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Chronic Thromboembolic Pulmonary Hypertension (CTEPH) Patient information booklet



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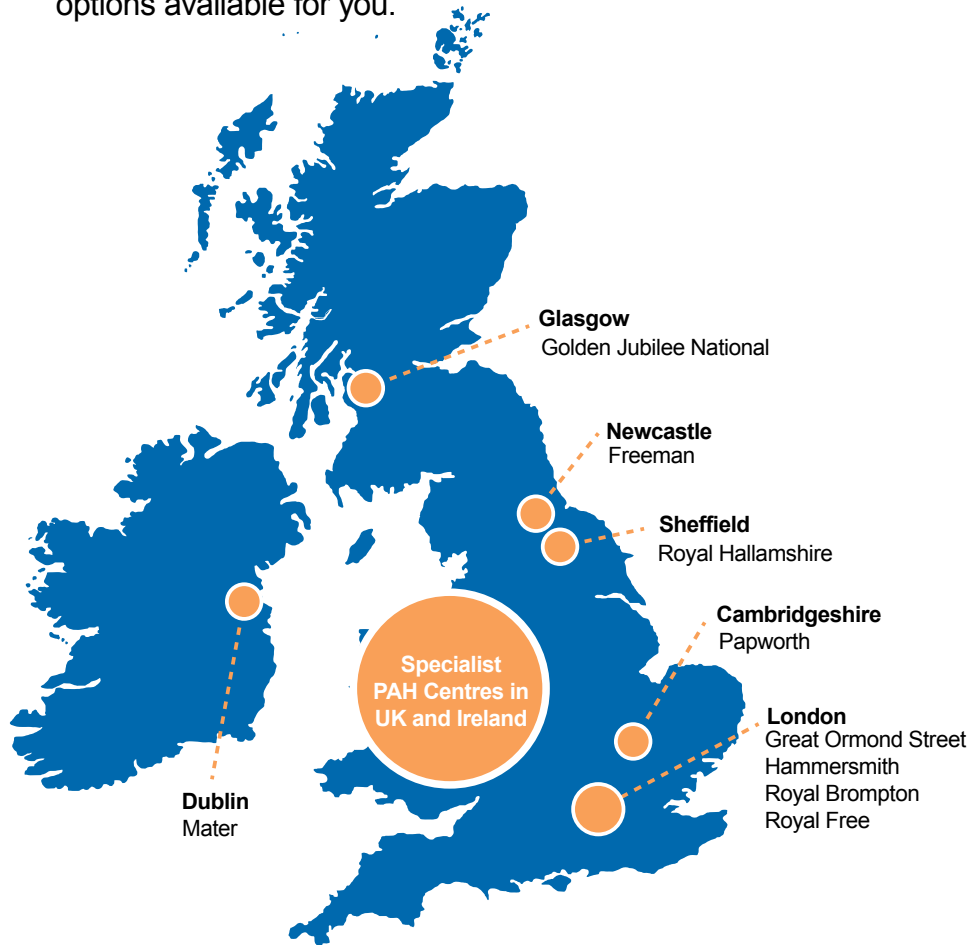


Introduction

What is CTEPH?

Pulmonary hypertension or PH is raised blood pressure in the blood vessels (arteries) of the lungs. Many people have systemic (rest of body) hypertension but PH is a rare condition. There are different types of PH and also different causes, but this booklet looks at PH caused by chronic (long standing or old) blood clots in the arteries of the lung. This type of PH is called chronic thromboembolic pulmonary hypertension, but you will most probably hear it being referred to as CTEPH. Lots of people develop blood clots (also called pulmonary emboli or PEs) in the lung arteries but usually your body breaks down the clots within 3 months and you return to normal. Patients with PEs will probably be given warfarin or another anticoagulant to prevent any new clots forming. Unfortunately, in a small number of patients who have a PE (approximately 2–4%) the blood clots do not break down fully and the patient will develop CTEPH.

CTEPH is a rare condition and is best treated at one of the seven National PH Centres shown on the map below. These centres have the experience and expertise to make an accurate diagnosis and provide you with information about the treatment options available for you.



