Idiopathic short structure is a general term used to describe a large group of children who have short stature, but in whom no specific diagnosis has been made. So, idiopathic short stature is not a specific entity in its own right, and in fact it’s not a diagnosis, but it is a general term to describe children with short stature. Idiopathic short stature, as a group of disorders, can be defined as children who have short stature, with a height less than -2 standard deviations below the mean. And that generally agrees with the third centile of normal population centile charts. They have normal birth weight. They do not have any chromosomal abnormality or dysmorphic syndrome. In particular, they do not have any specific endocrine abnormality, and they have normal growth hormone secretion. And finally, they do not have an intercurrent illness, which might be the cause of their poor growth. So having excluded these other causes of short stature, we can then come to describe a child as having idiopathic short stature.

Idiopathic short stature occurs very frequently. It is certainly the commonest cause of a child being referred for investigation. Because the organic causes of short stature are relatively rare and, statistically, 3% of the population are said to be short of the
childhood population. And I would say at least 50% of short children have idiopathic short stature. And over 50% of children referred for investigation to paediatricians or to specialist endocrine clinics would have idiopathic short stature. So it’s very common.

Idiopathic short stature can be subcategorised into three subcategories. The first is children who have parents who are short. And these children are described as having familial or genetic short stature. The second group are children who have parents of normal height, but these children are still short. And therefore they have non-familial idiopathic short stature. The third group which can be included in the general umbrella of idiopathic short stature are children with delay of growth. They are described as having constitutional delay of growth, and they also later have delayed puberty. This is a very large group of children; this is a very common problem, particularly in boys, and there has been some controversy as to whether they should be included under the general category of idiopathic short stature. But by and large, the consensus is that it is appropriate to include them under this general umbrella.

The assessment of the child with short stature is extremely important. Because when one first sees a child with short stature, we have really no idea as to the cause, and we have to keep an open mind. And therefore we start with a careful clinical assessment, and this begins with the accurate measurement of the child. We carry out so called auxological observations. Auxology is the study of growth. And that includes the careful measurement of a child’s height, maybe also of the sitting height of the child, and plotting the height accurately on an appropriate centile chart of the normal population.
We also take a careful history, and this is very important, because we need to know from the parents what is the history of short stature; has the child always been short? We need to know if there is a family history of short stature. We need to document the heights of the parents. And we also need, in the history, to have the child’s birth weight, and this is an important part of assessment of the child. We then go on with the history by asking questions about any possible intercurrent illnesses. And we go through a number of systems; for example the respiratory system, which may be appropriate for conditions such as cystic fibrosis; the gastrointestinal system, and we are looking for causes such as coeliac disease or Crohn’s disease, and/or, for example, the renal system; there may be renal dysfunction which may contribute to short stature.

So, so far, we have taken a careful history; we have started the physical assessment. We then go on to examine the child. We examine the basic systems of the body; the central nervous system; the respiratory system; the cardiovascular system. And we look, at this point, very carefully, for any possible dysmorphic features which the child may have, which may be a guide to the presence of a chromosomal abnormality or a dysmorphic syndrome.

Also, as part of the physical assessment, we assess the child’s puberty development, and document that. And we stage the puberty according to the criteria of Tanner. The appropriate investigations start with general paediatric investigations. We have to have an open mind as to possible causes of the child’s short stature. So we start with simple tests, such as full blood count, ESR, electrolytes, renal function, liver function tests. We then go on to measure the child’s thyroid function, which is very important. And
we also exclude tests for coeliac disease. And in all girls with short stature, we ask for karyotype analysis, to exclude Turner syndrome. When all the general investigations come back as normal, we are still faced with a child with abnormally short stature. So we then proceed to endocrine assessment. And this involves performing a growth hormone stimulation test, which will give us a level of peak growth hormone secretion, from which we can either confirm or exclude growth hormone deficiency. And we may also consider measuring serum IGF1, which is a marker of growth hormone secretion, or growth hormone resistance; that might well be helpful at this stage.

Finally, we may want to consider doing a bone age x ray. A bone age x ray is an x ray of the left hand and wrist, from which the development of the bones can be assessed and scored. And this gives us a score of bone age, which complies with the developmental age of the child; the age of physical development of the child. Bone age x ray is a popular investigation, but it is non-specific. And although it may be useful in some situations where there may be growth delay, it will not give a diagnosis. So it is not a diagnostic test.

The target height is very important, because the target height gives us an estimate of the genetic growth potential of the child. If we go back to plotting the child’s height, we plot the child’s height on the centile charts. We then take the height of the mother and the height of the father, and we plot these heights as centiles, also, on the child’s centile chart. Now we have to remember, if the child is a boy, we have a male centile chart. And we plot the father’s true height, and the mother’s height plus 13 centimetres. In other words, we have to correct. If the child is a girl, we are plotting the height on
a female chart. We plot the mother’s true height, and the father’s height minus 13 centimetres.

Now plotting the parents’ height centiles gives us the mid-parental height. And the mid-parental height, plus or minus nine centimetres, gives us a range which is known as the target range. And any child growing normally should have an adult height within their parental target range.

