Familial Amyloid Polyneuropathy

**Transthyretin (TTR)**

Transthyretin (TTR) is a normal blood protein, present in everybody. In healthy people, normal, so-called “wild-type” TTR functions as a transporter of thyroid hormone and vitamin A (retinol) within the bloodstream, hence the name: “trans-thy-retin”. Most TTR in the body is made in the liver and a small amount is made in the eye and the brain.

People who are born with inherited mutations (alterations) in the TTR gene produce abnormal, (“variant”) TTR throughout their lives. The “variant” TTR protein is amyloidogenic (amyloid forming). Over the course of several decades, usually after the age of 30 and often much later, people with inherited TTR gene mutations may develop symptoms of disease caused by the build-up of amyloid deposits.

More than 100 different mutations in the TTR gene have been observed. Many of these can cause the disease called familial amyloid polyneuropathy (FAP), in which amyloid deposits containing “variant” TTR affect the nerves, often the heart, and sometimes the kidneys and eyes.

Some people with inherited TTR gene mutations develop amyloid cardiomyopathy in which amyloid deposits containing “variant” TTR affect only the heart.

Some people without any mutations in the TTR gene develop senile systemic amyloidosis with advancing age in which amyloid deposits containing normal “wild type” TTR affect only the heart.

**Introduction**

Amyloidosis is a rare disease caused by abnormal deposition and accumulation of proteins in the tissues of the body. Amyloid deposits are primarily made up of protein fibres known as amyloid fibrils. These amyloid fibrils are formed when normally soluble body proteins aggregate (clump together) and then remain in the tissues instead of safely going away. About 30 different proteins are known to form amyloid deposits in humans. These amyloid forming (“amyloidogenic”) proteins are known as “precursor proteins.” Amyloid deposits cause disease by gradually accumulating within organs and thereby disrupting the structure and damaging the function of the affected tissues.

Different types of amyloidosis are named according to the precursor proteins which form the amyloid fibrils. All have the initial “A” denoting amyloidosis and letter(s) identifying the particular precursor protein which forms amyloid fibrils within the amyloid deposits.

In ATTR amyloidosis, a blood protein called transthyretin (TTR) is the amyloid precursor protein that forms the amyloid deposits. Familial amyloid polyneuropathy (FAP) is one of three distinct, different types of ATTR amyloidosis. It is the most commonly recognised form of hereditary systemic amyloidosis worldwide.
How common is FAP?

FAP is the commonest type of hereditary systemic amyloidosis. ("Systemic" means that several parts of the body are affected.) In overall terms it is nevertheless a very rare disease. We do not know exactly how many people around the world have FAP. The commonest type, associated with a particular mutation of the TTR gene (called Val30Met-associated FAP), is believed to affect about 10,000 people worldwide.

Who gets FAP?

FAP is a hereditary condition. This means that it runs in families. It may be inherited either from the patient’s mother or from the patient’s father. Patients with FAP are born with a mutation (alteration) in the TTR gene that causes the condition, although they usually only begin to experience symptoms in middle age. Some people with TTR gene mutations may never experience symptoms at all. People with a mutation in the TTR gene may pass the condition on to their children. Sometimes people diagnosed with FAP are not aware of anyone else in the family with the condition. This may be because the mutation first arose in that person, or because other family members were not diagnosed, or did not develop the disease despite having the mutation. For a more detailed explanation of the genetic principles underlying inheritance of FAP, see the appendix.

FAP was first described in 1952 in a number of families in Portugal. Since then it has been diagnosed in families from Japan, Sweden and County Donegal in North-West Ireland. Worldwide, most people with FAP have ancestors originating in one of these regions. In the UK, FAP is most common in people with Irish ancestry. It is estimated that 1% of the people in County Donegal have a TTR gene mutation.

What causes FAP?

People with mutations (alterations) in the TTR gene produce abnormal, “variant” TTR protein, throughout their lives. The “variant” TTR forms amyloid deposits inside body tissues, mainly in the nerves, heart, kidneys and eyes. The amyloid deposits build up slowly and cause damage to the organs affected, leading to the symptoms of FAP.