If you have just been diagnosed with CTEPH we understand that this is a difficult time for you and your family but we will do everything we can to help and support you. This booklet aims to provide clear information about what will happen next and answer some of your questions about the condition and its potential treatments.

If you have further questions after reading this booklet, there are several sources of good quality information available to you. You will be referred to a PH Specialist Centre and your PH physicians and specialist nurses will be pleased to answer your questions. The Pulmonary Hypertension Association UK (PHA UK) is an excellent, independent source of good quality information and advice. Contact details for the PHA UK are listed at the end of this booklet.

What is the circulatory system?

Learning about the heart, lungs and blood supply to the lungs will hopefully help you understand PH and CTEPH better.

The heart

The heart is a muscle made up of four parts or chambers. There are two chambers on the right side of the heart and two on the left, working like two separate pumps. The right side of the heart deals with the dirty or impure blood which is lacking in oxygen when it returns from the body (shown in blue in Figure 1). The upper chamber is called the right atrium and receives blood from the body. The lower chamber is called the right ventricle and pumps blood to the lungs through a blood vessel called the pulmonary artery. The left side of the heart deals with oxygen-rich blood (shown in red in Figure 1). The upper chamber is called the left atrium and the lower chamber is called the left ventricle. The left ventricle pumps oxygen-rich blood to the rest of the body. The flow of blood through the heart and lungs is called the pulmonary circulation and this is affected in PH.