This growth chart shows the height of a child, with several height points plotted and you can see the progression of the child’s growth. You will notice that the height of this child is below the third centile, and that as she grows, the growth pattern is essentially deviating away from the normal centile lines. This means that she is growing abnormally slowly. You will also see that the parents’ height centiles are plotted, and in this case, the parents’ heights are completely normal. So this child has idiopathic short stature which is non-familial. This child needs careful investigation, because it is crucial that we try to find the reason why this child is growing
abnormally slowly. Her height prognosis is not particularly good. It is unlikely that she will reach the height target of her parents, and we may want to consider some degree of growth therapy in this child.

Certainly, some children with idiopathic short stature may have some degree of growth hormone deficiency, or growth hormone resistance. The problem with making a diagnosis of growth hormone deficiency is that as the growth hormone deficiency becomes less severe, the tests that we depend on for making this diagnosis become less reliable. It is not difficult to diagnose extreme growth hormone deficiency. However, we take an arbitrary cut off for the peak growth hormone level during a growth hormone stimulation test. And this is a pharmacological test which can give rather unreproducible results. So it is very likely that we can categorise a patient as not having growth hormone deficiency because the peak growth hormone value exceeds our arbitrary cut off. And then that child will fall into the general category of idiopathic short stature.

The same applies to growth hormone resistance, which is a rather poorly defined entity, particularly at the mild end of the scale. Some children with idiopathic short stature, who we know have normal growth hormone secretion, because we’ve excluded growth hormone deficiency, will have low levels of serum IGF1. And therefore, by definition, they have normal growth hormone secretion, but the action of the growth hormone is not perfect. And this is the reason that they have low levels of serum IGF1. So they also very easily fall into the general category of children with idiopathic short stature.
Idiopathic short stature is not a licensed indication for growth hormone therapy in Europe. This has been carefully considered by the European Medicine Agency on a number of occasions. And they have decided, probably largely because of the vagueness in the definition of idiopathic short stature as a clinical entity, that this was not a justifiable indication for growth hormone treatment. In the United States, however, the FDA, in 2003, did approve idiopathic short stature as a licensed indication for growth hormone. They considered that children with heights below -2.25 standard deviations can be treated with growth hormone. And therefore growth hormone treatment is widely used in the United States, and also in some other countries that respects the FDA legislation.

If growth hormone is used for treatment of idiopathic short stature, it is very important that the growth of the child is very carefully monitored. For example, height should be measured accurately every six months after the start of growth hormone therapy. And if after one year of growth hormone treatment, the change in height standard deviation score has not exceeded 0.5, then the treatment should be stopped. And another variable used in discontinuation of growth hormone treatment is growth velocity. And if the growth velocity during the 12 months on treatment is not more than two centimetres per year, compared with pre-treatment growth velocity, growth hormone therapy should also be discontinued.

Alternatives for treatment of idiopathic short stature are really quite difficult to identify. Firstly, there are not good data showing real benefit from alternatives of therapy. The possible options are psychological counselling, and this can certainly be a help. And it is always a valid option to consider not giving hormone therapy for idiopathic short stature. And explaining to the child that really, the height prognosis is quite good, and that if no abnormal cause has
been identified, then it is likely that the child will reach a good height.

Other alternatives are firstly aromatase inhibitors. This treatment is still controversial; it is still essentially a research area. These treatments are not licensed. But in some boys with growth delay, the use of aromatase inhibitors has been found to be of some benefit. Anabolic steroids have been widely used for many years; over 20 to 30 years. They have a small effect on growth rate; particularly in children with delay of growth. They may for example increase the growth rate from, say, four centimetres per year, to, say, seven centimetres per year. And this can have some psychological benefit. These are mild androgens. They will not induce puberty development. And as I’ve said they can increase the growth velocity, but they are a short term measure. Other forms of treatment, for example GnRH analogue therapy, which is aimed to slow down puberty; to give further length of time for growth, are not recommended in idiopathic short stature.

In most studies of psychological status in children with idiopathic short stature, particularly those that were conducted in the community, children appear to adapt extremely well to their height, and the incidence of psychological disturbance is very low. If, however, you look at a selected group of children who are referred to hospital for investigation of their short stature, here we begin to see that there is a slightly increased incidence, for example, of bullying, and of low self esteem and low confidence in these children. But overall I would say that most children with idiopathic short stature are psychologically robust, and adapt extremely well.

The key points to bear in mind in terms of the management of a child with idiopathic short stature: first of all, one must never be
critical of parents who are concerned about the growth of their child. As a paediatric endocrinologist, I’m always happy to see a child whose parents are worried about their height, however short the child may be. Any child who is referred with idiopathic short stature needs careful assessment. And as we discussed, the principles of clinical management, consisting of history, investigation, careful examination, should be followed.

Often we will not find a cause of the child’s short stature. In this situation, it is important to follow the child carefully, take accurate measurements, and plot the child’s growth pattern carefully on an appropriate centile chart. If we find a cause of the short stature, that is good. It may or may not be treatable, but at least we can explain to the child and the family the reason why the child is short. If we do not find a cause, we are then describing the child as having idiopathic short stature. The child still needs to be followed, and as medical science develops, there may well be investigations which become available, which may allow us, in due course, to identify the cause of the child’s poor growth.