



Alström Syndrome

A guide to understanding this rare condition



Raising Awareness of Alström Syndrome

This booklet has been produced by Alström Syndrome UK to promote greater awareness, knowledge and understanding of Alström Syndrome.

It is hoped that the booklet will prove useful to medical and healthcare professionals and to parents anxious to know more about the Syndrome and the advances in methods of treatment.

This booklet uses a wide range of terms for medical conditions which may affect children and adults with Alström Syndrome. These are explained throughout the booklet and summarised in a glossary on page 17. Please note that the symptoms and conditions listed are intended to aid diagnosis and do not necessarily apply in every case of Alström Syndrome.

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Alström Syndrome UK (ASUK)

Alström Syndrome UK, is a registered charity, established in 1998 to provide support for families and professionals.

The charity has been instrumental in developing specialised medical screening clinics which are now held in Birmingham.

These multi-disciplinary clinics offer a carousel of tests and assessments to ensure personalised advice is given to each family. This helps patients find ways to manage their symptoms.

ASUK provide a conference which gives families a chance to hear talks from leading specialists on how best to manage this complex condition, hear research developments and meet others affected.

ASUK were delighted to be awarded the EURORDIS Patient Organisation Award. This prestigious award is given in recognition of extraordinary work and commitment to patient support and advocacy for people with Alström Syndrome.

For the latest information visit: www.alstrom.org.uk

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Introduction to Alström Syndrome

Alström Syndrome is a very rare recessively inherited condition. The symptoms are not always easily recognised. It was first described in 1959 by Carl Henry Alström in Sweden and the full characteristics of the syndrome became apparent in the subsequent 25 years [1,2]

Because it is so rare, many health professionals will not have come across Alström before - or perhaps have even heard of it [3].

It is estimated that many families in the UK could be suffering from Alström Syndrome but remain undiagnosed. This booklet is designed to create greater awareness and understanding of Alström Syndrome throughout Health, Education and Social Care Services. The aim is to provide guidance to families and professionals and to highlight the help and support that is currently available to both children and adults to enable them to lead a healthier life.

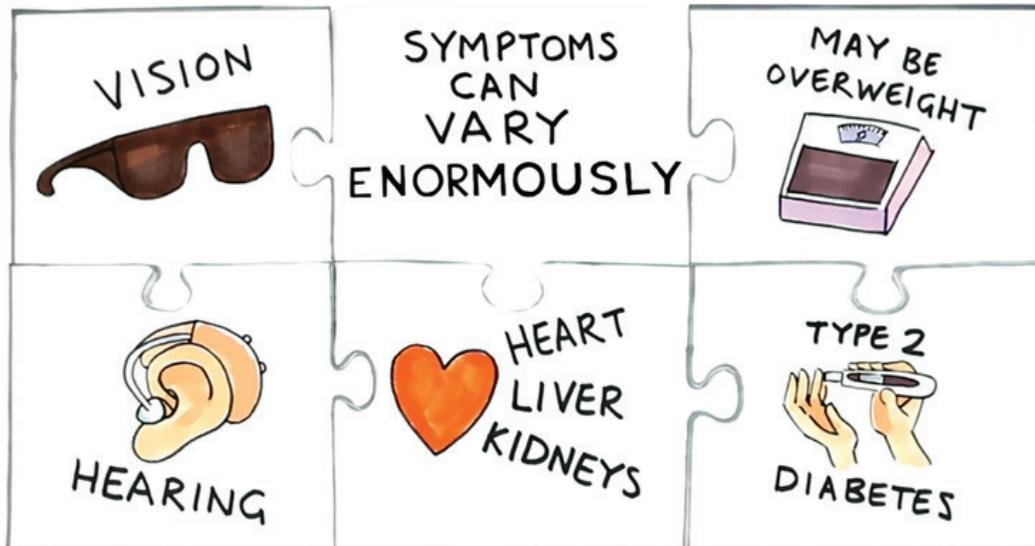
What is Alström Syndrome?

Alström Syndrome is characterised principally by:

- Retinal degeneration (inherited progressive eye disease)
- Nystagmus (wobbly eyes)
- Photophobia (sensitivity to light)
- Infant cardiomyopathy (potentially reversible infant heart failure)
- Sensorineural hearing loss (disorders of the cochlea)
- Obesity and Insulin resistance

Additional features from childhood can include:

- Renal and hepatic dysfunction (variable scarring of the kidneys and liver)
- Type 2 diabetes mellitus
- Hypertriglyceridaemia (elevation of fatty substances found in the bloodstream)
- Adolescent cardiomyopathy (poor cardiac function where the heart muscle is weakened and enlarged)
- Urethral detrusor dyskinesia (bladder spasms)
- Kyphoscoliosis (twisting of the spine)
- Reflux oesophagitis (heartburn)



N.B. It is important to emphasise that not all of the complications of the Syndrome occur in all those affected. A healthy lifestyle and appropriate therapies may minimise the impact of most of these problems. Even amongst siblings the symptoms may vary widely [4-6].

