largest organ in your body (the skin is first).
- The average liver weighs 1.5 kg (3.3lb).
- It is the body's 'engine' and performs over 500 different chemical functions.
- It filters over a litre of blood a minute. The blood comes from the gut as well as from the general circulation and this allows the liver to take up and process nutrients as well as filtering out harmful toxins.
- It makes the body's building blocks and regulates fat and sugar storage.
- It removes toxins entering from the bloodstream through eating, drinking and breathing. It converts these toxins into harmless substances that can be excreted in the urine or stool. Toxins include pesticides, cigarette smoke, alcohol and environmental chemicals.
- Liver disease is the fifth biggest cause of death in England and Wales.

There are a number of conditions that can damage the liver and lead to liver disease. These include:

- infections with viruses such as hepatitis B or C;
- drinking too much alcohol;
- obesity and some forms of diabetes which cause fatty liver disease;
- autoimmune diseases in which the patient's immune system, which is designed to fight infection, instead turns on liver cells.

Medications, prescribed drugs, illegal drugs and also herbal medicines can cause serious liver damage in some patients. Other causes of damage include genetic diseases where the patient is born with a defect which leads to the accumulation of toxic factors in the liver, such diseases include genetic haemochromatosis (excess iron); Wilson's disease (excess copper) and alpha I anti trypsin deficiency.

If liver damage persists the liver becomes inflamed (hepatitis) and eventually scarred (cirrhosis). Cirrhosis is not a disease itself but the final stage of all of the above conditions. If liver damage is severe the liver fails and is unable to make vital proteins/blood clotting factors, remove toxins and store energy. Liver disease can affect individuals in different ways. The majority of liver diseases do not show symptoms until the liver is severely inflamed or damaged, meaning that health professionals need to be aware of the possibility of liver disease, ask specific questions and order tests to look for early signs when the disease may still be treatable. Symptoms of liver disease can include tiredness, itching, yellow skin (jaundice), loss of muscle and body fat, bruising and in the advanced stages fluid retention, kidney failure, bleeding and confusion.

A Current Study

Clinical trials have strange titles, are packed full of medical terms and the jargon can make them difficult to understand. So here is a clear introduction to one of the current studies taking place at the Centre for Liver Research, NIHR Biomedical Research Unit, Birmingham

LEAN Study *(as featured on Midlands Today, October 7th 2011)*

Liraglutide's **E**ffect and **A**ctions in **N**on-alcoholic Steatohepatitis

Non-alcoholic fatty liver disease (NAFLD) is now the most common cause of liver disease in the western world. It occurs as a consequence of obesity and diabetes when fat deposited in the liver stimulates a harmful response termed steatohepatitis. There are currently no safe and effective drug therapies available for patients with the more severe forms of this disease.

LEAN is a study which investigates a new anti-diabetes drug, called Liraglutide, which was developed by the pharmaceutical company Novo Nordisk. It has been modified to mimic a naturally occurring hormone that is produced in humans after eating food. It comes in liquid form and has to be given by injection into the skin overlying the arm, thigh or the tummy. Injections are required once a day. The drug was originally developed for treating diabetes however, studies in rats and mice suggest that this drug may also be effective in liver disease. The drug works by improving the body's response to insulin, decreases appetite and slows the stomachs emptying of food, which in turn can cause weight loss. The latter has been shown in overweight patients with and without diabetes.

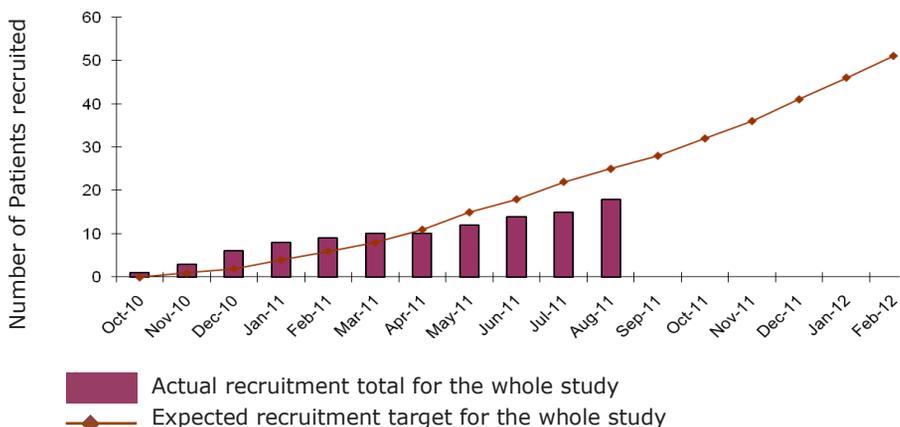
Liraglutide has been shown to improve liver blood tests in diabetics. This, in conjunction with the experimental studies in mice and rats indicates that Liraglutide

