Managing symptoms of AL amyloidosis and the side-effects of treatment

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AL amyloidosis: involves almost every system

Visible tissue infiltration
- bruising (especially around eyes)
- tongue (enlarged, stiffened)
- muscles (stiff and resistant)

Kidneys
- leak protein (ankle swelling)
- stop working (kidney failure)

Liver
- big liver (pressure symptoms such as feeling very full or sick after meal)
- liver failure rare

Heart
- breathlessness
- fatigue
- palpitations
- giddiness and blackouts
AL amyloidosis: involves almost every system

**Peripheral nerves**
- numbness
- pain (often burning or electric shock)
- muscle weakness

**Gut**
- weight loss/loss of appetite/bloating
- bleeding
- constipation/diarrhoea

**Autonomic nerves**
- giddiness
- bowel upset (diarrhoea/constipation)
- nausea, vomiting, sweating when eating
- coat hanger pain
- impotence
Supportive Treatment

Over the past 10 years patient survival has improved thanks to:

1. advances in treatments of the underlying diseases – chemotherapy
2. better supportive care

Cardiac symptoms

A build up of amyloid in the heart muscle can lead to:

- a heart that can't easily stretch (a stiff heart AKA diastolic failure)
- accumulation of excess water in the body – this always needs excess salt
- reduced blood flow through vital organs
- low blood pressure
### Cardiac symptoms

‘Heart failure’ describes the symptoms that arise:

- breathlessness
- swelling of the feet and ankles
- tiredness
- loss of appetite, weight loss, nausea
- disrupted sleep patterns
- dizziness and blackouts

### Diagnosis of amyloid cardiomyopathy

- Routine tests:
  - ECG
  - Echocardiography (ultrasound scans)
- MRI scans of the heart
- DPD scan – seems very helpful in picking up TTR amyloid in the heart
- Blood tests:
  - NT-proBNP
  - Troponin
  Used to track changes – both affected by kidney function
### Diagnosis of amyloid cardiomyopathy

- The SAP (whole body amyloid) scan is not able to demonstrate amyloid in the moving heart
- Occasionally a tiny heart muscle biopsy via a blood vessel in the heart or leg

**Why so many different tests?**
Because none are completely specific for amyloidosis. All tests have to be interpreted and can be affected by other conditions e.g. a history of high blood pressure; kidney disease; a previous heart attack or angina

### Treatment of cardiac failure: drugs

- Diuretics drugs (water tablets) form the mainstay of treatment by:
  - removing excess salt and water from the body into the urine
  - removal of excess body fluid reduces ankle swelling and breathlessness

- Diuretics increase the amount of urine produced (often easier to take them earlier in the day):
  - Frusemide/Bumetanide: often the first diuretic to be prescribed
  - 'high ceiling' – dose can be increased a lot (20mg a day up to 500 mg a day)
  - other diuretics e.g. spironolactone can be added to increase the effect (many only taken at much lower doses)
Monitoring diuretics

- blood pressure and weight
- blood tests – the tablets make the kidneys waste a variety of body salts and blood tests are required to make sure some of these (e.g. potassium, magnesium, sodium) are not becoming dangerously low

Sometimes tablets are not enough

- diuretics have to given by injection/infusion in hospital for a few days
- Dialysis is used occasionally to remove extra water

Many drugs prescribed in other common types of heart disease are not particularly helpful

‘heart failure’ drugs reduce already low blood pressure in patients with cardiac amyloidosis, and can worsen symptoms

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What can I do to help my heart?

Diet, diuretics and healthy heart

Diuretic drugs encourage loss of excess salt and water from the body. Their effect may be completely lost if your salt and water intake is too high:

- Reduce salt intake and do not add salt to your food or cooking
- Do not drink too much - around 1.5 litres daily is plenty
- Weigh yourself regularly (weekly or even daily) and write it down
- Most of the body is water - every litre of excess fluid retained weighs 1kg (2.2 pounds)
- Most people’s weight varies from week to week, or even day to day, by ± 1-2 kilograms
- Chemotherapy drugs – particularly steroids, can make the body hold onto salt and water
What is the right weight?
It varies – season, flesh weight etc.