What causes Alström Syndrome?

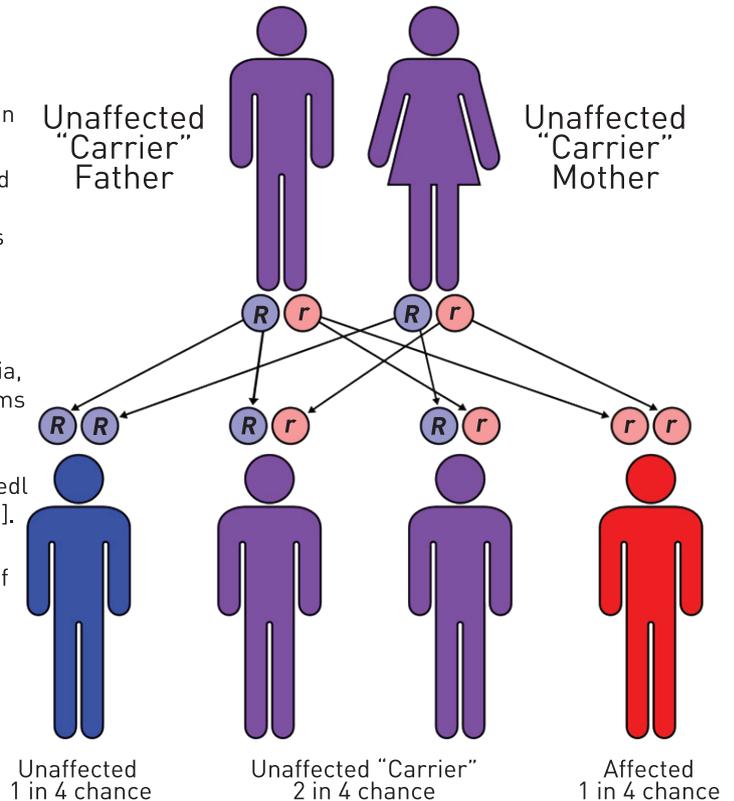
The condition is recessive, and the gene involved has been discovered [7,8] Mutations in both copies of the ALMS1 gene are required to cause the syndrome. Each parent will have one typical copy of the gene and one with a significant mutation (they are carriers with no known effects on their health).

On average one in four children of a couple who are both carriers will inherit both ALMS1 mutations and suffer from the condition. More than 80 pathological mutations in the ALMS1 gene have been identified in families with Alström Syndrome.

The ALMS1 protein, whose function is currently unknown, is found in the centrosome and/or the ciliary basal body. This suggests that Alström Syndrome is one of a growing collection of disorders known as 'ciliopathies' [9,10].

Cilia are like small antennae projecting from cell surfaces and perform diverse biological roles. Defects in cilia are associated with a range of human diseases, such as primary ciliary dyskinesia, hydrocephalus, polycystic liver and kidney disease, and some forms of retinal degeneration. Recent evidence indicates that ciliary defects can lead to a broader set of problems, with mutations in ciliary proteins now associated with nephronophthisis, Bardet-Biedl Syndrome, Alström Syndrome, and Meckel-Gruber Syndrome[10,11].

Early diagnosis of Alström Syndrome allows more appropriate clinical intervention, which may enable improvements in quality of life and longevity.



+ Medical terms explained

Centrosome (tiny organising centre of the cell)

Ciliopathies (genetic disorders caused by disturbance of the actions of the complex network of the hair like protrusion from each cell and their interaction with intracellular transport of proteins)

Ciliary dyskinesia (poor function of cilia especially in the respiratory system)

Hydrocephalus (excess water in the brain)

Nephronophthisis and nephropathy (disease affecting the kidney functions)

Annual review guide



Good medical practice involves a clear history, physical examination and investigation in any outpatient review

History from patient with Alström Syndrome

- General well-being
- Psychology - adjustment to condition
- Mobility
- Eyesight and visual aids - Braille, IT
- Hearing and appropriate hearing aids
- Growth and development
- Diet and exercise assessment

Ask if there is any:

- Shortness of breath
- Tiredness
- Problems with passing water
- Heartburn
- Treatment being taken

Examination

- Observe mobility
- Assess spine
- Weight, height, blood pressure
- Acanthosis nigricans (darkening and increase in thickness of cells in the skin)
- Condition of feet
- Listen to heart and lungs
- Palpate abdomen