may be a safe, novel treatment for patients with the more severe forms of fatty liver disease.

LEAN has been funded from a charity Wellcome Trust Fellowship programme. It aims to investigate whether 48 weeks' treatment with Liraglutide can reduce the amount of liver disease activity in patients with NASH (non-alcoholic steatohepatitis). NASH is a more aggressive form of NAFLD that can cause scarring (fibrosis) to the liver, which might progress to cirrhosis, which in turn can cause irreversible liver damage.

The aim is to treat 50 adult patients (with or without diabetes) who are currently under the care of liver specialists in the UK for fatty liver disease. Recruitment for this trial is likely to end in December 2012.

To request eligibility information for this study, please email: Liverresearch@contacts.bham.ac.uk



Highlighting Liver Research in the Big Apple



The Centre for Liver Research has received a generous donation of £1000 from marathon runner Éimhín Ní Mhuircheartaigh. Éimhín, who is a market risk analyst, completed the 41st New York Marathon and raised £2000, half of which has been given to the Centre for Liver Research at the University of Birmingham.

Éimhín was keen to donate some of the money raised to research as she has seen first-hand how liver disease can affect lives. "Supporting liver research is important to me as I have unfortunately seen the terrible effects of the condition primary sclerosing cholangitis (PSC)." Research is crucial if we are to develop better treatments and ways of preventing liver disease. Éimhín ran the 26 mile (42 km) course in 4.46 hours under difficult circumstances having sustained a knee injury after 90 minutes and running the remaining three hours in pain. "It was a great feeling crossing the finish line – despite being in agony!" Éimhín's donation has been gratefully received by the Centre for Liver Research and will help the team continue their work to understand the cause of PSC and to develop treatment for this devastating disease.

Volunteering at the Centre for Liver Research Biomedical Research Unit, Birmingham

Amross Richards tells us about his experience at this leading specialist liver unit



Two weeks may not seem like a long time, but the knowledge I gained during two weeks volunteering at the Liver Trials Unit has had an inspirational and profound effect on my ambitions and future career path. This introduction to clinical trials really highlighted to me how involved, detailed and precise these studies are from start to completion.

Being able to see the end result of many years of scientific research in the form of new treatments was incredibly rewarding. During my two weeks I had the opportunity to shadow various professionals at the Unit who imparted to me their experience and knowledge which made the placement very educational.

What made the experience most rewarding was having the opportunity to meet patients participating in studies; they offered me a unique perspective into being part of a clinical trial and reinforced how these studies and potential breakthroughs can give hope, transform lives and save lives.

Working in the Liver Trials Unit Birmingham was an enjoyable and insightful experience. Following the voluntary work I became a member of the Patient and Public Involvement panel (known as PPI). This group meets several times a year to hear how the liver studies are progressing. We provide our

opinions and advise doctors how we feel the results of these studies should be relayed to patients and members of the public. Being part of the PPI panel gives me an ongoing opportunity to develop my knowledge and impact on the development of future studies. As an undergraduate nearing the end of my degree I would wholeheartedly recommend the experience to any student interested in liver research.

If you would like to register your interest in joining the PPI voluntary liver review panel, then please contact us at the email address on the back page.

FOCUS ON: Professor David Adams

Head of the Centre for Liver Research, Birmingham



David Adams is Professor of Hepatology and Director of the Centre for Liver Research and the NIHR Biomedical Research Unit for Liver disease at the Queen Elizabeth Hospital. His clinical interests are liver transplantation and autoimmune liver disease. He is on the editorial boards of several international scientific journals that publish papers on liver disease.

