Marfan syndrome: diagnosis and management in childhood

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Abstract

Marfan syndrome (MFS; OMIM #154700) is an important pleiotropic genetic connective tissue disorder affecting multiple systems in the human body. Early diagnosis is vital to prevent sudden premature death. Many affected individuals are asymptomatic; leading normal lives, unaware that their aorta is dangerously enlarging and prone to catastrophic dissection/tear leading to blood vessel rupture. Males and females of all races are affected equally. MFS is inherited in an autosomal dominant mode and is caused by a genetic variation in the Fibrillin 1 gene (*FBN1*; OMIM *134797) located on the long arm of chromosome 15 (15q21). In most cases, 75% have inherited the condition from a parent, with 25% having *de novo* mutations. The most important systems to be affected are cardiovascular, ophthalmic, and skeletal. MFS is a highly penetrant condition with substantial intra- and interfamilial variability. With drug treatment and cardiac surgery, early medical interventions can lead to a lifespan into the seventh decade. Without treatment unexpected death can occur from a young age. In 97% of affected individuals a causative mutation can be found thereby enabling preconception genetic diagnosis to potentially prevent further offspring being affected. This review focuses on the major challenges those affected experience during childhood.

Keywords Adolescent; childhood; diagnosis; Loeys-Dietz; management; Marfan

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Classic Marfan syndrome

If two out of three major systems (eyes, heart, skeleton) are affected (following the original Ghent criteria (see Table 1), a clinical diagnosis of Marfan Syndrome should be entertained, and a mutation screen for Fibrillin-1 instituted to check this fibrous component of connective tissue should be done. A full family history, including height, build, early cardiac death, cardiac arrythmias and visual loss should be taken. The infant should be referred for echocardiogram and ocular examination for dislocated lenses and detached retina. If a causative variant is found, both parents and the other siblings should be examined and tested for the same variant.

Individuals with MFS have multiple systems affected and holistic care is needed. Specialists involved should include a geneticist, paediatric cardiologist, ophthalmologist, endocrinologist, dentist and orthodontist, physiotherapist, podiatrist, orthopaedic surgeon, rheumatologist, and GP. Usually, care is coordinated by a paediatrician or in some cases a paediatric cardiologist with a specialist nurse. Attending multiple appointments is expensive for families in terms of travel costs and time off work and school.

Diagnosis

Early diagnosis is vital. Since one quarter of all cases are sporadic with no other family members affected, affected individuals may die unexpectedly from a ruptured aortic aneurysm with the diagnosis of MFS only being made post-mortem. Typically, affected individuals are tall, slim, with long arm span, long fingers (arachnodactyly) and a high arched palate. Skin is thin and stretchy and stretch marks are common especially in the lower back. Charles de Gaulle was affected, and Julius Caesar, Osama Bin Laden and Tutankhamun may have been affected. There are affected individuals who look entirely normal which can lead to difficulty in the patient and their parents accepting the diagnosis and complying with treatment. These patients may be detected because of an incidental finding of aortic enlargement during a screening echocardiogram performed for a different reason such as a murmur.

Diagnosis can be made either by performing genetic testing for *FBN1* variants and confirming either ectopia lentis (dislocation of the crystalline eye lens) using a slit lamp, or aortic root enlargement by echocardiography. If a parent is affected, then genetic testing for the specific family variant is relatively quick and easy. There is no urgent requirement for a neonatal echocardiogram in this situation. A routine appointment at approximately 6 months of age can be arranged and if the genetics results are available by that time, a normal result will negate the requirement for an echocardiogram. Once a causative variant is detected and this is possible in 97% of cases, it can be used to screen all first-degree family members. Alternatively, a clinical diagnosis can be made using a complex scoring system based on the revised Ghent nosology. This assessment includes the finding of major criteria such as chest wall deformities [pectus excavatum (sunken breastbone) or pectus carinatum (pigeon chest)], positive wrist and thumb signs, flat feet (pes planus), scoliosis (spine curvature), aortic root enlargement or dissection, mitral valve prolapse (floppy mitral valve), and hypermobility.