Blood tests

- Urea, creatinine and electrolytes
- Full blood count
- Liver function tests
- Haemoglobin A1c
- Post prandial C-peptide and blood glucose
- Serum triglycerides and cholesterol
- Thyroid function
- Oestrogen or testosterone, FSH and LH
- Brain natriuretic peptide

Scans and other tests

- Bladder scan post micturition (after the passage of urine) if urinary symptoms
- ECG
- Echocardiogram
- Respiratory function
- Liver scan

From seven years and older standard respiratory function tests

- Peak Flow
- Forced Expiratory Volume in 1 second (FEV)
- Forced Vital Capacity (FVC)
- FEV1/FVC ratio
- Digital oximetry (determination of oxygen and carbon dioxide levels in the blood) at rest and after a five-minute walk

Making a diagnosis

The following key factors distinguish Alström Syndrome from most other cone rod dystrophies:

- Nystagmus and photophobia, usually but not always, in early infancy.
- Progressive pigmentary retinopathy (cone-rod dystrophy)
- Childhood obesity, often moderating to high-normal weight in adulthood.
- Mild to moderate bilateral sensorineural hearing loss.
- Congestive heart failure secondary to cardiomyopathy, in infancy or early adulthood.
- Hyperinsulinemia / insulin resistance.
- Non-insulin dependent diabetes mellitus (Type 2 diabetes or NIDDM) developing in early adulthood.
- Progressive chronic nephropathy.
- Varying degrees of development, with some reports of delayed developmental milestones.

It is important to emphasise that not all of the complications of the syndrome occur in all those affected. A healthy lifestyle and appropriate therapies may minimise the impact of most of these problems. Even amongst siblings the symptoms may vary widely [4-6]



A wide range of other conditions can be present in some, but not all, cases including hypothyroidism, portal hypertension, alopecia, scoliosis, hypertension, urinary tract infections, gastro-intestinal reflux, asthma and respiratory problems **(see the website www.alstrom.org.uk for a more comprehensive guide).**

The abnormality in the ALMS1 gene and consequent dysfunction/absence of the ALMS1 protein affect all the cells of the body. It follows that even protein or gene therapy would be unlikely to cure all the manifestations of Alström Syndrome. However significant improvements in well-being have been achieved by healthy lifestyle and established therapies for each system affected.

⊕ Medical terms explained

Nystagmus (wobbly eyes)

Photophobia (sensitivity to light)

Cone-Rod Dystrophy (CRD) (an inherited progressive eye disease)

Cardiomyopathy (weakness of the heart muscle cells)

Nephropathy (kidney disease)

Aetiology (study of causes and origins)



Looking for signs of Alström Syndrome

Clinical features

Eyes

This is often the first indication of the syndrome. Children who are affected may have an involuntary rapid movement of the eyes (wobbly eyes / nystagmus) and extreme photophobia (extreme sensitivity to light).

Eyesight often slowly deteriorates during childhood, and most young people who are affected may lose the ability to read print during the second decade. Protection of the retina from bright light with dark glasses is essential to avoid photophobia. It is not established whether this can slow down visual loss.

Progression of visual loss in Alström Syndrome is variable and sudden loss of vision has been described.

Treatment

Gene replacement therapy is at an early stage of research in general retina dystrophies.

Currently, there is nothing proven to prevent visual deterioration in sufferers. Ophthalmological advice is crucial to optimise life with low vision. Dark glasses will be needed indoors and out to combat the extreme photophobia experienced by patients with Alström Syndrome when young. Prescription glasses can also help. Teaching of IT and Braille should be introduced as early as is feasible.

⊕ Medical terms explained

Nystagmus (wobbly eyes)

Photophobia (sensitivity of light)

Sensorineural hearing loss (deafness due to problems with the inner ear and auditory nerve)

Glue ear (fluid in the middle ear preventing conduction of sound to the inner ear).

Hearing Loss

Hearing loss in patients with Alström Syndrome varies considerably in degree of severity and also age of onset. 'Glue ear' is common in childhood, often accompanied by very runny noses and should be treated. A small number of older patients have been treated successfully with Cochlear implants[12].

Treatment

Early recognition is vital to maintain educational and social development and regular hearing tests are advised. Hearing aids and other auditory devices can help considerably in alleviating problems and the patients should be fitted with the latest technology that is available.



Heart - Cardiomyopathy

Alström Syndrome can cause the heart muscle to pump less efficiently. This is known as a cardiomyopathy. This occurs in about 40% of infants with Alström Syndrome and the heart often recovers, although not completely, and can re-occur or present for the first time in later life[13,14].