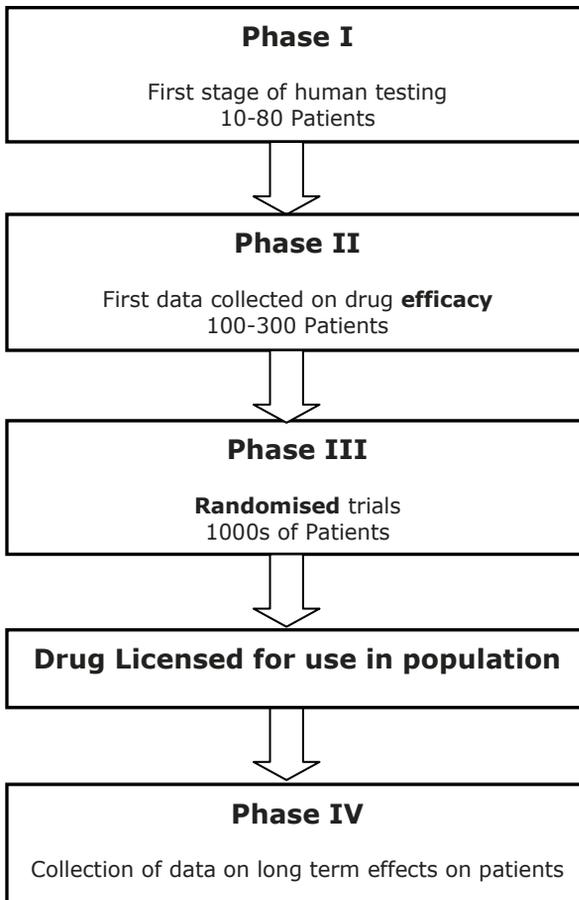
On the basis of his research into liver disease he was made a Fellow of the Academy of Medical Sciences in 2000. David has a long-standing interest in understanding how the immune system can cause liver damage in liver disease. He and his teams are using their research findings to find out more about the causes of liver disease and to develop new treatments.

Terminology, Lingo, Jargon, GobbledygookWhatever you call it, it can be confusing!



Here is our helpful breakdown of each stage of a clinical trial. Key words are in bold and explained below

The Clinical Trial:



Phase I: This is the first stage of human testing and is usually performed on a small number of patients (usually 10-80). This stage assesses:

- Safety and side effects
- How the treatment is absorbed and utilised by the body
- Which body systems are involved in the excretion of the drug from the body e.g. kidneys (urine production processes).

Phase II: Once the initial safety of the drug or treatment has been ascertained, phase II trials are performed on between 100-300 patients. Phase II assesses:

- How the treatment works in the body.
- Information on safety, side effects and limited data on **efficacy**.

Phase III: This stage can include thousands of patients and is usually **randomised**. Phase III studies provide a more thorough understanding of the effectiveness, risks and benefits of the drug or treatment, as well as a range of possible reactions and side effects. Only after successful completion of this phase can a treatment be used in the general population.

Phase IV: In this phase rare or long term effects can be assessed as the treatment is in general use.

Efficacy: How well the treatment affects the disease.

Randomised: A trial is randomised when some patients are randomly assigned one of a number of treatment options in the study. The patient or doctor does not select which treatment is used. In some cases no treatment or a **placebo** is one of the options. A trial may be **blinded**.

Placebo: A harmless substance which has no medical effect.

Blinded: This means that neither the doctor, nurse nor the patient knows whether the placebo or the treatment is being administered.

Have we missed off any medical terms that you would like explaining?
Then let us know!

Email: Liverresearch@contacts.bham.ac.uk.

Useful web links:

www.liver.bham.ac.uk and www.britishlivertrust.org.uk

Questions and Feedback

- Do you have any questions or comments?
- Have you undertaken any fundraising work for liver research?
- Do you want to suggest an item for the next edition of Liver Focus?

If so, please contact Diana Hull at the Centre for Liver Research on Liverresearch@contacts.bham.ac.uk or Donna Wiles on 0121 414 6955

And Finally ...

Congratulations to everyone who took part in the Birmingham BUPA half marathon on the 23rd October and raised funds for liver research!



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Produced by the Patient & Public Involvement liver review panel