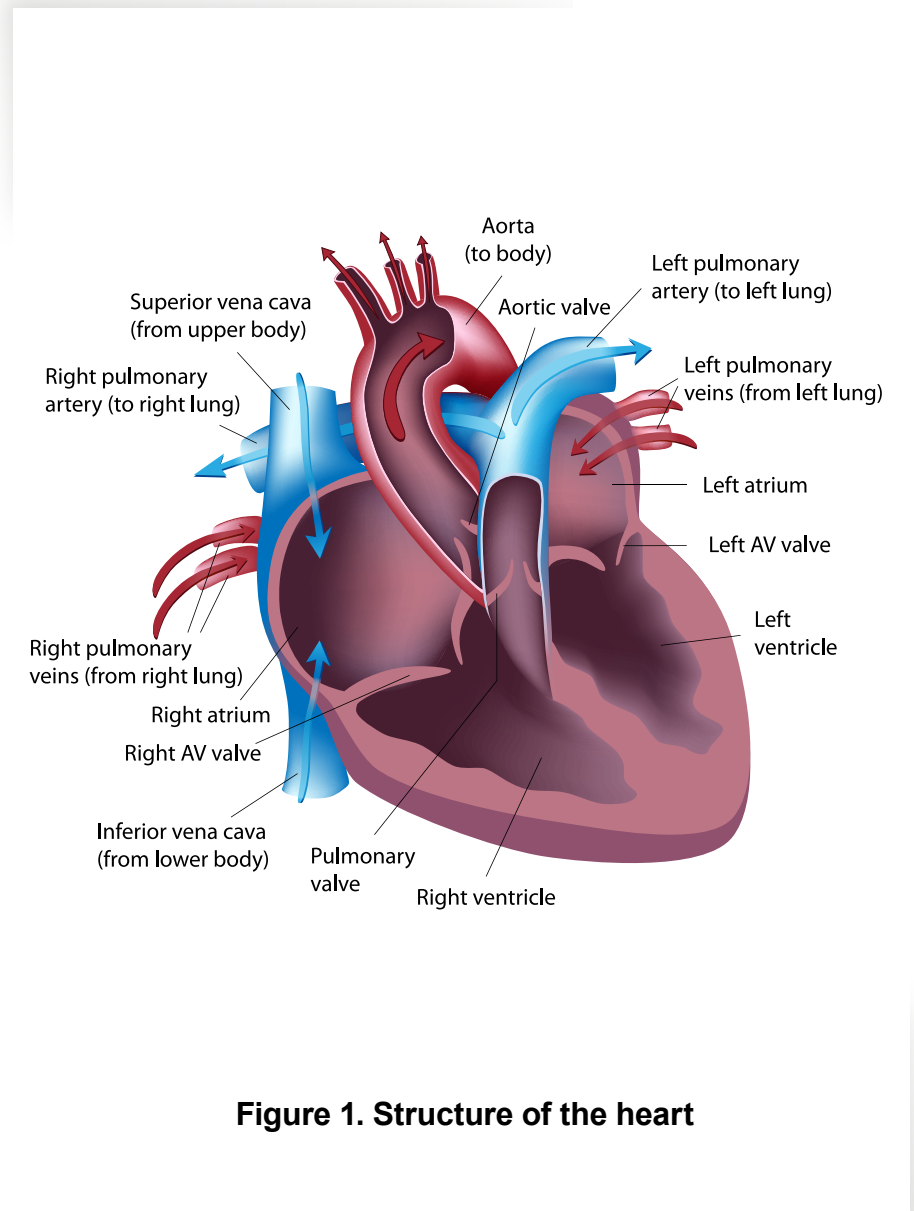


Figure 1. Structure of the heart

The lungs

You have two lungs, one on each side of the heart. Each lung is like a sponge made up of sections called lobes. When air is breathed in, it travels down the windpipe or trachea. The trachea divides into a left and right tube leading into each lung. Like the branches of a tree, these tubes keep dividing into smaller and smaller tubes and end in the lungs at tiny air sacs called alveoli, which look like bunches of grapes. There are over 300 million alveoli in healthy lungs (Figure 2).

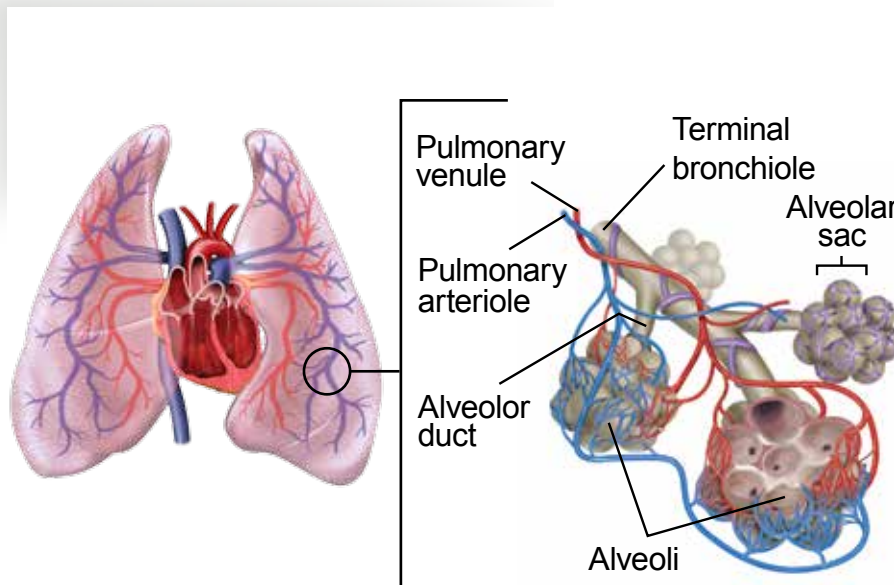


Figure 2. Structure of the lungs

The pulmonary circulation

The pulmonary circulation is made up of blood vessels that carry impure blood to the lungs and oxygen-rich blood from the lungs. Blood that contains waste gas (carbon dioxide) from all over the body is brought to the right side of the heart and is then pumped by the right ventricle through the pulmonary artery. Like the trachea, the pulmonary artery splits into two branches; one going to the right lung and the other to the left lung. These branches continue to divide again and again, becoming very small (see Figure 3). These thin blood vessels surround the alveoli in the lungs and allow the exchange of waste gas (carbon dioxide) and oxygen to take place. The pulmonary veins then take the oxygen-rich blood from the lungs to the left side of the heart and from here it is pumped to the rest of the body.