Symptoms of FAP

Symptoms of FAP may appear as early as age 20, or as late as age 80. Symptoms may include:

- Peripheral neuropathy: limb weakness and pain, loss of sensation.
- Autonomic neuropathy: disturbances of bowel, bladder and blood pressure and sexual dysfunction.
- Heart failure: symptoms result from stiffening of the heart due to amyloid deposits (restrictive cardiomyopathy). They may include:
  - shortness of breath, sometimes just after mild exertion
  - palpitations and abnormal heart rhythms, most frequently atrial fibrillation or atrial flutter
  - ankle swelling (oedema)
  - fatigue
  - fainting, which may occur after exertion, or after eating
  - angina (chest pain).
- Disease due to amyloid deposits in the:
  - eye
  - kidneys
  - thyroid gland
  - adrenal glands
  - blood vessels.

Different types of FAP

More than 100 different mutations in the TTR gene have been reported. Different mutations may cause a wide variety of different clinical symptoms. Within families the pattern is usually quite consistent for:

- age of onset
- rate of disease progression
- involvement of different body systems.
In some families all affected members have just neuropathy, while in other families all affected members have both neuropathy and cardiac disease. Certain mutations appear to cause particularly severe disease and others cause relatively mild disease.

Patients carrying a mutation in their genes do not always develop disease. Some cases have been reported where people over age 60 have no disease despite having two copies (one inherited from each parent) of the TTR mutation which results in production of the Val30Met TTR protein variant.

The TTR gene mutation that most commonly causes FAP in the UK results in production of another TTR variant, Thr60Ala (T60A), often seen in people with Irish ancestry. In these patients, symptoms tend to start relatively late, between ages 45 to 78, most often after age 60. The heart is almost always affected, and there is neuropathy in about two thirds of cases. Autonomic neuropathy symptoms such as diarrhoea and/or constipation are more common than peripheral neuropathy.

The TTR gene mutation that most commonly causes FAP worldwide results in production of the TTR protein variant called Val30Met (V30M). Most patients first experience symptoms in their 30s. Peripheral and autonomic neuropathy are the main symptoms in patients with this mutation, and heart problems are rare.

Another TTR gene mutation results in production of the TTR protein variant called Val122Ile (V122I), and is relatively common in the UK, especially in people with Afro-Caribbean or African American ancestry. This typically causes a condition called hereditary amyloid cardiomyopathy, where amyloid deposits are found only in the heart and the wrists, where they lead to carpal tunnel syndrome. Symptoms of heart disease usually appear after age 60. There is usually no neuropathy.

**Diagnosis**

When doctors suspect ATTR amyloidosis, the diagnosis can be confirmed (or eliminated) by tests including:

**Tissue biopsy**

This is a procedure where a small sample of tissue is obtained, processed and examined under the microscope. The tissue sample may be taken from a variety of sites.

Frequently, a small piece of fat tissue is taken from the skin of the stomach area (abdominal fat biopsy). The procedure is simple, quick, safe and relatively painless.

It proceeds as follows:
1. A small area of the skin in the stomach area is numbed with local anaesthetic.
2. A needle is inserted into the numb area to take out some fat cells from underneath the skin.
3. The fat cells are preserved and sent to the laboratory for analysis.

Amyloid may also sometimes be detected on biopsy of other regions such as the nerves, heart or rectum. Since hospitals usually preserve biopsy tissue, it is recommended that material suspected of containing amyloid is sent to the NAC for review and further staining.

In the laboratory a special staining technique using a dye called “Congo red” is used to identify amyloid deposits in the tissue sample. Then further stains are used to determine the protein composition of the amyloid fibrils. If amyloid fibrils composed of TTR are present along with a TTR mutation, then FAP is diagnosed.

**Genetic testing**

Genetic testing involves examination of the DNA from the patient’s cells. These tests are performed on blood samples taken from the patient’s vein.

These techniques can identify amyloidogenic mutations (abnormalities) in the TTR gene. There are over 100 known mutations in the TTR gene, and different mutations lead to different types of disease. The precise mutation identified may provide information about the likely clinical course. For example, the most common mutation worldwide, which results in production of the Val30Met TTR protein variant, usually leads to amyloid deposition affecting only the nerves and not the heart. In contrast, the mutation which results in production of the Thr60Ala TTR protein variant, typically in Irish individuals, may lead to disease affecting the nerves and the heart. The mutation which results in production of the Val122Ile protein variant usually leads to amyloid deposits just in the heart, and not the nerves.