Clinical diagnosis can be difficult in children as some of the features may develop with age. In Aberdeen, an audit over 7

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Revised Ghent criteria. Data from reference 1

System	Major criteria	Minor criteria
Skeletal	Pectus carinatum or excavatum requiring surgery Arm span:Height >1.05 Wrist and thumb signs Scoliosis >20 degrees or spondylolisthesis Elbow extension <170° Pes planus Protrusio acetabulae	Moderate pectus excavatum Joint hypermobility High arched palate with dental crowding Typical facial appearance (dolichocephaly, malar hypoplasia, enophthalmos, retrognathia, downward slanting palpebral fissures
Ocular	Ectopia lentis	Flat cornea Eye increased in axial length Hypoplastic iris/ciliary muscle
Cardiovascular	Dilated ascending aorta Dissection of ascending aorta	Mitral valve prolapse Dilated pulmonary artery <40 years of age (without pulmonary stenosis) Mitral annulus calcification <40 years Dilation or dissection of descending/abdominal aorta <50 years
Pulmonary		Spontaneous pneumothorax Apical blebs (on imaging)
Skin	Recurrent incisional hernia	Stretch marks without cause e.g. weight gain/pregnancy Recurrent of incisional hernia
Dura	Lumbosacral dural ectasia	
Family genetic/history	First degree relative with MFS Pathogenic FBN1 mutation	

Table 1

years of 232 patients found the Ghent nosology to be accurate for diagnosing MFS in 86% of cases. In the future as genetic testing becomes cheaper, quicker, and more widely available the Ghent nosology may become less important. Future research is focusing on diagnosing those individuals with no external phenotypic features of MFS but who still develop life threatening aortic aneurysms.

The differential diagnosis includes Ehlers-Danlos syndrome type 3 [also known as joint hypermobility syndrome, and hEDS (hypermobile Ehlers-Danlos syndrome)]. In Ehlers-Danlos syndrome the lumbar stretch marks are usually vertical, whilst in MFS they are horizontal. Other differentials include congenital contractural arachnodactyly (Beals' syndrome), Stickler syndromes. and Sotos syndrome (an overgrowth syndrome with learning difficulties and large head). Ectopia lentis can also occur in isolation. An important differential diagnosis in babies is homocystinuria (a condition due to the body's failure to metabolize the amino acid methionine) which must be diagnosed quickly by plasma amino acid analysis, as failure to treat can lead to preventable learning difficulties.

Genetics

The Human Gene Mutation database contains more than 3000 variants in the *FBN1* gene. The incidence of MFS is reported to be between 1 in 3,300[2] and 1 in 22,000.[3] The gene consists of 66 exon, of which 65 are coding; exon 2 is the first coding exon, and the gene encodes the fibrillin-1 protein (P35555). This protein found in the extracellular matrix is important as it makes the scaffolding of connective tissue throughout the body with elastin making elastic fibres. This protein also keeps transforming growth factor-β (TGF-β) in an inactive form. An important amino acid in the Fibrillin-1 protein is cysteine. Cysteine forms disulphide bridges which are crucial to the stability of fibrillin 1 protein. Variants that eliminate cysteine result in more severe cardiac problems. MFS results from a dominant-negative (DN) effect or haploinsufficiency (HI) of FBN1. Haploinsufficiency occurs when one of the two gene copies is nonfunctional, reducing protein production by approximately 50%, which leads to disease. Variants causing haploinsufficiency reduce the amount of fibrillin-1 protein in connective tissue, but all fibrillin-1 protein present is structurally normal. Other people with MFS have a variant that acts through a dominant-negative effect, in which the single mutant allele produces an abnormal protein that interacts abnormally with the protein from the normal allele, resulting in loss of function. In MFS caused by variants acting through a dominant-negative effect, connective tissue contains both normal and abnormal fibrillin-1 protein.[3]

Genetic testing can initially look at the *FBN1* gene using Next Generation Sequencing (NGS) and Sanger sequencing, followed, if negative, by multiplex ligation dependent probe amplification (MLPA) to screen for CNVs (copy number variants) of the *FBN1* and *TGFBR2* genes to maximise detection of the syndrome.

Another similar connective tissue disorder is Loeys-Dietz syndrome. Those affected have genetic variants in genes like

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TGFBR2 and *TGFBR1* as the main ones, and subtle dysmorphic features including hypertelorism (widely spaced eyes) and a bifid uvula but also get dangerous aortic enlargement and can even die of ruptured aneurysm before the age of 10 years.