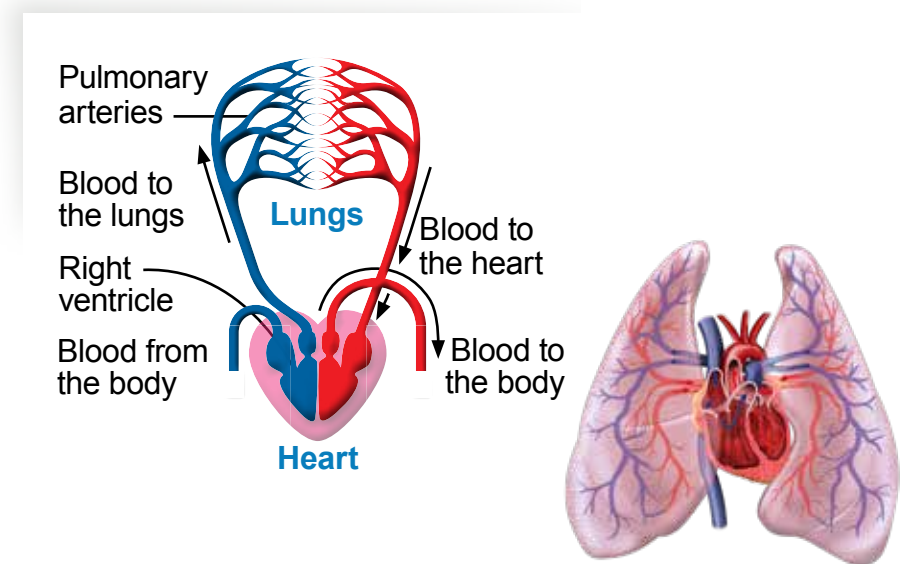


Figure 3. The pulmonary circulation



CTEPH

What causes CTEPH?

Some people are more likely to develop PE than others but in some cases there is no clear reason why a person develops a PE, and no one really understands why a small number of people with PEs then go on to develop CTEPH. Some known causes and risk factors for CTEPH include:

- Large or recurrent PEs
- A previous blood clot in a deep vein of the leg, also called deep vein thrombosis (DVT)
- Cancer or previous cancer
- Removal of the spleen (splenectomy)
- Chronic inflammatory diseases, such as inflammatory bowel disease
- Certain blood clotting disorders, such as antiphospholipid syndrome (a disorder of the immune system that causes an increased risk of blood clots).

What are the symptoms of CTEPH?

Many people who have CTEPH will go through a period of time where they do not experience any symptoms or only mild breathlessness when they exercise. This is known as 'the honeymoon period'. Some patients will have some improvement of their breathlessness within 3 months after a PE. Others have no history of a PE or DVT and the early symptoms of CTEPH are similar to those for airway problems, such as asthma or heart disease. This can make it difficult to diagnose CTEPH and so it can take some time and many tests to get a correct diagnosis.

Early symptoms of CTEPH include:

- Shortness of breath on exercise
- Chest discomfort
- Tiredness or fatigue.

As the condition progresses, the breathlessness gets worse and you may experience dizziness, fainting or symptoms of right heart failure, including swelling in the ankles, legs or abdomen (fluid retention), and/or blue tinged fingers and toes.

How common is CTEPH?

CTEPH is seen in all races, both sexes and at any age. It is a rare condition, especially in children, but the true estimation of how many people in the UK population may have CTEPH remains unknown. Recent studies estimate that most people with CTEPH are between 50 and 60 years old.

How is CTEPH diagnosed?

A number of things are used to diagnose CTEPH. These are listed below.

- **Medical history** — your doctor will take your full medical history. This may include a history of unexplained breathlessness or one or more of the risk factors mentioned above.
- **Physical examination** — you may have none, one or a few of the following signs:
 - o Breathlessness when exercising
 - o Heart palpitations
 - o Chest pains
 - o Fluid retention, swollen legs or tummy
 - o Enlarged liver
 - o Blue fingers or toes
 - o A visibly full jugular vein (the blood vessel in your neck)
 - o Heart murmurs. These reflect turbulent blood flow through a leaky heart valve, usually the tricuspid valve (the valve between the right atrium and right ventricle) in PH. These are heard using a stethoscope.
 - o Parasternal heave. In advanced PH, when the right side of the heart contracts, it has to work harder than usual because it is pushing against the high pressure in the lungs. The physician can feel the right side ‘heave’ as it contracts, by placing a hand on your chest. This ‘heave’ is not normally present when there is no PH

- **Tests and investigations** — these could include:
 - o Blood tests
 - o Electrocardiogram (ECG)
 - o Chest x-ray
 - o Echocardiogram
 - o Lung function tests
 - o Walk tests
 - o Cardiopulmonary exercise test (CPET)
 - o CT pulmonary angiography (CTPA) scan
 - o MRI pulmonary angiography (MRPA) scan
 - o Ventilation/perfusion (V/Q) scan
 - o Quality of life assessment
 - o Right heart catheter
 - o Conventional pulmonary angiography.

