

Riley-Day Syndrome (Familial Dysautonomia) and the Spine

A patient guide

In brief: Riley-Day syndrome, more properly called familial dysautonomia and classified as hereditary sensory and autonomic neuropathy type III (HSAN III), is a rare inherited disorder of the nervous system in which the nerves that control automatic body functions, and those that carry sensation, fail to develop and survive normally. It is described here not as a general account of the autonomic nervous system but from the particular vantage point of the spine, because spinal deformity is one of the defining orthopaedic features of the condition. The great majority of people with familial dysautonomia develop scoliosis, a sideways curvature of the spine, and many develop kyphoscoliosis, a curvature that also bends the spine forwards. These deformities tend to appear early in childhood and to progress, and they arise from the underlying neuromuscular and neuropathic nature of the disease rather than from any fault of posture. What makes the spine in familial dysautonomia such a demanding subject is not only the frequency of the curvature but the formidable difficulty of treating it surgically, because the same autonomic instability, respiratory fragility and poor bone quality that characterise the condition turn spinal deformity surgery into one of the most perilous undertakings in the field. The single most important idea is that this is spinal deformity occurring against a backdrop of a whole-body neurological disorder, which is why it demands extreme care.

What familial dysautonomia is, and why the spine is so often involved

Familial dysautonomia is a genetic disorder, inherited in an autosomal recessive manner, caused in almost all cases by a mutation in the gene known as IKBKAP, also called ELP1. It occurs overwhelmingly in people of Ashkenazi Jewish descent, in whom it is one of the more common inherited conditions, though it remains rare in absolute terms. The mutation disturbs the development and survival of certain nerve cells, particularly those of the autonomic nervous system, which governs functions that happen without conscious thought, and those of the sensory system, which carries information about pain, temperature and the position of the body.

The consequences of this nerve loss are widespread. Blood pressure may swing unpredictably, swallowing may be uncoordinated, tears may be absent, temperature control may be erratic, and the perception of pain and of where the limbs lie in space may be blunted. These features explain why familial dysautonomia is a systemic condition and not simply an orthopaedic one. Yet running through this systemic disorder is a strong and early tendency to deform the spine.

The reason the spine is so frequently involved lies in the neuromuscular and neuropathic character of the disease. The muscles that surround and balance the spinal column depend on a steady flow of nervous signals to hold the trunk upright and symmetrical. When the sensory feedback that tells the body where it is in space is impaired, and when the control of the muscles that stabilise the spine is uneven, the column is no longer held in balance. Over the years of growth this imbalance allows the spine to drift into a curve, much as it does in other neuromuscular conditions where muscle control around the trunk is disturbed. The deformity in familial dysautonomia is therefore best understood as neuromuscular and neuropathic in origin, a consequence of the disordered nervous system acting on a growing skeleton.

How common spinal deformity is in familial dysautonomia

Spinal deformity is not an occasional complication of familial dysautonomia but one of its defining orthopaedic hallmarks. Across the published series, the large majority of people with the condition develop a curvature of the

spine, and the reported prevalence is strikingly high. One of the largest reviews of spinal deformity in the condition, drawn from a major dysautonomia centre, described curvature of the spine in the great majority of patients studied, with figures in the region of eight in ten. Other reviews of the orthopaedic manifestations of the condition have reported similar proportions, placing scoliosis and kyphoscoliosis among the most consistent skeletal features of the disorder.

The pattern of the deformity is also characteristic. Many people develop not a simple sideways curve but a kyphoscoliosis, in which the spine bends both to the side and forwards, producing a combined deformity that is more complex than ordinary adolescent scoliosis. The curves tend to begin in childhood, often earlier than the idiopathic scoliosis seen in otherwise healthy adolescents, and they have a strong tendency to progress as the child grows. This early onset and progressive nature are themselves consequences of the neuromuscular mechanism, since the imbalance driving the curve is present throughout growth rather than appearing only in the adolescent years.

Because the deformity is so common and so often progressive, it occupies a central place in the orthopaedic care of people with familial dysautonomia. It is one of the features that brings these patients to the attention of a spinal surgeon, and it is the reason the condition is discussed here in the context of the spine.

Why the deformity behaves like a neuromuscular scoliosis

It is useful to set the spinal deformity of familial dysautonomia alongside the more familiar idiopathic scoliosis of healthy adolescents, because the two behave quite differently, and the differences flow directly from the underlying mechanism.

Idiopathic scoliosis arises in an otherwise normal nervous system and a structurally normal trunk, tends to appear around adolescence, and follows reasonably well understood patterns. The scoliosis of familial dysautonomia, by contrast, belongs to the family of neuromuscular curvatures. Here the spine deforms because the nervous control of the muscles that balance it is disturbed, and because the sensory feedback that would normally keep the trunk centred is impaired. Curves of this kind tend to start earlier, to be longer and more sweeping in shape, to extend further down towards the pelvis, and to keep progressing for as long as the underlying imbalance persists.