**Imaging studies of the heart**

ECG, echocardiogram, DPD scanning and in some cases cardiac magnetic resonance (CMR) scanning may give helpful information. SAP scanning may not be helpful as it does not show amyloid deposits in the heart or nerves.
Treatment

Treatment of all types of amyloidosis is based on the following principles:

1. Reducing the supply of amyloid forming precursor proteins
2. Supporting the function of organs containing amyloid.

Liver transplantation

Most of the TTR in the bloodstream is made in the liver. Liver transplantation is therefore a treatment option for some patients with FAP. The liver which makes the abnormal “variant” TTR is removed and replaced by a donor liver making normal, “wild type” TTR. The aim is to prevent the formation of further amyloid deposits by reducing the supply of the amyloid-forming precursor TTR.

Over the last 20 years, liver transplantation has been performed in hundreds of patients with FAP around the world. In many cases this has been successful, leading to stabilisation of disease. Success is greatest when transplantation is performed:

- early in the course of disease before there has been too much damage to the nerves or the heart
- in younger patients
- in patients with the TTR Val30Met variant.

Unfortunately amyloid deposits in the heart sometimes continue to progress even after liver transplantation. It seems that amyloid deposits composed of abnormal (variant) TTR, present before liver transplantation, act as a template encouraging deposition of normal TTR as amyloid. Thus the normal TTR protein (“wild type” TTR) produced by the new liver builds up on top of the existing ‘variant’ TTR amyloid deposits. This problem has appeared most often in older patients with variants other than TTR Val30Met.

Combined heart and liver transplant has been performed in a few dozen patients with FAP around the world. This operation is only an option for a minority of patients, and it carries significant risks.

Supportive treatment

Peripheral neuropathy

Medications that may help to alleviate neuropathic pain include amitriptyline, gabapentin, pregabalin and duloxetine. Medical staff can give advice regarding appropriate foot care and footwear. This is important in order to prevent painless ulcers at pressure points and to protect areas of the foot that lack sensation.

Autonomic neuropathy

If there is orthostatic hypotension (drops in blood pressure and faintness on standing up from sitting or lying positions), elastic stockings may be recommended. Drug treatment with midodrine may also be helpful. Care should be taken to avoid dehydration if there is vomiting and diarrhoea. Intravenous fluids and anti-nausea drugs may be necessary.

There are drugs that can help to control diarrhoea and constipation, and others that can help to combat erectile dysfunction. If there are disturbances of heart rhythm, drug therapy or implantation of a pacemaker may be necessary.

Heart disease

Treatment of heart disease in patients with FAP is symptomatic and supportive for the majority of patients. Many standard medications used for heart failure are not effective for patients with amyloid deposits in the heart, but the following measures can be very helpful:

Fluid balance

Patients with cardiac amyloidosis should limit their fluid intake.

The most important principle of treatment for cardiac amyloidosis is strict fluid balance control. Specialist heart failure nurse involvement may be valuable.

When there is cardiac amyloidosis, the heart is often too stiff to pump the blood efficiently. This may lead to fluid build-up, causing leg swelling (oedema) and breathlessness due to fluid in the lungs. This problem is exacerbated if the patient drinks too much fluid.

There may be episodes of worsening symptoms if there is even a small fluid excess. It is preferable to catch and treat heart failure symptoms at an early stage, before they become overwhelming.
Fluid excess can be avoided by careful attention to the 3 Ds:

1. **Diet**
2. **Diuretics**
3. **Daily weights**

**1. Diet:**
Fluid intake should be *steady* and should usually not exceed **1.5 litres per day**.

Salt intake should be strictly limited. Salt should not be added to food. In addition, this includes attention not just to salt added to the food from the salt pot, but also to food with high salt content such as crisps, bacon, canned meats, sausages, canned soups and smoked fish. It can be very helpful to meet with a dietician for precise and personalised dietary advice.

If salt and fluid intake is too high, the benefits of diuretic drugs can be completely lost.

**2. Diuretics:**
Doctors may prescribe diuretics (water tablets) which help the body to clear excess salt and water via the urine. Taking these drugs is not a substitute for avoidance of excessive dietary salt and water. If patients consume too much salt and drink too much fluid, the benefits of diuretics may be lost.

Removal of excess fluid from the body leads to reduced ankle swelling and breathlessness. The first diuretic prescribed is often furosemide. Other diuretics such as spironolactone may be added on later to increase the effect. Diuretics lead to increased amounts of urine and should be taken first thing in the morning, sometimes with an additional lunchtime dose. It is important to follow the doctor’s advice carefully regarding diuretic dose and the time of day when the tablet should be taken.