The heart muscle develops lots of small scars (fibrosis), myocardial fibrosis, usually in a patchy manner. In infants the heart may stretch or dilate, but in older patients fibrosis (scarring) makes the heart stiff and inflexible, termed 'restrictive' cardiomyopathy.

Other causes of cardiomyopathy, such as viruses, may be suspected until other signs of Alström develop e.g. wobbly eyes (nystagmus) and photophobia (sensitivity to light).

Cardiomyopathy can also occur during adolescence when the outcome may not be so good. It is often misdiagnosed as asthma in children and young people because it can cause breathlessness and wheeze.

It is important to recognise cardiomyopathy early, so treatment can be started promptly. It is recommended that patients who have had cardiomyopathy should have:

- An annual cardiac review, with an echocardiogram (echo) - a painless ultrasound scan which looks at the structure and function of the heart.
- An ECG (electrocardiogram) which traces electrical activity in the heart.

Ideally, blood oxygen levels should also be monitored, together with exercise capacity. The role of blood hormone tests and cardiac MRI scanning is being evaluated.

It is also recommended that even if patients have not had cardiomyopathy they should have annual cardiac review with a detailed discussion of exercise capacity and ECG.

Change in ECG results should trigger an echo. It is helpful if the person doing the echocardiogram knows to look for evidence of 'restrictive' cardiomyopathy because the signs are often subtle. New echo techniques (Tissue Doppler) will improve this.

Treatment

Cardiomyopathy in Alström Syndrome affects both the right and left sides of the heart, which is important as treatment may differ depending on which side is more severely affected.

Effective treatments to improve symptoms have included: Digoxin, furosemide, angiotensin converting enzyme (ACE) inhibitors, beta-blockers and spironolactone.

Ischaemic heart disease

It has recently been shown that the early onset of diabetes and high blood fats in Alström Syndrome can lead to coronary artery blockages and ischaemic heart disease. This is distinct from cardiomyopathy and may well be prevented by healthy lifestyle and treatments to lower blood fats[15,16].



Caution



Both patients and their doctors should be aware that cardiomyopathy can happen suddenly in people affected by Alström Syndrome and patients are vulnerable during intercurrent illness and surgery. At these times, close monitoring is essential and expert advice should be sought as needed.

Obesity

Children with Alström Syndrome may gain weight rapidly. In some increased appetite (hyperphagia) is a factor. They may also have limited ability for physical exercise due to sensory impairment and decreasing eyesight. Help from a dietitian should be sought at an early age for specific help and advice.

Adults have been seen to benefit from modest restriction of carbohydrate as well as calorie control and exercise[6,17]. Culture may be an important factor to consider. Particularly as there is evidence to suggest there is a difference in the progression of obesity in Alström Syndrome, in people affected in Italy and Canada for example.

Treatment

Diet and exercise are very important in managing weight in people affected by Alström Syndrome. Avoiding energy dense convenience foods accompanied by regular exercise are crucial. Children may also benefit from a modified healthy eating plan with a reduction in carbohydrate and life long regular exercise is emphasised. ASUK encourage healthy lifestyle choices, by providing grants for families and individuals affected to fund specialised trikes and tandems, fitness monitors and gym membership.

Dietary advice will always be tailored to the patient's individual and cultural needs.



ASUK encourage exercise and provide a bike club where tandems and trikes can be loaned.

Type 2 diabetes

Insulin resistance is present from infancy, but progression to type 2 diabetes is influenced by lifestyle as described. From UK clinical experience, diabetes occurs in 50% of adults affected.

There are a small number of patients who have type 1 and type 2 diabetes.

Treatment

The 'first-line' treatment is dietary advice, weight control and physical activity. If the blood glucose level remains high despite these measures, then tablets to reduce the blood glucose level are usually advised. Other treatments include reducing blood pressure if it is high, and other measures to reduce the risk of complications. Treatments include:

- More detailed and targeted dietary advice
- Exercise programmes
- Metformin or Exenatide or Liraglutide
- Insulin - in those who lose some of the capacity to produce insulin and when blood glucose levels continue to increase despite diet and oral therapy. Early evidence suggests that post-prandial C-peptide/glucose ratio can reflect insulin deficiency [6].

Lipid disorders

As is common in other insulin resistant conditions patients with Alström Syndrome tend to have high serum triglyceride levels, low HDL cholesterol and variable increases in total serum cholesterol.

Hypertriglyceridaemia if severe ($\rightarrow 10\text{mmol/l}$) will respond acutely to fasting and long term to nicotinic acid. With milder dyslipidaemia long term statin therapy is indicated [4,20]. As the high risk of coronary artery disease has now been well demonstrated in the syndrome, statin therapy should be introduced from adolescence.