<table>
<thead>
<tr>
<th>Happy heart</th>
<th>Happy lungs</th>
<th>Happy guts</th>
<th>Happy blood pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>minimal ankle swelling (but still a little bit if you press)</td>
<td>not breathless at rest or gentle exertion</td>
<td>not feeling bloated nor permanently full</td>
<td>- not giddy when you stand up - warm fingers and toes</td>
</tr>
</tbody>
</table>

Aims:

If I have questions where can I get help?

Specialist heart failure nurses
- provide information
- guide you in the day to day management of 'heart failure', often via the telephone
- help with management of disease symptoms as well as disease-related anxiety and stress

GP or hospital specialist
- e.g. cardiologist, nephrologist, haematologist
- may provide help with management of heart failure

Doctors and nurses at the Nation Amyloidosis Centre
- can be contacted between 8am – 6pm Mon-Fri
**Palpitations**

- when you are aware of your heart beating
- sometimes normal, sometimes the heart is going:
  - too fast (tachycardia)
  - too slow (bradycardia)
  - irregularly (atrial fibrillation)
- **diagnosis**
  - ECG and/or 24-hour tape/implanted reveal device
- **treatments**
  - drugs depending on what the rhythm problem is
- **pacemaker**
  - implanted electric device which fixes the slowest speed at which the heart will pump
- **defibrillator**
  - implanted electric device which can shock the heart if it goes much too fast

**Nephrotic syndrome:**
when the kidneys leak normal healthy blood proteins

**Defined as:**

- **Significant proteinuria**
  - normal blood protein (albumin) leaks into the urine
- **Hypoalbuminemia**
  - too low levels of the healthy protein albumin in the blood
- **Peripheral oedema**
  - swelling of the legs and around the eyes due to the abnormal collection of fluids in the tissues

May be accompanied by kidney failure
Potential complications of severe nephrotic syndrome

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
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<tbody>
<tr>
<td>Oedema</td>
<td>Water that should be trapped in blood leaks into tissues</td>
</tr>
<tr>
<td>Hypovolaemia</td>
<td>• too little fluid in blood stream</td>
</tr>
<tr>
<td></td>
<td>• low blood pressure causing weakness, giddiness or blackouts</td>
</tr>
<tr>
<td>Blood clots</td>
<td>• factors normally protecting blood from clotting are also lost</td>
</tr>
<tr>
<td></td>
<td>• risk of blood clots in the legs, lungs or other sites</td>
</tr>
<tr>
<td>Infections</td>
<td>• greater risk of bacterial infection of the blood – septicaemia</td>
</tr>
<tr>
<td>Kidney failure</td>
<td>• it’s not good for kidneys to leak a lot of protein – esp. if not seeing enough blood flow (low blood pressure)</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>• the blood fat cholesterol rises because of the over production by the liver as part of making more albumin (the healthy blood protein)</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>• the body needs to replace the protein it loses</td>
</tr>
<tr>
<td></td>
<td>• if there is a lot of oedema the gut can get ‘soggy’ and that reduces appetite</td>
</tr>
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</table>

Treating the symptoms of nephrotic syndrome

- **Proteinuria** — Treatments that lower the blood pressure in the kidney may reduce the amount of protein lost and protect against renal failure
  - most common treatment is blood pressure tablets (ACE inhibitors) aiming for a blood pressure of <120/80 mmHg
  - dietary protein restriction is not a good idea as it tends to worsen malnutrition
- **Oedema** — due to water and salt retention by the kidneys and treated with:
  - dietary salt restriction
  - pressure stockings
  - water pills (diuretics) – gently to avoid low blood fluid levels and low BP
  - injections of albumin may be required in severe cases
- **Elevated blood lipids** — Increases in blood cholesterol often seen with the nephrotic syndrome
  - if the nephrotic syndrome persists, treatment may be given to lower cholesterol.
  - Cutting out fats doesn’t usually help and risks malnutrition
  - use of lipid lowering drugs - class of drugs called statins
- **Blood clots** — Blood thinners can be given
  - carries real risks of bleeding and needs to be considered carefully for each individual
What is Postural Hypotension?