This neuromuscular character has practical consequences for the whole subject. Neuromuscular curves are generally less responsive to bracing than idiopathic ones, because a brace can hold a passive trunk but cannot correct the active imbalance of nervous control that is driving the curve. They tend to involve a longer stretch of the spine, which has implications for any operation undertaken. And they occur in a body that is, in familial dysautonomia, fragile in many other respects at the same time. Understanding the deformity as neuromuscular rather than idiopathic is the key that explains why it is both so common and so difficult to manage.

The bone in familial dysautonomia

A further thread running through the spine in familial dysautonomia is the quality of the bone itself, which is frequently poor. People with the condition have a well-documented tendency towards low bone mineral density and towards fractures, and studies measuring bone density have found a substantial proportion with values well below the normal range, including at the spine. Fractures, including silent fractures of the vertebrae and ribs that cause no pain because of the blunted sensation, are reported in a large share of patients.

Several strands of the condition come together to weaken the bone. The impaired sensation means that the protective signals which normally guard the skeleton are diminished, and the disordered autonomic control and altered patterns of weight-bearing further affect how bone is laid down and maintained. The result is a skeleton that is often softer and more friable than normal, a feature that surgeons operating on these patients have long remarked upon, describing bone that holds metalwork poorly and yields under the forces of correction.

This poor bone quality is not a side issue but a central part of why spinal surgery in familial dysautonomia is so demanding. An operation to correct a curvature relies on anchoring metal implants firmly into the vertebrae and on

the bone fusing solidly afterwards. When the bone is weak, the anchors hold less securely, the correction is harder to achieve and to maintain, and the fusion is slower and less certain to take. The state of the bone therefore shapes the whole approach to the deformity.

The perioperative challenge: autonomic instability

If the deformity is the reason these patients reach a spinal surgeon, the perioperative danger is the reason such surgery must be approached with extreme caution. The foremost hazard is autonomic instability. Because the autonomic nervous system in familial dysautonomia is profoundly disordered, the body's automatic regulation of blood pressure, heart rate and other vital functions is unreliable, and the stresses of anaesthesia and major surgery can provoke dramatic swings.

Blood pressure in these patients can rise and fall steeply and unpredictably during an operation, and reviews of anaesthesia in the condition have documented marked cardiovascular lability, including episodes severe enough to threaten life. A particular feature of the disorder is the dysautonomic crisis, a storm of autonomic overactivity that can be triggered by stress, in which blood pressure surges, the heart races, vomiting and agitation occur, and the whole regulatory system is thrown into turmoil. The major physiological stress of spinal deformity surgery is exactly the kind of trigger that can set off such a crisis, and the prolonged nature of these operations gives ample time for instability to develop.

The implications are considerable. Anaesthesia for these patients is a specialist undertaking, demanding meticulous attention to fluid balance, blood pressure and the choice and dosing of drugs, because the usual responses to anaesthetic agents are altered and the buffering mechanisms that protect a normal patient are absent. The accumulated anaesthetic experience in the condition, gathered largely at specialist centres, underlines that these patients tolerate the cardiovascular stresses of major surgery far less well than others, and that the management of their autonomic instability is one of the principal determinants of a safe outcome.

The perioperative challenge: respiratory and aspiration risk

Running alongside the autonomic danger is a serious respiratory and aspiration risk, which is especially relevant to long operations on the spine. Swallowing in familial dysautonomia is frequently uncoordinated, and the reflexes that normally protect the airway from inhaled food, fluid and secretions are impaired. As a result, material is repeatedly drawn down into the lungs over the years, a process known as aspiration, and the chest in these patients commonly shows the consequences in the form of recurrent infection and scarred, damaged lung.

Detailed studies of the chest in familial dysautonomia have documented widespread changes consistent with long-standing aspiration, and respiratory reviews have found that the great majority of patients have some combination of upper airway obstruction, lower airway disease and a restrictive pattern of lung function, the last of these compounded by the scoliosis itself, which by deforming the chest wall reduces the volume the lungs can occupy. The spine and the lungs are thus bound together, because a severe curvature physically restricts breathing at the same time as the underlying disease damages the lung.

For surgery this combination is formidable. A patient whose airway is poorly protected and whose lungs are already compromised faces a heightened risk of aspiration during and after anaesthesia, of chest infection, and of difficulty in weaning from breathing support once the operation is over. These respiratory hazards weigh heavily in any consideration of major spinal surgery, and they are among the reasons such surgery in familial dysautonomia carries a high complication rate.