**3. Daily weights:**

Patients should monitor and record their weight daily. Weight should be measured consistently, using the same scales, at the same time of day, usually first thing in the morning after passing urine, just wearing underclothes.

Each litre of excess fluid weighs one kilogram. Several litres of fluid can accumulate in the body without it being very noticeable. But an increase in weight can be an early warning sign of fluid retention.

Variations from week to week or even from day to day of about ± 1-2 kilograms are normal. If there is greater variation in weight, the doctor or nurse treating the patient can recommend appropriate measures. These may include increasing or reducing the diuretic dose. Some patients learn over time how to make appropriate small adjustments to the diuretic dose according to their weight fluctuations.

The aim is to detect and treat any excess fluid, before the patient feels unwell because of the fluid overload.

Support stockings can be helpful for patients with leg oedema (swelling in ankles and lower legs).

Monitor your weight and blood pressure daily. It is helpful if you record them in a chart that you can show your local heart failure team during regular reviews. It is important for your local cardiology/haematology teams to agree to an exact, pre-determined plan for monitoring your fluid balance and adjusting diuretic doses in the event of unexpected fluid retention.

**Medications**
Many standard heart failure medications reduce the already low blood pressure in patients with cardiac amyloidosis, and can actually worsen the symptoms. Others may cause toxicity in the setting of amyloidosis.

The following drugs should be used with caution:
- calcium channel blockers
- digoxin
- beta blockers
- angiotensin converting enzyme (ACE) inhibitors
- angiotensin receptor blockers

There may be interactions between heart failure drugs and drugs used to treat AL amyloidosis.

If you are concerned, ask your doctor whether any of the medicines you are taking interact. Follow your doctor’s advice carefully and take the medicines your doctor prescribes for you.
Under certain circumstances some other treatments may be helpful. For example:

- Alpha agonist drugs such as midodrine may help to maintain blood pressure and allow higher diuretic doses.
- In some cases anticoagulation (warfarin) may be recommended.
- Pacemakers may be recommended if there is a slow or irregular heart rate.

Patients should inform all their doctors of all medications they are taking, including any complementary or alternative treatments, to avoid any ill effects from drug interactions or side effects.

**Exercise**

It is believed that limited, light exercise is beneficial for the general well-being of patients with amyloid in the heart. However, it is important to be careful, and to exercise within limits, to avoid exhaustion. If there are symptoms on exercise, patients should not push themselves.

**Drugs in development for ATTR amyloidosis**

**Diflunisal**

This belongs to a class of drugs called “non-steroidal anti-inflammatory drugs” (NSAIDs). This class of drugs are in common use as pain killers, for conditions such as arthritis. Diflunisal is bound by TTR in the blood. This binding is thought to make the TTR less amyloidogenic. Trials are currently underway to assess the effect of diflunisal on the progression of neuropathy in patients with FAP. However, it is important to note that NSAIDs such as diflunisal may have serious side effects, which may be especially dangerous in patients who are already unwell with amyloidosis.

These side effects include:

- bleeding from the stomach and gut
- worsening of kidney function
- worsening of heart failure

Diflunisal use for ATTR amyloidosis is an off-label indication, and only amyloidosis specialists should prescribe it.

**Tafamidis**

Tafamidis was developed as a specific drug for ATTR amyloidosis. It is bound by TTR in the blood. This binding stabilises the TTR and makes it less amyloidogenic. Tafamidis has been studied in a trial involving 91 patients with early FAP. Progression of neuropathy was slightly slower in patients who received the drug than in those who did not. However, the difference was not statistically significant. Given the major clinical unmet need, tafamidis has been approved in Europe, but only for polyneuropathy caused by hereditary ATTR amyloid. Since the evidence that tafamidis has a beneficial effect on polyneuropathy is not strong, it has not been approved by the FDA in the USA or by NICE in the UK. Tafamidis has not received approval for cardiac ATTR amyloidosis.
Other therapies that are currently in early stages of development and clinical trials include:

**Genetic based therapies**
- Small interfering RNA
- Antisense oligonucleotides

These two approaches aim to “switch off” the gene for TTR in liver cells, so that TTR is simply not produced.

**Antibody mediated amyloid elimination**

Serum amyloid P component (SAP) is a normal blood protein, present in everybody, which is always present in amyloid deposits, in all types of amyloidosis, because it binds strongly to amyloid fibrils of all types. The Wolfson Drug Discovery Unit has developed a drug called CPHPC, which clears all the SAP from the blood but leaves some SAP bound to the amyloid deposits. After CPHPC has been administered, it is therefore safe and feasible to administer antibodies to SAP which target the amyloid.