A fall in blood pressure (hypotension) which occurs on sitting or standing up (postural) and which may result in a range of symptoms due to lack of blood to the organs.

This can be due to:

- heart failure
- nephrotic syndrome
- damage to the autonomic nervous system: automatically regulates the flow of blood to desire areas and controls the volume of fluid in the circulation
  - a complex system that should maintain a constant blood supply to vital organs such as the brain and the heart
  - also provides a supply to other areas when needed for everyday activities e.g. eating or walking

What are the symptoms of postural hypotension?

Symptoms arise because of decreased blood supply to the brain, muscles or other parts of the body:

**Brain:**
- dizziness or light-headedness
- visual changes, e.g. blurred or tunnel vision, greying or blacking vision
- feeling of impending doom
- decreasing level of awareness, leading on occasion to confusion
- loss of consciousness (blackout/faint) with or without warning

**Muscles:**
- pain across the back of the shoulders or neck – coat hanger pain
- pain in the lower back, buttocks
- angina-type chest pain

**General:**
- sweating
- weakness
- Fatigue
- confusion
When are they likely to happen?

Whenever there is an increased demand for blood for activities throughout the day:

- In the **morning**, as blood volume is lower
- **Sudden movement**, particularly from a lying to a sitting or standing position
  - Mechanisms that raise your BP cannot be activated swiftly enough
- **On exertion**, as the demand from exercising muscles deprives the brain of blood
- **After meals**, when the digestive system needs blood
  - **Alcohol** has a similar effect
- After **inactivity**, especially bed rest
- In the **warmth** of a centrally heated room, hot bath or a warm summer day
  - More blood goes to the skin (i.e flushing), thus lowering blood pressure
- **When constipated** the effort of straining causes symptoms
  - They can also occur when coughing or if there is any effort involved in passing urine
- **Illness**, from a cold to more serious conditions.
- **Anxiety** can cause overbreathing which lowers blood pressure
- A variety of **drugs** can lower blood pressure
  - Always check new medication with your doctor

Strategies you can use

**Exercises** – help pump blood back to the heart

These can all be used while in bed, sitting or standing:

- leg exercises, flexing the ankle and foot up and down, or squeezing the calf muscle
- gentle “marching” movements
- crossing and uncrossing the legs

**Manoeuvres**

- crouching or squatting
- bending forward
- stomach pressing: this can be used when bending forward and is the position most people adopt when they feel faint

Techniques can be used discreetly (e.g. crouching down to tie a shoe-lace) at the first sign of symptoms or before starting an activity which causes symptoms
Emergency measures

If you feel dizzy or faint, **sit down or lie down immediately** until the feeling passes

- derby-stick or shooting-sticks that convert to a seat, allow you to rest whenever, wherever

If loss of consciousness (blackout) occurs, your family or carers should:

- lie you down flat
- make you safe – remove any dangers such as hot drinks
- check your airway, breathing and circulation (simple first aid checks)
- raise your legs above the hips and hold them there for 3-5 minutes

This usually works quite quickly but if there is no response **get urgent medical attention**