Kidneys - Renal Failure

Renal failure (poor kidney function) can occur in patients affected by Alström Syndrome [21]. It is not related to diabetes or pyelonephritis (UK clinical experience).

It is recommended that all patients receive regular blood monitoring, and annual urine testing and serum creatinine testing.

In patients with Alström Syndrome acute renal failure has occurred in some patients with ileal conduits (part of the intestine used as a urinary conduit) and chronic kidney failure is more prevalent from the third decade of life. Currently the cause is not fully understood but, like the heart, the kidneys may develop fibrosis.

Renal failure is described as a decrease in the glomerular filtration rate. Each kidney contains over one million tiny filtering units, called glomeruli, which remove waste chemicals etc from the blood.

Problems frequently encountered are abnormal fluid levels in the body, imbalanced pH levels, abnormal levels of potassium, calcium, phosphate, hematuria (blood in the urine) and (in the longer term) anaemia. Long-term kidney problems can impact on other diseases e.g. cardiovascular disease.

Acute renal failure

People with Alström Syndrome very occasionally experience sudden decline in kidney function (acute renal failure) because of reduced blood pressure associated with cardiomyopathy, infection (see pneumonia) and therapies prescribed for diabetes, the heart, and hypertension. Treatment is urgent and consists of rehydration, temporary withdrawal of hypotensive therapies and intensive treatment of infection.

Chronic kidney disease

More than 50% of those affected will have a degree of chronic kidney disease which is usually slowly progressive, due to diffuse renal fibrosis and has been successfully managed short term with haemodialysis and good results from renal transplantation in some cases UK clinical experience[16].

Methods of measurement for CKD

Chronic kidney failure is measured in five stages, which are calculated using a patient's GFR, or glomerular filtration rate. Stage 1 and 2 CKD may be associated with normal kidney function, but increased loss of protein in urine and high blood pressure. However, if there are other signs of damage to the kidneys close monitoring may be necessary. Stages 3 and 4 need increasing levels of supportive care from their medical providers to slow and treat their renal dysfunction.

Patients in stages 4 and 5 usually involve active treatment. Stage 5 CKD is considered a severe illness and requires some form of renal replacement therapy (dialysis) or kidney transplant whenever feasible.

Glomerular filtration rate

A normal GFR varies according to many factors, including sex, age, body size and ethnicity. Renal professionals consider the GFR to be the best overall index of kidney function. The National Kidney Foundation offers an easy to use on-line GFR calculator for anyone who is interested in knowing their glomerular filtration rate (a serum creatinine level, a simple blood test, is needed to use the calculator).

Further information can be found at www.kidney.org.uk.

Transplants

Transplants

Transplants need to be carefully thought through with the multi-disciplinary specialist teams in Birmingham and the patients local teams to enable a joint approach.

Endocrine / Fertility / Genitalia

Males

Delayed puberty and hypogonadism is common[14]. Treatment with testosterone is usually given by monthly depot injections if required. Fertility has not been conclusively proven, and testicular histology has been shown to demonstrate fibrosis[2.]

Acanthosis nigricans

Darkening and velvety thickening of skin in the flexures (neck, axillae, groins and knuckles is common). It is a sign of insulin resistance, may decrease with reduction in insulin with diet and exercise. It is not caused by lack of personal hygiene and cannot be washed clean (UK clinical experience).

Respiratory changes

The combination of kyphoscoliosis, restrictive lung function and subtle pulmonary fibrosis can impair exercise capacity in some patients affected. Rarely this may lead to hypoxia during surgery or intercurrent pneumonia [22].

Vaccinations

At the clinics in the UK families and individuals are recommended to have annual influenza vaccination and 5 yearly pneumococcal immunisation.

Other Conditions

Treatment

The AS physiotherapy team in Birmingham can personalise exercise routines and give guidance about poor core stability, which some patients are affected by. In our experience, patients often find insoles in their shoes can also help flat foot (fallen arches in the feet), which some patients are affected by. Painful joints can also be a problem and personal guidance and exercises should be discussed with your physiotherapist for the best course of treatment and advice. Further information about arthritis and spinal changes can be found on the next page.



Rheumatology and Orthopaedic changes

Growth and Postural changes

The majority of those with Alström Syndrome have advanced bone age and epiphyseal fusion (maturation of the growing ends of bones at wrist, knee and in the spine) resulting in short stature.

Excessive curvature of the cervical spine (neck) can result in an arching forward of the head and neck. This is reversible in younger patients but can become fixed in adulthood. This is not seen in other causes of early blindness and affects less than 50%. It is not yet clear whether exercises can prevent this effect.

