

The Clinical Trials and Evaluation Unit (CTEU) continued to grow during 2009-2010. Three clinical trial co-ordinators, two trainee co-ordinators, a research fellow, a medical statistician and two database managers have joined the team. The unit now has 25 staff members who contribute to the management of leading clinical research. The CTEU currently has ten randomised control trials which are recruiting patients and two which are being set up. This newsletter will focus on the progress of a selection of these trials.



Cardiac Surgery: On-Pump or Off Pump?

Traditionally, coronary artery bypass surgery is carried out 'on-pump'. This involves stopping the heart, and using a heart-lung machine (pictured) to pump the blood around the body. However, some surgeons prefer to carry out the operation 'off-pump', meaning that surgery is performed without using a heart-lung machine and without stopping the heart.

Previous studies comparing these two types of surgery found no difference in the risk of death between the two methods, but did show that the risk of complications was less with off-pump surgery. These studies were mainly in patients without other health problems. They did not include patients who have a slightly increased risk of surgical complications due to factors such as their age and current health state.

The purpose of the **CRISP** trial is to find out which method is best for these 'high risk' patients. We started recruitment in November last year and plan to recruit 5,400 patients worldwide. Here in the BHI we are looking to recruit 200 patients over 2 years. There are currently 5 other UK centres taking part and many more centres are preparing to start. Centres overseas are also going to join and we have already had interest from centres in Brazil, Hungary, Canada, Australia and USA.



ProMPT

Can General Anaesthetic Protect the Heart During Cardiac Surgery?

During on-pump cardiac surgery, cardioplegia (heart stopping) solution is injected in to the heart and a heart-lung machine is used to pump blood around the body. This allows the surgeon to operate while the heart is still and bloodless. However, when the blood flow to the heart is restarted, damage to the heart can occur. The damage is mainly caused by highly reactive molecules known as 'free radicals', which are formed in the heart muscle when it is stopped. It has been suggested that propofol, a general anaesthetic, can protect the heart against this damage.

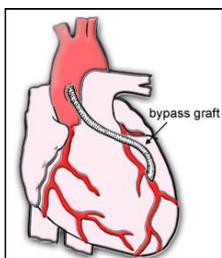
The purpose of the **ProMPT** trial is to assess the benefits of adding propofol to the cardioplegia solution. We will do this by studying chemicals released by the heart and other organs in the body when they are damaged or stressed. Ninety-six patients having surgery in the BHI will be randomised to receive cardioplegia containing propofol or not.

HARVeST

Increasing the Life of Bypass Vein Grafts

Up to 40% of vein grafts created during coronary artery bypass surgery become blocked within 12 years, causing angina symptoms to recur and increasing the risk of heart attack and death. When the vein is taken from the leg it is current practice to remove the fat surrounding the vein and to check the vein for leaks by filling it with fluid at high pressure.

Recent research suggests that the fat surrounding the vein may be important for the health of a vein graft and that filling it at high pressure may cause damage to the inside lining of the vein.



Alternative techniques that involve removing the vein with its surrounding fat and testing for leaks at lower pressure are being compared with current practice in the **HARVeST** trial. Ninety-six patients will be recruited from the BHI and will be followed for one year after surgery, during which time they will have detailed investigations of their vein grafts. So far 10 patients have joined this trial.

Blood Conservation Research

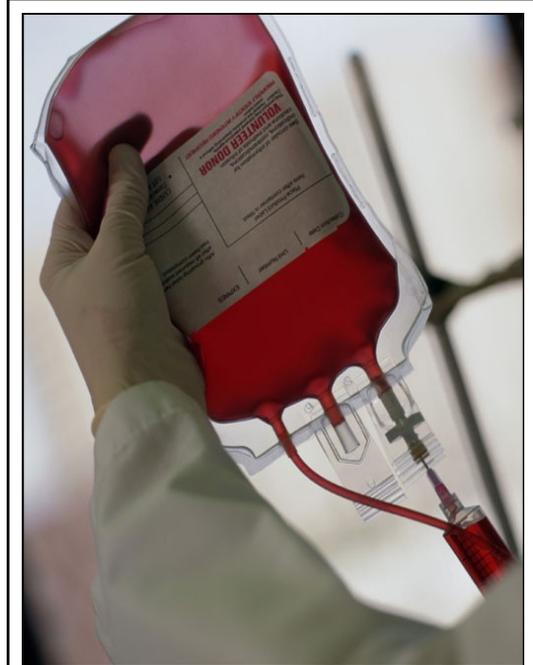
Last year, we explained how we were preparing to start the TITRe2 trial (now recruiting well!), which aims to help doctors to maximise the benefit from blood transfusions after cardiac surgery. Mr Murphy (one of the academic surgeons) has been successful in obtaining an additional £1.75m in funding for further research into how to optimise the use of blood in cardiac surgery. Two of these studies which the CTEU is coordinating (COPTIC and PASPORT) are described below.

COPTIC

Improving How Blood is Analysed and Used During Cardiac Surgery

6% of blood donated in the UK is used for blood transfusions during and after heart surgery. One major reason for this high statistic is that heart surgery patients often have abnormal blood clotting. The **COPTIC** research project is part of the NHS strategic priority to look at improving how blood is used.

Over the 2-years from April 2010 until March 2012, all heart surgery patients at the BHI are being asked to donate two small blood samples, which will be taken at the start and the end of their operation. Tests of how well the blood from each of these samples clots will help us to find out how useful it is to perform the tests. It will also allow us to look at how abnormal blood clotting results relate to the amount of bleeding and other complications after surgery.

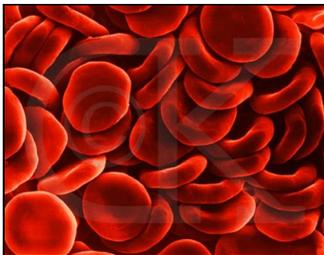


PASPORT

Measuring Oxygen Levels to Decide When a Patient Needs a Blood Transfusion During Cardiac Surgery



During on-pump cardiac surgery it is important to ensure that a patient's organs are receiving the correct amount of oxygen. At present, counting a patient's red blood cells (the 'haematocrit' level) is the standard method of measuring the oxygen level. When the haematocrit drops below a certain level (threshold) a transfusion is given. This threshold is the same in all patients. This may not be the best method because the oxygen supply to an individual organ can be low (which can cause injury) while the overall haematocrit level remains within the normal range. On the other hand, transfusing blood unnecessarily may cause the body more stress and reduce its ability to fight infection.



In the **PASPORT** trial a patient-specific method for deciding when to transfuse, based on the amount of oxygen reaching the brain during the operation, is being compared with the standard method using the same threshold for transfusion for all patients. We will use 'near infra-red spectroscopy' (NIRS) to monitor oxygen levels in the brain and help guide surgeons in transfusion decisions. This is a non-invasive technology that is thought to be the best device for measuring oxygen supply.

The trial is due to recruit 150 patients from the BHI who are having valve or combined valve and coronary surgery. We will investigate whether using NIRS to guide decision making improves oxygen levels in the brain and reduces complications. So far 13 patients have joined the PASPORT trial.

Gratefully acknowledging the support of:

- ◆ British Heart Foundation
- ◆ NIHR
- ◆ Garfield Weston Trust
- ◆ MRC
- ◆ HTA



Clinical Trials and Evaluation Unit:

0117 342 3398 ◆ 0117 342 2374
Bristol Heart Institute,
Freeport SWB2225, Bristol, BS2 8ZZ