Summary of helpful options

<table>
<thead>
<tr>
<th>Things to avoid</th>
<th>Things to do</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lying flat</td>
<td>Raise your head of the bed so that your head is higher than your feet (use blocks for the bed legs, a foam wedge or an electric bed raiser)</td>
</tr>
<tr>
<td>Sitting/standing up quickly, especially on waking</td>
<td>Get up slowly, change position in gradual stages. Use exercises and positions</td>
</tr>
<tr>
<td>Early morning activity</td>
<td>Plan important activities for your best time of day, usually late morning or early evening</td>
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<tr>
<td>Inactivity</td>
<td>Choose gentle exercise where you can take frequent rests (e.g. vacuuming, swimming)</td>
</tr>
<tr>
<td>Warm environment</td>
<td>Keep cool, use fans, take extra fluid and salt</td>
</tr>
<tr>
<td>Straining when constipated</td>
<td>High fibre diet and high fluid intake help prevent constipation. Consider daily laxatives</td>
</tr>
<tr>
<td>Large meals, refined sugar and alcohol</td>
<td>Eat 5/6 small meals daily Increase salt intake (add to cooking/meals) Include salty snacks (e.g. crisps/nuts) Drinks during the day; coffee and drinks with caffeine help, esp. when taken with food</td>
</tr>
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Drug management of postural hypotension

Often useful but lots of serious side effects:

- **Mineralocorticoids** – a type of steroid
  - Salt retention/expand blood volume
    - Fludrocortisone
    - Nandrolone

- **Alpha-adrenergic agonists** – make the heart pump harder and faster and make the blood vessels in your peripheries close up
  - Midodrine

- **Inotropes** – make the heart pump harder and faster
  - Ephedrine

- **Vasopressors** – help the kidneys hold on to water
  - DDAVP
## Nausea and diarrhoea

- **both contribute to malnutrition**
  - stopping eating is *not* a good way to handle the symptoms

- **nausea and vomiting**
  - metoclopramide and erythromycin tablets can help
  - anti sickness drugs work best if taken 10-20 minutes before you eat
  - small frequent meals

- **diarrhoea**
  - can be sometimes be helped by antibiotics
  - Imodium is often helpful and can be combined with codeine phosphate
  - injected agents such as somatostatin sometimes help

## Nutrition and supplements

- It is very easy to lose weight with amyloidosis but not a good idea
- **Common problems that put people off eating are:**
  - fatigue
  - changed or decreased sense of taste
  - dry mouth
  - sore tongue, blood blisters inside mouth
  - feeling full very quickly
  - drug side effects

- If you do not think you are eating enough
  - do not rely on feeling hungry – plan small frequent meals, ‘sloppy’ foods are easier than meat or bread
  - with a very sore mouth – soft plastic ‘baby spoons’ can be more comfortable than metal cutlery
  - you need to see a dietician early

- **Food restriction**
  - makes you more tired
  - is not a good idea – we often ask you to avoid salt but not protein or fat

- **Supplements**
  - help but don’t replace eating - should be used early
  - if you don’t like the taste get a selection of different makes and flavours and see if you like any other ones better
Fatigue

• A very difficult symptom with no good treatment
• Typically in amyloidosis it comes and goes
• Trying to sleep at night helps
  – if you are not sleeping at night try to avoid excessive day time naps
  – a cool dark bedroom can help a bit
  – there is a lot of advice of the web – try searching for sleep hygiene
• eating enough helps
• planning so that you only do vital or enjoyable activities helps to make the best of your energy

Pain

• Amyloidosis not usually painful
• Joint capsule amyloid is rare but can be very sore – tends to affect the shoulders
  – Prednisolone can help
• Neuropathy - damage to the nerves can cause electric shock or burning pains in feet and hands
  – A cradle to keep the bed clothes off the legs can help
  – Counter irritation by rubbing the skin with slightly tingling creams can help
  – Medications include:
    • amitriptyline
    • Gabapentin/pregabalin
      These can help but have several side effects which can limit their use
  – Injection/surgery for carpal tunnel syndrome
Exercise

• within reason, some level of exercise is good
• exercise is important for general well-being but avoid exhaustion
• do not push yourself if you or your symptoms are telling you to stop!

Summary

• Amyloidosis can produce a lot of symptoms
• Management can be difficult and often requires a combination of:
  – behavioural changes
  – medication changes
  – patience with a lot of gentle fiddling until matters are as good as possible