Why complication rates are high

When the strands above are drawn together, it becomes clear why spinal deformity surgery in familial dysautonomia is recognised as carrying a high rate of complications. The operation itself is major: correcting a long neuromuscular curve usually involves fusing a substantial length of the spine and anchoring metalwork into many vertebrae. Onto this demanding procedure are layered the particular vulnerabilities of the condition. The

bone is often weak, so anchors hold less securely and fusion is less certain. The autonomic system is unstable, so the cardiovascular stresses of the operation are poorly tolerated. The lungs are already compromised and the airway poorly protected, so respiratory complications and infection are more likely. Wound healing and the response to infection may be affected by the altered physiology of the condition.

The published surgical experience reflects this. Series describing operative treatment of scoliosis in familial dysautonomia have reported meaningful but limited correction of the curve, friable osteoporotic bone that complicates fixation, and complication rates well above those seen in straightforward adolescent scoliosis. More recent reports have continued to emphasise the heightened risk of infection and the special measures sometimes taken to guard against it. The picture across the literature is consistent: this is surgery that can achieve worthwhile improvement, but only at the cost of considerable risk, and only when undertaken with extensive specialist support.

It is precisely this combination, a deformity that is common and progressive on the one hand, and a surgical undertaking that is exceptionally hazardous on the other, that places familial dysautonomia among the conditions a spinal surgeon must treat with the greatest caution and care.

How the spine is assessed and monitored

The assessment of the spine in familial dysautonomia rests on the same imaging tools used in other spinal deformities, applied with awareness of the particular features of the condition. Plain X-rays of the whole spine, taken in the standing position where possible, are the standard means of measuring the size and shape of the curve and of following it over time, since the tendency of these curves to progress makes serial measurement central to understanding them.

Because the curves often begin early and progress through growth, the spine is typically followed from childhood, with repeated imaging to track whether and how fast the deformity is advancing. Where surgery is contemplated, more detailed imaging such as computed tomography may be used to examine the bony anatomy and to plan the placement of implants, and assessment of bone quality forms part of the wider picture, given how often the bone is weak. Alongside the imaging of the spine itself, assessment of the lungs and of swallowing, and of cardiovascular stability, forms an essential part of evaluating any person with familial dysautonomia in whom spinal surgery is being considered, because the fitness of these other systems bears directly on the safety of the operation.

This broad assessment, extending well beyond the spine to the lungs, the swallow and the autonomic system, reflects the systemic nature of the condition and is one of the ways in which the care of these patients differs from the care of an otherwise healthy adolescent with a curved spine.

What the evidence shows about management

It is important to be clear that the evidence base for managing the spine in familial dysautonomia is built on observational series, reviews of specialist experience and case reports rather than on large randomised trials, which the rarity of the condition makes impractical. The descriptions that follow report what the literature observes, not guidance for any individual, and decisions in practice are highly individualised and made by specialist teams.

Bracing has been examined as a means of controlling the curve, particularly in younger children, but the published experience suggests that it is of limited effect, with curves frequently progressing despite a brace. This is consistent with the neuromuscular nature of the deformity, since a brace cannot correct the active imbalance of nervous control that drives the curve. The literature therefore describes bracing as, at best, a way of delaying progression rather than a definitive solution.

Surgery, in the form of spinal fusion to correct and stabilise the curve, is the intervention described for severe or progressive deformity, and the surgical series report that worthwhile correction can be achieved. Yet the same series are emphatic about the hazards already described: the friable bone, the autonomic instability, the respiratory fragility and the consequent high complication rate. The literature thus presents spinal surgery in familial

dysautonomia as a serious undertaking reserved for significant deformity, demanding the involvement of an experienced spinal surgeon working alongside specialists in anaesthesia, respiratory medicine and the management of the dysautonomia itself. Across the published experience the recurring theme is that the outcome depends not only on the technical conduct of the operation but on the meticulous management of the whole patient through the perioperative period.

Outlook

The outlook for the spine in familial dysautonomia is bound up with the outlook for the condition as a whole, which has improved considerably as specialist care has advanced, even as it remains a serious lifelong disorder. The spinal deformity is common, tends to appear early and to progress, and frequently reaches a degree at which it affects posture, sitting balance and, through restriction of the chest, breathing.

Where surgery is undertaken, the published experience shows that the curve can be improved and stabilised, but it also shows that this comes with a real burden of risk, arising from the bone, the autonomic system and the lungs together. The outlook in any individual case therefore depends on many factors at once: the size and flexibility of the curve, the quality of the bone, the state of the lungs and the swallow, the stability of the autonomic system, and the experience and support available to the surgical team.

Across the whole field the consistent themes are that spinal deformity is one of the defining orthopaedic features of familial dysautonomia, that it behaves as a progressive neuromuscular curvature rather than an ordinary adolescent one, and that any surgery to correct it must be weighed against the formidable perioperative hazards of the condition. Any individual outlook is a matter for careful assessment by the treating team rather than something that can be read from a category or a measurement alone.