Medications

Many standard heart failure medications reduce the already low blood pressure in patients with cardiac amyloidosis, and can sometimes worsen symptoms. The following drugs should be used with caution:

- calcium channel blockers
- digoxin
- beta blockers
- angiotensin converting enzyme (ACE) inhibitors
- angiotensin receptor blockers

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 may be recommended.
- A pacemaker may be recommended if there is a slow or irregular heart rate.
- An implantable cardioverter defibrillator (ICD) may occasionally be recommended if there is an abnormally fast heart rate leading to dizziness or loss of consciousness.

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.

Neuropathy

If there is orthostatic hypotension, 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. Medications that may help to alleviate neuropathic pain include 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.

Liver transplantation

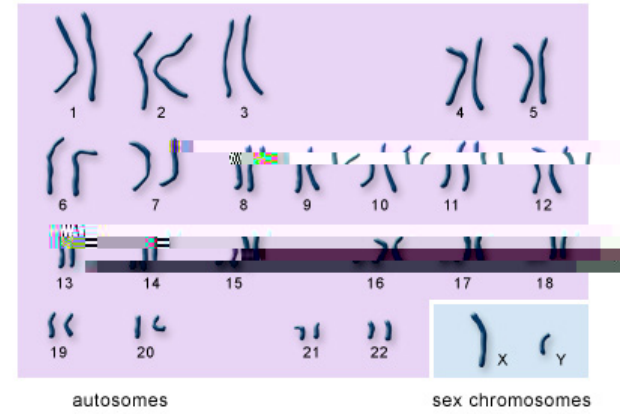
Most TTR in the body is produced in the liver, and liver transplantation has been helpful in some patients with familial amyloid polyneuropathy caused by mutations other than Thr60Ala. However, liver transplantation does not prevent the progression of cardiac ATTR amyloid deposits in Thr60Ala amyloidosis. When patients with this condition have undergone liver transplantation, normal 'wild-type' ATTR from the transplanted liver has formed new amyloid deposits in the heart, that build up over the template of the pre-existing ATTR Thr60Ala amyloid deposits. Liver transplantation is therefore not effective for patients with ATTR Thr60Ala.

Heart transplantation

Appendix 1

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.



U.S. National Library of Medicine

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.

All the other 44 chromosomes apart from the X and Y chromosomes are referred to as 'autosomes'. Diseases that result from mutations in genes within the autosomes may be passed on from parent to child by 'autosomal dominant' inheritance or by 'autosomal recessive' inheritance.

ATTR Thr60Ala amyloidosis 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 ATTR amyloidosis have important effects on the abnormal so-called 'variant' TTR whose production they determine. The differences in structure between the normal and the amyloidogenic variant TTR are usually extremely small but nonetheless they have very important effects on the behaviour of the variant TTR. The variant TTR proteins have an increased tendency to misfold, clump together and form amyloid fibrils. Thus even a very small change in the TTR gene can lead to serious disease.

DPD scanning and SPECT are safe tests. There is only slight exposure to radiation from the tracer and the CT scan.

: DPD scan. : fused CT/SPECT scan.
Both scans show TTR cardiac amyloidosis.
The arrows point at the