Tests and investigations

Some of these tests may sound a little alarming, but they are usually very straightforward.

Let’s look at some of them in more detail.

- **Blood tests** — a small amount of blood is taken usually from a vein in your arm. This does not usually hurt but may sting. The blood sample is then sent to the laboratory where scientists carry out tests to check that you do not have anaemia and that your liver and kidneys are working properly. They may also do a test known as a ‘thrombophilia screen’. This is to see if you have any

coagulation disorders. Another blood test, known as NTpro-BNP, can give an indication of heart stretch and the severity of the condition.

- **Electrocardiography (ECG)** — small electrodes are attached to the chest with sticky pads. These pick up the electrical activity of the heart and produce a graph of the heart rhythm. This is an entirely painless procedure and may provide evidence that you have PH.
- **Chest x-ray** — a chest x-ray may show that the heart and/or the main blood vessels in the lungs have become enlarged because of the raised blood pressure in the lungs. This is a noninvasive and painless test.
- **Echocardiography (Echo)** — this noninvasive and painless test involves using ultrasound to detect changes in the structure of the heart and estimate the blood pressure in the lung blood vessels.
- **Lung function tests** — these tests give information about how well your lungs are working. They can be used to detect what may be causing your breathlessness, such as damage to the lungs caused by smoking. It is important to find out if you have any other ‘airway’ problems to maximise treatment options. Again, these tests are noninvasive and painless, but the breathing tests may make you puff!
- **Walk tests** — these tests give information about how much exercise you can do. The tests are usually repeated at each visit to your PH Specialist Centre to give an idea of how effective your treatment has been. Some patients can find the walk tests challenging but it is important to do your best with the test. There are two types of walk tests used in the assessment of PH:

- o 6-minute walk test — the 6-minute walk test is exactly that! You are asked to walk up and down a corridor for six minutes. During this time a technician makes a note of how far you walk, how breathless you get and what happens to your pulse and oxygen levels (this is done by wearing a small monitor on the wrist, forehead or ear)
- o Shuttle walk test — the shuttle walk test is used in some PH Specialist Centres. It involves walking up and down a 10 metre stretch in response to automated ‘bleeps’ until you are unable to keep up with the bleeps. The bleeps may be set at a constant pace (endurance shuttle walk) or become closer together meaning you will need to increase your walking speed (incremental shuttle walk).

- **Cardiopulmonary exercise test (CPET)** — this exercise test is usually carried out on an exercise bike. You will be asked to wear a mask to monitor how your lungs are working and ECG electrodes will be placed on your chest to monitor your heart rhythm. To start with, you will pedal the bike without any resistance but over time the resistance will slowly be increased (which will feel like you are peddling uphill) until you cannot peddle anymore. This useful test allows specialist doctors to confirm that it is PH which is limiting you rather than another cause, e.g. emphysema.
- **CTPA scan** — this scan creates 3D images from a series of x-rays known as slices. This is an essential test in CTEPH. It can diagnose or rule out other lung conditions, such as emphysema, and can also identify signs of CTEPH. Before the scan, a cannula (small tube) is put into a blood vessel in your arm so that a ‘contrast dye’ which shows up the blood vessels in your lung during the CT scan can be

injected. The images are taken as you lie on your back and passed through the CT scanner. The scan is entirely painless but inserting the cannula can sting a little and you may get a warm sensation when you are injected with the contrast dye. There is a small chance that you will have an allergic reaction to the dye but the doctors and nurses will watch for this and treat you if needed. The contrast dye is removed by the kidneys and it is important to let the doctors know if you have any kidney problems or diabetes.