Familial Thoracic Ascending Aortic Aneurysm and Dissection [FTAAD] is a condition which also causes fatal aneurysms but those affected do not look marfanoid. They seem to look completely normal and have different genetic mutations.

Early-onset Marfan syndrome

This is also known as neonatal Marfan syndrome (nMFS) and is the most severe and rare type; the genetic defect is mainly concentrated in an specific area of the gene called neonatal region (most cases are between coding exons 24 and 32, but nMFS has also been observed outside of this region) whereas classical MFS affects coding exon 2−66. The neonatal form is sporadic arising from a *de novo FBN1* variant. They have a typical appearance with progeria, pulmonary emphysema, joint contractures, crumpled ears, loose skin, ectopia lentis, arachnodactyly, diaphragmatic hernia and pneumothorax, severe mitral and/or tricuspid regurgitation. Death usually occurs without treatment within the first 2 years of life from heart failure. The authors are unaware of any affected individual having their own offspring.

The decision as to whether to proceed with cardiac interventions early in life in this group involves complex ethical decision making which should be made with early involvement of experts with experience of caring for children with this rare severe condition including a geneticist, paediatric cardiologist and paediatric respiratory specialist.[4] The authors are aware of a single affected individual living until the age of 26 years. Long term survival usually depends on the degree of respiratory compromise. Survival beyond early childhood is associated with high morbidity with frequent hospital admissions due to severe repeated complications throughout the body.

Cardiovascular involvement

The main concern is the development of progressive aortic root dilation leading to aneurysm formation and eventual aortic dissection. Although dissection in childhood is very rare it is often catastrophic. Chest pain is extremely common in childhood and dissection is seldom considered as a potential cause by GPs and paediatricians due to the common misconception that aortic dissection only occurs in adults. Normal ECG and normal cardiac enzymes cannot exclude dissection. In any child with acute severe chest/back pain it is important to quickly consider whether there could be an undiagnosed connective tissue disorder. If this is a possibility or the child has known MFS then immediate discussion with a paediatric cardiologist and urgent CT scan is advised.

Any child with a confirmed genetic diagnosis of MFS should be monitored at least annually by a paediatric cardiologist with serial echocardiograms. In childhood MFS the aorta first enlarges at the aortic root comprising of the aortic sinus, valve and sino tubular junction. The aortic root accepts the cyclic pressure load from the blood ejected from the left ventricle making it more likely to dilate than other parts of the aorta. The sinus has the highest content of elastin in the entire arterial circulation. Abnormal elastin in MFS will therefore manifest first in this area.[5] This progressive enlargement can begin at any age and has even been noted *in utero*. Aortic root dilation is seen in 75−80% of affected children and is a hallmark of MFS.[5] There is no predictable pattern with some MFS children having a normal echo appearance throughout childhood whilst others have progressive dilation from early life even without typical external features of marfanoid habitus.

The aorta is measured in the parasternal long axis view. The largest measurement is at sinus level (European paediatric recommendation is to measure inner edge to inner edge in systole) and compared to body surface area, creating a Z score which is given. Measurements are also taken at valve level, ST junction, ascending aorta, arch, descending and abdominal aortic levels. A Z score greater than 2 is abnormal and medical treatment is indicated.

Management of cardiovascular complications

Daily oral beta blocker (reduce arterial wall strain) and/or angiotensin receptor blocker (ARB) treatment (attenuates TGFβ activity, possibly leading to reduction in extracellular matrix degeneration in vessel wall and lowers blood pressure) with either losartan or irbesartan have been proven to reduce and in some cases prevent aortic enlargement. Maximally tolerated doses are recommended if the aorta is dilated. Initially single therapy is given but combined treatment is given if rapid progression of aortic dilation is occurring and for aortas greater than 40 mm in size.[6] Atenolol is available in liquid form and hence is often given to affected young children.[7] Recently there has been a trend to commence medication even if aortic size is normal with the aim of delaying or even preventing the need for aortic surgery later in life.