In experimental models these antibodies trigger the body’s normally very efficient systems for removal of debris from tissues to act on the amyloid.

Questions or enquiries:

Specialist heart failure nurses are well qualified to guide you with day to day heart failure management. They can often be consulted by telephone, and can help both with heart failure symptoms and with anxiety and stress related to disease. GPs and hospital specialists can also be helpful.

The doctors and nurses at the National Amyloidosis Centre can be contacted between 08:00 – 17:30 Monday to Friday at +44 (0)20 7433 2738.
Basic genetics - understanding inheritance

The human body is made up of millions of tiny cells, each of which contains identical copies of the genes which we inherit from our parents. These genes function like an instruction manual, or a recipe book for the cells to construct the proteins and other substances which make up the body. Human cells each contain about 25,000 different genes.

Each cell contains two copies of each gene, one from each of our parents. Within each cell, the genes are arranged into forty six long strings, called chromosomes. Twenty three chromosomes come from the father and twenty three from the mother. Complicated interactions between the two copies of each gene determine how the body is composed, inside and out. External traits, like hair colour, eye colour and height and internal traits like blood group are all a consequence of which genes we inherit from our parents. The sex chromosomes determine whether a person is a man or a woman. Women have two X chromosomes and men have one X and one Y chromosome in every cell of their bodies. The illustration above shows the chromosomes from the cell of a man.

When a gene is located within one of the sex chromosomes, the way in which it is inherited is called “sex-linked.” Diseases that result from a mutation (abnormality) in a gene within a sex chromosome may be passed from parent to child by “sex-linked” inheritance.

FAP is inherited by autosomal dominant inheritance, discussed below.

How do mutations cause amyloidosis?

The genes act like an instruction manual or a recipe for protein production inside every cell of the body. Sometimes an alteration or error may arise within a gene. This is called a mutation.

Anyone who has ever baked a cake knows that a single error in the recipe may have a number of different effects on the final product. It may lead to complete disaster, for example if you put in salt instead of sugar, or forgot the baking powder. Alternatively, there may be little effect on the final product, for example if you used margarine instead of butter.

Similarly, a mutation in a gene may have a number of different effects. Some mutations have minimal effects or no effects either on the proteins produced or on the person’s health. Other mutations may lead to abnormal protein production, causing a wide variety of diseases.

The mutated genes that cause hereditary systemic amyloidosis have important effects on the abnormal so-called “variant” proteins whose production they determine. The differences in structure between the normal and the amyloidogenic variant proteins are usually extremely small but nonetheless they have very important effects on the behaviour of the variant proteins. In all cases the variants have an increased tendency to clump together and form amyloid fibrils. Thus even a very small change in a gene can lead to serious disease.
Autosomal dominant inheritance

Complex rules control the inheritance of many characteristics, and of many diseases. Hereditary systemic amyloidosis syndromes are inherited in a fashion known as autosomal dominant. This means that the presence of just one copy of a mutated gene can cause the disease.

Autosomal dominant inheritance is illustrated in the figure. The yellow box represents an unaffected gene and the blue box represents an affected gene, carrying a mutation. The two columns next to each person in the figure represent two identical chromosomes (strings of genes) each person inherits, one from each parent.

In the figure, the father has one copy of a mutated gene, and one copy of a normal gene. He therefore suffers from the disease, since, as mentioned above, in this type of disorder, just one copy of a mutated gene is enough to cause disease. The mother, like the vast majority of the population, has two normal genes and is healthy. Each child gets one copy of each gene from their mother, and one from their father.

When there is simple autosomal dominant inheritance of a condition:

- Each child has a 50% (1 in 2) chance of receiving a mutated copy of the gene from the affected parent.
- Each child has a 50% (1 in 2) chance of receiving a normal copy of the gene from the affected parent.
- Half of the children have a mutated gene and develop the disease. They can then pass the mutated gene and the disease on to half of their children.
- Half of the children have two copies of the normal gene. They are healthy and they cannot pass the disease on to their children.
- Brothers and sisters of people with the disease have a 50% (1 in 2) chance of having the mutated gene and developing disease.
- Men and women have equal chances of receiving the mutated gene and of developing disease.