- **MRPA scan** — magnetic resonance imaging (MRI) is a type of scan that uses strong magnetic fields and radio waves to produce detailed images of the inside of your body, including the heart and blood vessels in the lungs. It does not involve any radiation. Like the CTPA scan, you lie on your back and pass inside the scanner. The MRI scanner is narrower than a CT scanner and at certain times during the scan it will make loud tapping noises. This is the electric current in the scanner coils being turned on and off. You will be given earplugs or headphones to wear. You may find the scanner uncomfortable if you have claustrophobia (fear of enclosed spaces), but hopefully you will find this manageable with support from the radiographer. Throughout the scan you will be able to talk to the radiographer through an intercom and they will be able to see you on a television monitor. As with the CTPA scan you will be injected with a contrast dye, which is removed by the kidneys and it is important to let the doctors know if you have any kidney problems.
- **Ventilation/perfusion (VQ) scan** — this scan is used to assess the flow of air and blood within the lungs. This is a two-part test. The ventilation part looks at how well air reaches all parts of your lungs when you breathe in and

the perfusion part looks at how well blood circulates in the lungs. This is a particularly useful test for confirming or excluding CTEPH as a cause of your PH. If you have a VQ scan you will be asked to lie down under a scanner. In the first part of the test you are asked to wear a mask over the nose and mouth and inhale a small amount of radioactive substance. This is used to trace how air flows in your lungs. The second part of the test involves injecting a tiny amount of a radioactive substance into a blood vessel usually in your arm. This is used to trace the blood circulating in the lungs. A scanner then creates images of the lungs to build up a picture of both ventilation and perfusion. The injection can sting, but otherwise this is a painless test.

- **Quality of life assessment** — symptoms of CTEPH can have a negative effect on your physical activities and how you interact with the people and world around you. So one of the most important aims of treatment for CTEPH is to improve and maintain quality of life. Quality of life is assessed using several tools. Two of the most commonly used tools are the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) and the emPHasis-10. Both of these tools are paper questionnaires, which take about 10–15 minutes to complete.
- **Right heart catheter** — this test is needed to confirm a diagnosis of PH and assess how well your heart is currently coping with the extra work it is being asked to do. It helps the doctors looking after you to work out which treatments you may need. The test is a minor invasive procedure that is performed while you are awake but under local anaesthesia. In most cases it can be performed as a day case procedure. You will be taken to a special x-ray room and asked to lie flat on your back on a narrow bed. A local anaesthetic is injected usually into your neck but sometimes

in your arm or groin. A catheter is then inserted into a vein in the neck (or arm or groin) and then gently manoeuvred to the right side of the heart and the pulmonary artery. To get accurate readings on how well your heart is working you will need to lie still for about half an hour. The local anaesthetic stings at first and the insertion of the catheter can feel uncomfortable. Some patients also report feeling their heart 'thump' as the catheter is passed through the right side of the heart. In centres experienced with this procedure, serious complications are rare from this procedure and most patients who undergo right heart catheter do not have any problems. The risks will be explained to you as part of the consent procedure.

- **Conventional pulmonary angiography** — this is a test that is sometimes carried out at the same time as your right heart catheter test. For this test, the catheter is placed in the pulmonary artery. You will be asked to hold your breath for a short period while a contrast dye is injected along different places in the pulmonary artery. Images are then taken to locate where the clots are. You may get a warm sensation as the dye is injected. There is a small chance that you will have an allergic reaction to the dye but the doctors and nurses will watch for this and treat you if needed. The contrast dye is removed by the kidneys and it is important to let the doctors know if you have any kidney problems or diabetes.

Please note: Tests involving small doses of radiation include X-rays, CTPA, and VQ scans. More information on radiation doses is available at <https://www.gov.uk/government/publications/medical-radiation-patient-doses>. For all X-rays, you should let the hospital know if you are pregnant.



Treatments for CTEPH

Treatment for your CTEPH falls into one of four categories:

- Anticoagulation
- Pulmonary endarterectomy (PEA) surgery
- Balloon pulmonary angioplasty (BPA)
- Medical treatment with drugs.