Dizziness is the commonest medication side effect due to excessive hypotension. Consideration should be given to briefly omitting medication or reducing dose when unwell, septic, dehydrated or undergoing anaesthesia, to prevent dangerous hypotension. ARBs can also detrimentally affect renal function and are contraindicated in pregnancy. It is important to remind affected teenage girls of this. Calcium channel blockers should be avoided in MFS as they may increase the risk of an acute aortic event. Activities which promote aortic enlargement (e.g. lifting more than 1/3 of body weight, contact sports) should be avoided if the Z score is greater than 2. If the aorta is normal in size, then exercise restriction is not required from a cardiac perspective.

If despite medical treatment the aorta continues to grow (due to severe cardiac phenotype, poor medication compliance or late diagnosis in childhood) then surgery may be required to prevent dissection. This is usually considered between 45 and 50 mm, with lower values being considered if there is a worrying family history of early dissection or if there has been rapid change in aortic size.

There are rare but reported cases of dissection under the age of 10 years; most dissections in childhood occur in adolescence accounting for 0.5% of all aortic dissections occurring in the MFS population.[6] The PEARS surgical procedure has grown in popularity. This involves placement of a personalized 3D printed sock-like textile wrap, made of a soft pliable polymer, around the ascending aorta, strengthening its wall preventing dissection. This procedure has been performed on children as young as 3

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years of age. Aortic valve sparing surgery is always preferred to valve replacement. More traditional surgeries include the reimplantation technique (David V procedure) and the remodelling technique (Yacoub procedure).

Mitral valve prolapse with or without mitral regurgitation may also occur in MFS children. Childhood surgical mitral valve repair is usually only required for those with Neonatal Marfan Syndrome.

Hypertension must be avoided. It is particularly important to monitor for this in those treated for Attention Deficit Hyperactivity Disorder (ADHD) which can coexist with MFS (up to 50% of cases of MFS have some type of neurological deficit, ADHD being the most common). The US FDA has approved the use of stimulant and non-stimulant medication in ADHD patients with MFS.

Eye abnormalities

Everyone with Marfan syndrome should be examined at regular intervals by an ophthalmologist. The condition of the eyes will determine how often the eyes need to be reviewed and whether they can be cared for by the local optician or if they need continued specialist care. Generally, myopia is a feature (>50% of cases). Strabismus may need correcting. There is an increased risk of eye emergencies including retinal detachment or lens dislocation (ectopia lentis 60%).

Glaucoma and early cataracts can also occur. Contact sports should be avoided, and protective eyewear should be used where necessary to try to reduce the risk of retinal detachment. The symptoms of retinal detachment include a curtain or shadow in the patient's vision, sudden sight loss or double vision, severe eye pain, sudden flashes, or floaters in the eye. If the lens is dislocated and interferes with normal vision, it can be removed and replaced, with a new lens introduced into the anterior eye segment.[8] It is important to note that there are other genes that can cause isolated ectopia lentis,[9] which can be differentiated from MFS by careful family history to determine mode of inheritance, and physical examination including negative echocardiogram.

Musculoskeletal involvement

Fibrillin-1 is an important constituent of bone, cartilage, periosteum, tendons, ligaments, and muscle. It has a special function in providing insertion of ligaments into bones. Common problems in Marfan Syndrome include scoliosis, spinal pain, arthralgia, ligament injury, dislocation or subluxation of joints, myalgia or muscle injury, cervical spondylosis, knee meniscus injury, anterior knee pain, pes planus and hammer toes, and occasional early osteoarthritis.

Scoliosis is very common in Marfan Syndrome appearing from 7 years and often progressing more rapidly than in other conditions. Screening examination with the 'Forward Bending Test' should be carried out annually between the ages of 7 and 17. Referral to an orthopaedic surgeon specializing in scoliosis should be performed if the curve is seen to be progressing. Surgery at an age when the child is still actively growing is most effective, and telescopic rods can be inserted, and lengthened in the office magnetically.

Pectus deformity, either pectus carinatum (pigeon chest) or pectus excavatum (a dip in the chest) are common in Marfan Syndrome children, due to rib overgrowth. While of cosmetic and psychological importance to the child, surgical correction is most indicated for severe pectus deformity, such as pectus excavatum which interferes with cardiac or lung function. Rarely cardiac arrhythmia may occur.