Developmental spinal changes

A varying degree of forward curvature of the thoracic spine (around the chest area) is extremely common in those with Alström Syndrome. This is rarely severe but may contribute to neck aches and can slightly reduce lung function by restricting lung volume and chest expansion.

In a smaller number, the spine can be twisted sideways (scoliosis). This can also cause pain in the back and if the lower ribs rub against the top of the hip on one side. Regular stretching exercises can relieve discomfort though if kyphoscoliosis (curvature and twisting of the spine) is severe from a young age then major surgery might be needed.

Secondary spinal changes

Excessive thickening of the spine (spondylitis), which is known to occur sporadically in persons affected by type 2 diabetes, rarely occurs in Alström Syndrome. If the bony thickening rubs on nerves flowing from the neck, then pains and weakness can exceptionally occur. Surgery for this is very specialised and its place in the syndrome is uncertain.

Arthritis

A minority of young adults have painful joints not yet well characterised.

Therapy

Stretching exercises, swimming, dancing and walking as well as massage - all have a place in relieving symptoms. Weight reduction in obesity cases has also helped to relieve backache.



Considerations where surgery is involved

Blindness due to retinal degeneration and sensorineural partial hearing loss may be accompanied by obesity and insulin resistance. Other manifestations such as infant and/or adult cardiomyopathy, kyphosis and pulmonary fibrosis are variable in occurrence and severity.

This combination of cardio-respiratory changes can predispose to unexpectedly severe hypoxia during episodes of infection or post-operatively. Metabolic disturbances can include hypertriglyceridaemia, and insulin-resistant diabetes.

The severity and responsiveness to treatment of hyperglycaemia is variable, just as in adult type 2 diabetes. A few patients require up to 500 insulin in very high doses long term, but many respond to Metformin and/or Glitazones providing cardiac and renal function are good. Hypertriglyceridaemia if severe ($\rightarrow 10\text{mmol/l}$) will respond acutely to fasting and long term to nicotinic acid.

In preoperative assessment, therefore, we would advise:

- Echocardiogram
- Pulse oximetry before and after exercise
- Blood glucose
- Serum triglycerides
- Renal and hepatic function tests

Peri-operatively and post-operatively:

Very careful monitoring of heart and oxygenation until fully recovered and ambulant. Monitoring of blood glucose - levels

of both blood glucose and serum triglycerides normalise in 24-48 hours during fasting and do not usually require intravenous insulin.

NB Photophobia and nystagmus can be troublesome for people affected by Alström Syndrome. Every effort should be made to adjust the surroundings to make the patient more comfortable and avoid bright lighting. It is best to consider a period of ventilation of lungs on intensive care after surgery in people affected by Alström Syndrome. [22]

Even for relatively minor procedures under general anaesthetic HDU or ITU should be considered post-operatively.

Pulmonary Oedema:

Patients with Alström Syndrome may be more prone to pulmonary oedema, particularly if cardiomyopathy is present. This should be anticipated and planned for and steps such as procedures being undertaken when a dialysis session, for example, is booked for the next day as opposed to having a procedure on a Friday with a weekend in between sessions.

⊕ Medical terms explained

Hypertriglyceridaemia and triglycerides (elevation of fatty substances found in the bloodstream)

Pulmonary oedema (fluid on the lungs)



Unexpected severe hypoxia can occur during episodes of infection and post - operatively. Even for relatively minor procedures under general anaesthetic HDU or ITU should be considered for post operatively and very careful monitoring of the heart and oxygenation until fully recovered and ambulant.

Genetics

Alström Syndrome is an autosomal recessive condition; meaning that both parents must carry one copy of the ALMS1 gene with a significant mutation to have a child who is affected. There is a 1 in 4 chance of having a child affected by Alström Syndrome with each pregnancy.

The gene responsible for Alström Syndrome was discovered by scientists at the Jackson Laboratory in Maine, USA, and scientists at Southampton University, England, simultaneously.

The ALMS1 gene provides instructions for making a protein whose function is unknown. Researchers believe that the protein may play a role in hearing, vision, regulation of body weight, and functions of the heart, kidney, lungs, and liver. It may also affect how the pancreas regulates insulin, a hormone that helps control blood sugar levels (see www.alstrom.org.uk for more guidance).

One fifth of the world's population live in communities where consanguineous marriages are common (of the same blood origin). In the UK, these may include those of Pakistani, Middle Eastern, Bangladeshi, Turkish and some groups of Indian origin, plus the Irish travelling community. Where an autosomal recessive condition like Alström Syndrome is identified within these populations, parents and extended family members are at increased risk of having additional children affected.