Anticoagulants

A diagnosis of CTEPH brings with it a need for life-long anticoagulation medication, unless there is a medical reason for not taking it. Anticoagulants are used to prevent further clots forming rather than breaking down the chronic clots that are already present. The most commonly used anticoagulant is warfarin. Patients on warfarin are monitored by a regular blood test called the INR (international normalised ratio), which monitors how quickly your blood clots. For most patients in the UK prescribed warfarin, the target INR is 2.5, with a range of 2.0–3.0.

Other patients are treated with injections of low molecular weight heparin, e.g. enoxaparin (Clexane®) or dalteparin (Fragmin®) or a synthetic anticoagulant called Fondaparinux. These are most commonly used if your INR is less than 2 or if you have had recurrent PEs despite treatment with warfarin.

There are an increasing number of alternative oral anticoagulants to warfarin, such as apixaban, dabigatran and rivaroxaban, that do not need to be monitored but their effectiveness has not been assessed in patients with CTEPH.

PEA surgery

PEA is an operation to remove the scars made by old blood clots in the pulmonary arteries. Approximately 60–70% of patients with CTEPH are suitable for PEA. It is complex surgery and Papworth Hospital is the only centre in the UK that performs this operation. PEA is the treatment of choice for patients with CTEPH because it is potentially curative. It can also significantly improve patient symptoms, quality of life and gives the best chance of long-term survival. However, there are risks as well as benefits with PEA and some patients may not benefit fully due to residual PH after the surgery.

BPA

BPA is a new procedure that can potentially be offered to carefully selected patients who are not suitable for PEA surgery. This is performed under local anaesthetic and sedation. The treatment usually requires 2–5 procedures where small balloons are inflated in the lung vessels to push the scars (old clots) to one side, which allows blood to flow freely. At the moment, there

are promising short-term data that this procedure improves exercise capacity, quality of life and reduces the blood pressure in the lungs, but long-term data are needed.

Medical treatment

Tablets are used for the treatment of patients with CTEPH in two main scenarios:

- To improve symptoms while waiting for PEA. This will usually be sildenafil and is an unlicensed treatment. The drug is well tolerated and is usually stopped immediately after your surgery.
- In patients where the distribution of the scars are not suitable for PEA or who have residual PH following surgery. This will usually be riociguat (Adempas®) and is the only licensed therapy for patients with CTEPH. This has been shown to improve exercise capacity and breathlessness in patients with CTEPH. Riociguat is taken 3 times a day and the dose is slowly increased over 8 weeks until the optimum treatment dose is reached.

Both of these tablets have been shown to interact with medicines called nitrates which are used to treat ischaemic heart disease (also known as coronary heart disease) such as angina (chest pain), heart attacks and heart failure, so they cannot be used by patients who are taking these medicines. If you are taking nitrates and your CTEPH is not suitable for surgery, your Specialist PH Centre may consider other treatment options including endothelin receptor antagonists or prostanoid medication. Your specialist physician will discuss these options with you.

CTEPH and surgery: What happens next?

If you have been diagnosed with CTEPH, your case will usually be referred to the Multi-Disciplinary Team (MDT) at Papworth Hospital, Cambridgeshire to assess your suitability for surgery or potentially balloon pulmonary angioplasty. This is the only Specialist PH Centre in the UK that performs these procedures at present.

Am I suitable for surgery?

PEA surgery is a big operation and the level of risk versus the benefit will vary from person to person depending on where the scars are, how severe your CTEPH is, your general health, age and other medical conditions. The MDT will carefully review your case and test results before deciding whether PEA surgery is an option for you. The surgeon can only remove scar tissue from the larger pulmonary blood vessels, which is called proximal disease. Unfortunately, surgery can't help everyone because sometimes the blockages are only in the tiny vessels deep within the lungs that are impossible to reach. This is known as 'distal disease'. Some patients have a mixture of proximal and distal blockages making the decision of whether to do surgery more difficult. You may still be offered surgery if the MDT feels it may be beneficial for you.