There is a UK national network of surgeons capable of correcting pectus deformities, and (after a brief hiatus in funding between 2019 and 2023) the NHS once more offers to fund surgery for severe cases.[10] A randomized trial of surgery versus no treatment to restore cardiopulmonary function in severe pectus excavatum (The Restore Trial) is underway.

Most MFS children's height is above the 97% percentile for age. If the final predicted height is excessive, cyclical hormone therapy to limit the pubertal growth spurt needs to be considered in a growth clinic, from height 150 cm. Hypermobile joints may require supports or splints. Seventy percent of children (70%) experience symptoms of pain. It is important to allow the child to participate in school and family events to the extent of their ability, but rest should be permitted if pain is the result. Sports which do not traumatize lax joints are preferred, e.g. swimming and badminton. Heavy weightlifting, long-distance running, and rugby are not recommended. A tendency to costochondritis, especially in rapidly growing adolescents, may lead to worries about chest pain, erroneously thought to be coming from the heart. This is best treated with reassurance, non-steroidal anti-inflammatory drugs, and review of possible triggering events. Any acute severe chest or back pain must always be taken seriously, and only once dissection is excluded can other more common conditions be considered. Fibrillin deficiency probably also plays a role in the easy fatiguability common in children. Shoes with arch and ankle support may be used to improve joint stability and reduce pain during activity. Pes planus is a feature and flat long feet require very careful shoe fitting, with orthotics.

Surgery and wound healing

Healing after surgery is often delayed, therefore sutures need to be strong and left in somewhat longer than for the average patient. Antibiotic cover should be provided to prevent endocarditis, and at any surgery, an experienced anaesthetist should be utilized since patients with MFS might be difficult to intubate due to a high palate, limited neck extension and narrow trachea.

Dental aspects

The most common oral signs are a high arched palate and dental crowding. Malocclusion and open bite tend to be associated. Often there is mandibular prognathism. Prognathism, and hyperextensibility of the ligaments and muscle of the temporomandibular joint can lead to dysfunction and dislocations or subluxations of the joint. Developmental abnormalities may also be evident such as the development of supernumerary teeth.

Ear, nose and throat problems

Due to the long narrow skull, sinuses tend to drain poorly. This may be contributed to by nasal septum asymmetry. Also, ear canals tend to be slanted more, with resultant poorer drainage. Together with enlarged tonsils and adenoids, the child may have frequent ear infections which can lead to loss of hearing unless

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antibiotics are commenced early in any throat or ear infection. Tonsil and adenoid removal may be required in children with obstruction, infection and/or sleep apnoea.

Respiratory issues

Pulmonary complications occur in up to 10% of patients. Lung involvement may present in infancy or childhood, with complications in adolescence. Within the lung, flaccidity of small airways and terminal bronchioles predisposes to premature airway closure, obstruction, and air trapping, resulting in abnormal lung function. Asthma is common. Chest x-ray or CT scan often reveals apical bullae, which are associated with an increased incidence of pneumothorax (4–14%) especially in adolescent males. Bronchiectasis, fibrosis, and a tendency to recurrent lung infections, including unusual fungal infections, is reported. Obstructive sleep apnoea may be a cause of daytime fatigue in children and adults.

Gastrointestinal problems

Irritable bowel syndrome is twice as common in the Marfan population as it is in the general population. Difficulty swallowing, nausea and vomiting, abdominal bloating, constipation, or diarrhoea may be symptoms.[11] Occasionally, nasogastric tube feeding may be necessary. Allergy testing may reveal a likely cause but more generally reducing caffeine and fatty processed food may help, as might adding a probiotic. Additional help from a dietician or a gastroenterologist may be required. Hernias can also occasionally be a problem.

Dural ectasia

Dural ectasia (DE) is present in a high proportion of children but is usually asymptomatic.[12] One study found that around 40% of children with Marfan Syndrome had signs of DE, and another showed a prevalence of about 90%. The presence of DE can be a useful diagnostic tool in the absence of other major criteria. It is defined as an enlargement of the neural canal anywhere along the spinal column. The dura surrounding the spinal cord enlarges, especially in the lower lumbosacral region where cerebral spinal fluid pressure is greatest. If symptoms are present, the most common are headache, low back pain, nerve pain in the legs or buttocks, loss of sensation above and below the affected area, rectal pain, or genital pain. Symptoms can be aggravated by lying face downward and are relieved by lying on the back. Pain can also be postural (worse when standing up) as the cerebrospinal fluid will pool in the dilated area.