Genetic counselling is available locally and can be accessed via the specialised multi-disciplinary clinics in Birmingham. This can provide the whole family with relevant information to enable informed choices about future pregnancies and to understand the genetic basis of the condition.

An introductory guide, *Consanguineous Marriage and Inherited Disorders* is now available from Dr Aamra Darr BSc (Hons), PhD, Director of Genetics Communication Diversity (GCD) www.g-c-d.org.uk

Genetic Alliance UK can help families who may be worried that they will pass on a genetic condition to their child.

Further information about genetics is provided by Genetic Alliance UK with specific information sheets available to download, including:

- Living with a Genetic Condition
- Learn about Genetics
- Services and Testing

<https://www.geneticalliance.org.uk/information/>



Alström Syndrome UK

ASUK has a wealth of knowledge about Alström Syndrome. We are developing pioneering research projects, as well as raising awareness to improve diagnosis. ASUK work in partnership with the NHS Trusts at Birmingham Children's Hospital and the Queen Elizabeth Hospital in Birmingham to offer multi-disciplinary specialist clinics and medical advice from leading experts.

Patients are encouraged to attend the AS multi-disciplinary clinics to seek the best treatments and help manage their condition.

ASUK is led by those directly affected, their family members and professionals who have the passion and dedication to make a difference.

Alström Syndrome UK has three key aims:

- ✓ To support people with Alström Syndrome - to provide support for them, their carers and the professionals who are working with them.
- ✓ To raise awareness amongst both the public and medical professionals of Alström Syndrome.
- ✓ To raise funds to promote research into Alström Syndrome and create opportunities for those affected by AS and their families.



Alström Syndrome UK

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or email-info@alstrom.org.uk
Web: www.alstrom.org.uk

Today ASUK provide a website giving up-to-date information www.alstrom.org.uk, regular newsletters, help and support services, a family and professional conference and regular multi-disciplinary clinics at Birmingham Children's Hospital for children with the condition and Queen Elizabeth Hospital, Birmingham for the adults.

Alström Syndrome UK is an equal partner in providing the Alström clinical services and maintains the only UK database of those affected by this disorder.

ASUK pride themselves on their personalised family support services, offering help and support to families and individuals affected. Including supporting young people through all stages of transition, through our T-KASH (Transition - Knowledge, And Skills in Healthcare) resources which were developed by young people for young people. These resources support young people and the professionals working with them to think about and plan their future throughout all stages of growing up, to manage their healthcare effectively.

Thanks to the ongoing fundraising efforts of our dedicated supporters we have now been able to buy specialised equipment, family holidays, support volunteering opportunities and offer personalised transition support for young people. We also run a Bike Club where families can borrow a tandem or adapted trike to enable them to exercise freely in a safe and fun way.



Highly Specialist Clinics for children and adults

World's first multi-disciplinary clinics for the dedicated care of patients with Alström Syndrome in the UK.

The clinics are based at Birmingham Children's Hospital and Queen Elizabeth Hospital in Birmingham (for adults) and have now become an established part of the NHS.

A wide range of related tests and consultations (eg cardiology, respiratory tests, diabetes and metabolism) can be carried out under 'one roof.' Additional visits for extra consultations or tests can also be arranged. Accommodation and meals are provided whilst attending the clinic.

Patients can be referred via their GP, consultant or through the Alström Syndrome UK charity.



If you would like to attend either of the clinics or would like to speak to a medical expert, please contact ASUK www.alstrom.org.uk



ASUK Team supporting patients during an AS clinic

Research

Research into Alström Syndrome to learn more about this complex condition, has been gathering momentum over the past few years. The current research being conducted in the UK, Europe and America is investigating why mistakes in the Alström Syndrome gene cause the syndrome. Our hope for the future is people affected will be quickly diagnosed, quality of life for patients will be improved and further understanding of this rare condition will be learnt to enable further treatments to be developed.

Research Highlights

- National clinical database of patients affected by Alström Syndrome in the UK
- Alström Syndrome tissue bank and stem cell research into Alström Syndrome
- EURO-WABB – European registry to seek further treatments and prognosis
- Lifestyle study, researching how a healthy lifestyle can affect symptoms and disease progression
- First clinical trial for people affected by Alström Syndrome in the UK began in 2016

Alström Syndrome UK works in partnership with other like-minded charities such as EURORDIS, Genetic Alliance UK, Council for Disabled Children, Rare Disease UK and many more to promote the needs of patients who are affected by rare diseases.

This collaborative work enables patients to be empowered and have their voice heard on an International level.

Clinical Trial

ASUK is pleased to announce that we are working in partnership with the Canadian Pharmaceutical Company ProMetic Bio therapeutics Ltd and the specialist clinical team at the Queen Elizabeth Hospital, Birmingham to support the first clinical trial for people affected by Alström Syndrome in the UK.