The consensus opinion from the MDT is fed back to the referring team. If the MDT decides that you may be a candidate for PEA surgery you will be invited to an all-day out-patient appointment at Papworth Hospital to meet the surgeon and PEA specialist nurses. During the visit you will be provided with verbal and written information, including a booklet about PEA surgery and the potential risks and benefits in your particular case. It is important to realise that coming to clinic at Papworth Hospital

does not mean that you will be definitely offered surgery nor do you have to agree to the surgery if it is offered to you. You may also be given the opportunity to meet a patient who has already undergone the procedure so that you can ask them questions. You will be encouraged to bring someone with you to this consultation as there will be a lot of information to take in. If the MDT decide that you are not suitable for surgery then the PEA specialist nurse will contact the PH specialist nurse at your local Specialist PH Centre.

You may make the decision whether or not to accept an offer of surgery on the day of the visit or you may wish to take some time at home to discuss this option with your family. The PEA specialist nurses will be happy to answer any further questions you may have in order to help you come to a decision.

Whether you choose surgery or other treatments it is important that your choice is well informed, so please feel free to ask as many questions as necessary.

CTEPH and BPA: What happens next?

In patients who are not suitable for PEA, the MDT may feel you are suitable for BPA treatment. You may be invited to an outpatient clinic at Papworth Hospital with a specialist interventional cardiologist, PH physician and PH specialist nurse to discuss BPA. Similar to the surgical clinic the risks and benefits of the procedure will be carefully discussed with you and you will have the opportunity to ask questions so that you can make your decision whether to accept the offer of this procedure.

This procedure may become available at other specialist centres in the future.

Living with CTEPH

The physical symptoms of CTEPH can affect:

- Everyday activities
- Your ability to work or attend education. This may also place a financial burden on some patients.

We also understand that people with CTEPH can have:

- Emotional and psychological issues
- Issues associated with living with uncertainty
- Effects on relationships.

Healthcare professionals may provide you with information and advice about CTEPH and living with the disease. They may also direct you to other sources of support such as social workers, counsellors or charities. Please let your healthcare professional know if you are having problems coping with your diagnosis. They will do their best to get you the support you need.

Pregnancy

You are strongly advised not to become pregnant if you have CTEPH because the disease increases the risk of death associated with pregnancy and childbirth. Anticoagulants that you need to take may also affect the baby's development. Some of the diagnostic tests involve exposure to radiation. If you think you may be pregnant please speak to your PH specialist physician or nurse as soon as possible.

Support groups

Support groups can help you and your family cope with the emotional effects of CTEPH. The PHA-UK is the national support group for patients with all forms of PH. The PHA-UK will also be able to provide you with details of any local groups that meet in your area. Details for the PHA-UK can be found at the end of this booklet.

Summary

There are significant challenges associated with a diagnosis of CTEPH. We hope this booklet has gone some way to reassure you that you are not alone as you face the next steps along the path of diagnosis and treatment. Your specialist teams are here to work with you to achieve the best possible outcome for you.

Useful contacts

Pulmonary Hypertension Specialist Centres in the UK

Freeman Hospital

William Leach Centre Freeman Hospital Freeman Road Newcastle upon Tyne NE7 7DN

Tel: 0191 223 1968 Fax: 0191 223 1489

www.newcastle-hospitals.org.uk

Golden Jubilee Hospital

Scottish Pulmonary Vascular Unit Golden Jubilee Hospital Beardmore Street Glasgow Scotland G81 4HX

Tel: 0141 951 5497

www.spvu.co.uk

Great Ormond Street Hospital (children only)

L6 Main Nurses Home Great Ormond Street Hospital Great Ormond Street London WC1N 3JH

Tel: 020 7405 9200 (ext. 1005, 1007, 8495)

www.ich.ucl.ac.uk

Hammersmith Hospital, Imperial College Healthcare NHS Trust

Hammersmith Hospital Du Cane Road Hammersmith London W12 0HS

Tel: 020 8383 2330 Fax: 020 8383 2331

www.pulmonary-hypertension.org.uk

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Cambridge Pulmonary Vascular Centre Cambridge CB23 3RE

Tel: 01480364223

www.papworthhospital.nhs.uk

Royal Brompton Hospital

Royal Brompton Hospital Sydney Street London SW3 6NP

Tel: 020 7351 8362 Fax: 020 7351 8629

www.rbht.nhs.uk

Royal Free Hospital

Royal Free Hospital Pond Street London NW3 2QG

Tel: 020 7794 0500 (ext 8648)

www.royalfree.nhs.uk