Magnetic resonance imaging (MRI) is usually used to diagnose DE as it is better at imaging the dural sac than computed tomography (CT) although this can be used if MRI is contraindicated. Referral to a neurosurgeon is indicated if the symptoms are not relieved with medication.

Transition

During the teenage years, planning transition to adult services particularly cardiology is important to ensure no loss of follow-up as well as harnessing the opportunity to enable the young person to learn more about their lifelong multisystem condition giving them the ability to self-advocate and make the best decisions for their futures. The importance of medication compliance, endocarditis prophylaxis, avoidance of body piercing, tattoos, smoking, vaping, and illicit drug use is emphasized. Career guidance is given. A diagnosis of MFS may disqualify entry into certain jobs e.g. pilot, serving in the armed forces. Ways of explaining MFS to a partner are touched on. Meeting other teenagers with MFS can be invaluable in terms of peer psychological support. The Marfan Trust (www.marfantrust.org) can help to facilitate this.

Contraception must be discussed. The importance of carefully planning pregnancy must be stressed. Medication may need changing; for example, angiotensinogen receptor blockers should be stopped as potentially dangerous to the foetus' developing renal system. Women with MFS need extra cardiac monitoring during pregnancy by an adult cardiologist with expertise in pregnancy as well as MFS to watch for potentially dangerous aortic enlargement with risk of dissection which is most frequent during the post-partum period. Delivery must be carefully planned. Regional anaesthesia reduces the risk of pain related extreme fluctuations in blood pressure and heart rate. As part of preconception counselling, imaging of the spine is recommended to check for dural ectasia which can be asymptomatic. If DE is present, then a pre-delivery consultation with the anaesthetist is important.

Preconception counselling

When it is deemed suitable, a couple in which one has Marfan Syndrome should be advised to have preconception counselling. The risk of conceiving a child with MFS is 50%. However, with modern technology this can be prevented using preimplantation genetic diagnosis. In the UK the Human Fertilization Embryology Authority has approved this for MFS since 2010.

Alternatively, if pregnancy has already occurred prenatal diagnosis can be performed by chorionic villus sampling or amniocentesis. Cells are removed and genetically tested for the FBN1 gene mutation. Both procedures carry a small 1% risk of miscarriage.

Exercise

Regular physical exercise elevates the mood, helps health, and drives energy. It provides benefits for physical and emotional wellbeing and gentle regular exercise can be safely integrated into the life and daily routine of someone with Marfan Syndrome. In general, non-contact sports are recommended, and competition at high level should be avoided. However, a holistic individualized approach to patients, with joint decision making together with the child and parents is important. If a tall child with MFS is talented at basketball or netball and is obtaining self-esteem, confidence, and popularity from being in a team, and aortic size is under control with good medication compliance, forbidding competitive sport in this situation may not be in the child's best interests.

The authors have cared for a number of children with MFS who have competed in a variety of sports successfully representing Great Britain at international and even Olympic level who have experienced no abnormal aortic dilation. Every patient is different.

Current expert advice is that in children $\leq$10 years of age all sports can be undertaken. Above 10 years power sports should

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be avoided but as long as the aortic root Z score is less than 3 then any intensity recreational skill, mixed or endurance sport can be undertaken. If the Z score is ≥3 or the absolute size is ≥40 mm then these activities should only be undertaken at a moderate level (defined as being able to hold a conversation whilst exercising).

Exercises such as yoga, tai chi and pilates ensure that muscles get stretched thus avoiding pain. Resistance and strengthening exercises can be encouraged, but strenuous exercise which leads to a sharp rise in blood pressure, thus putting a strain on the aorta, is to be avoided. Exercise should involve movement at a comfortable pace during which conversation can still be held. To avoid damage to the eyes, contact sports such as rugby should be avoided. Basketball is fine.

Medications such as beta blockers may lower blood pressure and heart rate so that heart rate cannot be used as a monitor of the efficacy of exercise.