The primary aim of the trial is to evaluate the safety and tolerability of PBI-4050 and its effects on inflammatory, fibrosis, diabetes and obesity biomarkers in people affected by Alström Syndrome.

It is early days and there are no guarantees that patients taking part in the trial will have any clinical benefit, but we hope this trial will enable us to further develop our understanding of this complex condition and add to the body of knowledge about Alström Syndrome.

Further information about Alström Syndrome can be found via our website www.alstrom.org.uk. Further information about the clinical trial can be found via the website www.clinicaltrials.gov, using the trial reference number NCT02739217.



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Glossary

of medical terms

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Acanthosis (darkening and increase in thickness of cells in the skin)

Adult phenotypes (characteristics displayed by an organism)

Aetiology (study of causes and origins)

Centrosome (tiny organising centre of the cell)

Ciliary dyskensia (progressive disorder affecting organ systems)

Digital oximetry (determination of oxygen and protein levels in the blood)

Dilated cardiomyopathy (poor cardiac function where the heart muscle is weakened and enlarged)

Glomerular filtration (each kidney contains over one million filtering units called glomeruli which remove waste chemical etc from the blood)

Heterogeneous (consisting of elements that are not of the same kind or nature)

Hydrocephalus (‘water on the brain’)

Hypertriglyceridaemia and tryglycerides (elevation of fatty substances found in the bloodstream)

Hypogonadism (defect of the reproductive system)

Ileal conduits (part of the intestine used as a urinary conduit)

Nephronophthisis and nephropathy (structures and function of the kidneys)

Organelles (components of cells)

Post micturition (after the passage of urine)

Pulmonary oedema (fluid on the lungs)

Renal and hepatic dysfunction (affecting the kidneys and liver)

Sensorineural hearing loss (disorders of the cochlear part of the ear)

An acknowledgement and thanks from ASUK

**Dedicated to the Alström Community
In memory of those who have sadly passed away and those who inspire us every day**

Sue Manzoor describes her inspirational niece;

“My beautiful, funny, history-loving niece, Maariyah, was born in December 1999. Within days of being born she was rushed to the Children’s hospital in Birmingham where they found she had a problem with her heart. They discovered my tiny niece had a rare illness called Alström Syndrome. This is an illness which can affect many parts of the body including the heart, vision, hearing, fibrosis, scoliosis and the children are prone to diabetes. Although my niece’s heart, lungs, spine, hearing and vision were affected this did not stop her one bit, she was always smiling and laughing and she certainly never let anything stand in her way.

Maariyah loved socialising with her family and friends; and also loved the time she spent with the members of Alström Syndrome UK the Acorns Children’s Hospice team and her beloved Priestley Smith Specialist School.

She was wise beyond her years and at the same time had the pure innocence only a child has. She was extremely brave and courageous; the number of hospital visits and cannulas made her an expert in how to get to her blood. Maariyah was full of confidence and would speak her mind in a way that made you laugh and love her at the same time, she was never afraid to remind everyone of the importance of listening to the voices of young people.

On 2nd December 2016, shortly before her 17th birthday Maariyah sadly left us, her heart had done all the work it could. Anyone who knew or met Maariyah couldn’t help loving her, she was a character who stole your heart, she was our princess and we miss her dearly.”

Alström Syndrome is an ultra-rare genetic condition which can be complex, due to the many organs in the body that can be affected. This guide aims to highlight the symptoms, raise awareness, improve knowledge and ensure anyone with Alström Syndrome can access the AS multi-disciplinary clinics. During these clinics patients are monitored regularly and receive the most up to date treatments and advice to help manage the condition.

Alström Syndrome UK is a registered charity, providing support services to individuals and those who care for them. We are a patient led organisation, inspired to help improve the lives of children and adults who are affected by AS and to find effective treatments.

Extraordinary clinical teams

The multidisciplinary clinics are supported by Professor Tim Barrett at Birmingham Children’s Hospital and by Dr Tarek Hiwot at Queen Elizabeth Hospital Birmingham. Long term thanks will always go to Dr. Richard Paisey and Dr Cathy Carey at Torbay Hospital, who were instrumental in establishing the first Alström Clinics. We are grateful to Kay and John Parkinson who began the charity in 1998 and wish them well in their future pursuits.

Thank you

To all our donors, families and individuals who raise funds and give their time to support ASUK. Your generosity makes a positive difference to the lives of children and adults with Alström Syndrome.

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This booklet is meant as a guide only. If you feel concerned about anything you have read please seek medical advice from your GP or consultant.



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