Incomplete penetrance

For many of the diseases that are passed on by autosomal dominant inheritance, all people with a mutation in the gene develop disease. However, in the case of the hereditary systemic amyloidosis, this is not the case. An additional genetic principle called incomplete penetrance operates, making the situation more complicated.

Incomplete penetrance means that:

- Some people who inherit a mutated copy of the gene do not develop any amyloid at all.
- Some people who inherit a mutated copy of the gene develop only a small amount of amyloid and do not suffer from any clinical problems.
- Some patients diagnosed with hereditary systemic amyloidosis have no family history of the disease.

Information about a particular family is important for evaluation of the likelihood that a young healthy person with a mutation will develop disease.
Appendix 2

Tests that help to diagnose amyloid in the heart

Tests that can help doctors to detect amyloid deposits in the heart include:

**Blood tests: cardiac biomarkers**
When heart muscle is damaged by amyloid deposits, blood tests may detect raised levels of **NT-proBNP** (N-terminal fragment of brain natriuretic peptide) and **high sensitivity troponin**. These are known as “cardiac biomarkers”. Patients with ATTR amyloid in the heart may have cardiac biomarker levels that are higher than normal.

**Electrocardiogram (ECG)**
The ECG test is a safe, rapid, painless method whereby the electrical impulses controlling the heart’s contractions can be detected, measured and represented as a tracing on graph paper. Some ECG appearances are suggestive of amyloidosis in the heart.

**Echocardiogram**
Echocardiography is an ultrasound test. It is safe and painless and does not involve any exposure to radiation. This test is routinely performed when patients visit the NAC. When amyloidosis in the heart is advanced, it is usually clearly visible on the echocardiogram. However, the findings may be less clear at the early stages of amyloid heart disease.

**Cardiac magnetic resonance (CMR)**
CMR is a method whereby a magnetic field and radio waves are used to obtain detailed pictures of the heart. It is safe and painless, and does not involve any exposure to radiation. CMR provides very detailed information on the structure of the heart. CMR has been available at the NAC since our new, state of the art CMR unit opened in early 2016. In some patients, echocardiography may not be able to determine whether heart wall thickening is due to amyloidosis or to another cause such as high blood pressure (hypertension). In such patients, CMR imaging can help to distinguish between these different causes of heart wall thickening.

When doctors analyse CMR scans, they can often clearly visualise the amyloid deposits within the heart walls, between the heart cells. It is expected that in the future it may be possible to use CMR to accurately measure the quantity of amyloid within the heart wall. Such measurements could then be repeated to follow the build-up of amyloid deposits and their regression with treatment.

**Radionuclide imaging (DPD scan)**
SAP scanning does not provide adequate information about body organs that are moving. The heart is in constant motion, so SAP scanning is not of use for assessment of amyloid deposits in the heart.

A different radioactive marker that does home in on amyloid in the heart is called **99mTc-DPD**, or just DPD. DPD scans are routinely undertaken at the National Amyloidosis Centre in patients with suspected ATTR amyloid in the heart.

DPD scans are most useful when the deposits are of TTR type, and the amount of DPD taken up by the heart correlates with the size of ATTR amyloid deposits. Asymptomatic “early stage” ATTR amyloid deposits can be detected in the heart by DPD scans when other heart tests appear normal.

The DPD scan is made in 3D by a method called single photon emission computed tomography (SPECT), and is combined with a standard CT scan. The doctors can then assess both the structure of the heart and the extent of amyloid deposits.

DPD scanning and SPECT are safe tests. There may be minor discomfort when the tracer is injected, but the tests are otherwise painless. There is only slight exposure to radiation from the tracer and the CT scan.

**Heart biopsy**
Heart muscle biopsy involves removal of a small sample of heart muscle which is then examined in the microscope to detect amyloid deposits. It is the “gold standard” for diagnosing amyloid deposits in the heart. This means that it is the best available test, against which all other tests are measured. This test is performed by cardiologists or cardiothoracic surgeons.

Patients are usually sedated during the biopsy, which usually takes less than an hour. During the procedure, the doctor numbs a small area of skin in the neck, then inserts a long, narrow tube called a catheter into a blood vessel and threads it through to the heart. X-rays are performed to ensure that the catheter tip is positioned next to the heart wall. Then a grasping device at the end of the catheter is used to remove a tiny sample of heart tissue. The catheter is then withdrawn, bringing the heart tissue with it. The tissue is sent to the laboratory for analysis. The procedure is usually safe and painless, and does not require admission to hospital.
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