Psychosocial aspects

Children and adolescents with Marfan Syndrome look and feel different from their peer group, because of their long, thin, body build, poor eyesight, lax painful joints, and cardiac problems. School absence may be frequent because of hospital appointments. In addition, other affected members of their family (perhaps a parent) may have been ill, required surgery, or even died suddenly, possibly at an early age. Despite normal intellectual and gross motor development children may fail to perform to the best of their ability because of short sightedness and clumsiness due to lax joints and long thin body build. Attendance at mainstream school is the norm with a care plan in place for emergencies and extra time requested for examinations. They may be teased or bullied at school from a young age due to looking noticeably different.

Behavioural problems, low self-esteem, anxiety, and depression are not unusual. These issues tend to worsen during the pubertal growth spurt when discomfort with body image can become a major source of distress. Alerting teachers and parents to anticipate these challenges for the young person enables early identification and prompt intervention which can reduce suffering. Professional psychological counselling can improve feelings about self-image, worth and social interactions. Children should be taught about Marfan Syndrome from an early age and should be encouraged to be comfortable educating their classmates about their condition. A positive self-image of the child may be fostered by praising their talents, especially by encouraging musical ability or computer skills, for example, to compensate for possible lack of physical ability. Group activities such as joining a choir may provide instant social groups. A sense of humour is vital for coping with teasing.

Time off school should be minimized by asking for hospital appointments and operations to be arranged wherever possible during holidays. Unfortunately, this can mean that holidays are spent in hospital waiting rooms, negatively impacting on unaffected siblings and the whole family.

Patient support

In the UK the Marfan Trust (www.marfantrust.org) is a charitable organization of Marfan syndrome and Loeys-Dietz syndrome families who all share genetic problems. The Marfan Trust website and social media sites are full of helpful videos, pamphlets, and patient stories. The Trust provides a telephone and e mail helpline, advice from an expert nurse, and medical specialist panel, holding two National Patient Education and Advocacy Conferences per annum, one face to face, and one remote, as well as promoting local support groups. Child-to-child partnerships can also be arranged where children of similar ages are linked to prevent isolation and provide an opportunity to celebrate their shared experiences of facing the world with Marfan Syndrome.

Conclusion

Marfan syndrome is a complex, multisystem connective tissue disorder that demands early recognition, careful lifelong monitoring, and truly holistic care. Advances in genetic testing, cardiac imaging, and medical therapy have transformed outcomes, allowing many affected children to grow into healthy, independent adults. Yet the condition's variability means that each child's needs—medical, developmental, and psychological—must be approached individually. Coordinated specialist input, proactive surveillance of the heart and eyes, thoughtful guidance around exercise, school, and lifestyle, and strong psychosocial support are all essential. With timely diagnosis, personalized care, and robust family and community support, children and young people with Marfan syndrome can lead full, active, and rewarding lives. ◆

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FURTHER READING AND RECOMMENDED WEBSITES

A guide for young adults with Marfan syndrome: www.marfantrust.org/information.

Child AH, ed. Diagnosis and management of Marfan syndrome. London Springer-Verlag, 2016.

Marfan Trust: Paediatric Guide: www.marfantrust.org/information.

National Marfan Foundation (USA): www.marfan.org.

Practice points

- Think of Marfan syndrome early in any tall, slim child with long limbs, scoliosis, joint hypermobility, pectus deformity, myopia, or a family history of early cardiac disease or lens dislocation. Early referral for echocardiography, ophthalmology, and genetics can be lifesaving
- Do not dismiss chest or back pain in a child with known or suspected Marfan syndrome. Although rare, aortic dissection can occur in childhood; urgent discussion with a paediatric cardiologist and prompt imaging (usually CT) is essential if symptoms are severe
- Multisystem care is often required and follow-up with cardiology (at least annually), ophthalmology, orthopaedics, physiotherapy, and dentistry is required
- Non-contact and moderate-intensity exercise is generally encouraged, but power sports and heavy lifting should be avoided once the aortic root Z score exceeds 2. Reinforce medication adherence and avoidance of stimulants that raise blood pressure unless specifically approved
- Children with Marfan syndrome often face pain, fatigue, visual problems, and body-image concerns. Be alert to anxiety, low mood, bullying, and school difficulties; early counselling, school care plans, and links with patient support groups such as the Marfan Trust can make a significant difference

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