RTS support group

Rubinstein-Taybi Syndrome:

INTERNATIONAL CONSENSUS GUIDELINES ON DIAGNOSIS AND MANAGEMENT

Your summary in clear language, from the RTS Support Group

Rubinstein-Taybi syndrome (RTS) is a genetic condition that is there from birth (congenital). It's named after the two doctors who first recognised and described it in 1963.

A set of guidelines has been developed by a group of experts, working alongside people from RTS patient groups. They outline best practice in diagnosing and looking after children and adults with RTS. They list the physical signs and symptoms needed for a diagnosis of RTS as well as guidelines for tests and management. They also make a number of recommendations. This summary is a clear language version of these guidelines.

This is a plain English version of "Diagnosis and management in Rubinstein-Taybi syndrome: first international consensus statement. Lacombe D, Bloch-Zupan A, Bredrup C, et al. Journal of Medical Genetics. 2024;61(6):503-519". It is not intended as a substitute for the original work and should be read in conjunction with it. If you have any concerns or queries about Rubinstein-Taybi Syndrome, you should speak to your own (or your child's) doctor.

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Diagnosing RTS

Having a reliable way of diagnosing RTS enables people with RTS and their families to identify and understand the syndrome, and the features which are associated with it, seeking medical advice as needed and considering helpful ways to support an individual with RTS. It also enables families to connect with each other and to provide mutual support.

Type 1 and Type 2 RTS

There are two genes involved in RTS, called CREBBP and EP300. People with RTS have a change in one of these genes, or more rarely it may be missing altogether. You can have the mutation and not have RTS and vice versa, you can have RTS and not have the mutation.

A change in the CREBBP gene is known as type 1 and EP300 type 2. The types have features in common, but these overlap and vary too much to separate people with RTS into two separate groups.

Doctors can now use the guidelines to score RTS features and make a diagnosis. Some features are essential. Other features support a diagnosis but are not essential. Points are allocated based on the existence of these features. A score of 12 or more (including essential features) means a definite diagnosis of RTS. Lower scores will indicate a likely, possible or unlikely diagnosis. If the score indicates a possible diagnosis, doctors should do a blood test for RTS genes before confirming it. (Full details of the scoring system are outlined in the original consensus statement).

Essential Features

Facial characteristics

To count as essential, there should be at least 3 of the following:

- a nose that curves outwards and forwards
- eyes that slant downwards
- high arched eyebrows
- the fleshy part between the nostrils being lower than the sides of the nostrils
- the roof of the mouth being higher and narrower than usual
- a typical smile.

Doctors may need to take family likeness into account when scoring facial features for RTS in case this explains their existence.

Thumbs and big toes

Someone with RTS **may** have:

- thumbs or big toes (or both) that look wider than usual
- thumbs or big toes (or both) that bend outwards.

Diagnosing RTS

Growth
People with RTS may be born with a head that is smaller than usual. This is more common in babies with type 2 RTS. Babies and children with RTS usually grow more slowly.

Delay in development
Babies and children with RTS tend to be slower to reach milestones. They usually have some learning disability, but how much each person is affected varies a lot.

Supporting Features

There are 3 other features that don't affect everyone with RTS, but are more likely. The scoring system takes these into account. They are:

- a medical condition that affects the mother shortly before birth, called pre-eclampsia
- a tendency to form raised scars (keloids) after injury
- having a lot of body hair.

Doctors with expertise in RTS intend to work with families to identify the factors that most affect the lives of those with RTS. This will include physical features, behaviour and learning difficulties.

Having a baby with RTS

Many of the features of RTS develop as a child grows. So they're not all visible in newborn babies. But around 7 out of 10 babies with RTS (70%) are diagnosed when they're born. Babies may have a prominent forehead with a red birth mark in the centre. They may also have widely spaced eyes, with long eyelashes and unusually thick, black hair.

It's very rare for RTS to run in families. At most, there's a 1 in 100 likelihood (1%) of having another baby with RTS. If someone with RTS has a baby, there is a 1 in 2 likelihood (50%).

Testing is not generally done while the baby is in the womb. But it can be done if the parents have already had a child with a known RTS gene.

Feeding

Babies with RTS often have feeding problems. The roof of the mouth being arched and a tendency to be a bit 'floppy' mean that they can have difficulty sucking and swallowing.

About 1 in 2 babies with RTS (50%) are able to breastfeed. Mothers who wish to try should have help and support from midwives and health visitors.

If your baby has feeding problems, seeing a dietician may help.

Some babies will need to be fed through a tube, at least to start with. Tube feeding is usually done when a baby isn't gaining enough weight. Or if they are inhaling some of their feed into the lungs when swallowing. Usually, these problems go away by the age of one.

Tests and Scans

The gene changes in RTS mean that people are prone to a number of other conditions.

All babies with RTS should have eye examinations, heart tests and a kidney ultrasound scan. These are to pick up any problems early so they can be treated.

Babies should also have all the other care and vaccinations that any baby would have.

There is more information on the following pages about conditions people with RTS are prone to. These conditions do not affect every individual with RTS and the degree to which they are affected can vary greatly.

Hormonal Issues (Endocrinology)

Low blood sugar sometimes happens in newborn babies with RTS but this is usually easily managed and doesn't last. Much more rarely, low blood sugar can be due to babies producing too much insulin. Although still rare, this is more common in type 2 RTS. It may not last, but in some cases it's permanent.

If your baby is jittery, has weak muscles or has seizures, the doctor should test for low blood sugar.

Slow growth and physical development is typical of RTS, usually within a few months of birth.

Growth in babies and children should be measured against a growth chart specific for RTS.

Children with growth that is slower than is usual in RTS, should have their growth hormone level tested.

There isn't the usual teenage growth spurt. So adults will be shorter than average.

Growth hormone levels are usually normal, but if not, giving growth hormone may help to increase adult height.

Children with RTS tend to go through puberty at the usual age. RTS doesn't affect fertility, so it's possible for them to become pregnant or father a child.

Teenagers and adults with RTS need sex education and contraceptive care that is in keeping with their emotional development and level of understanding.

Digestive System

Acid reflux is common in babies and children with RTS. Doctors call this gastro-oesophageal reflux disease or GORD. Symptoms include feeding problems, repeated chest infections, restlessness and poor sleep. Long term, it can damage teeth and cause inflammation of the food pipe (oesophagus).

Your child's doctor will help you manage acid reflux with diet and treatment. But if this doesn't help, they should refer you to a specialist (a gastroenterologist).

Constipation is very common in all age groups with RTS. There's no obvious reason for this.

Constipation is mostly managed as it would be with anyone, by increasing fibre and fluids. Sometimes laxatives that draw water into the bowel are necessary.

Heart and Lungs

Heart defects from birth are more common in RTS and may affect 1 in 3 babies. They may have a hole between the major blood vessels or within the chambers of the heart. Usually these would have closed by the time a baby is born.

Other problems with the heart and circulation (such as high blood pressure) are less common in RTS and are managed as for anyone else.

Everyone with RTS should have heart tests, when they are diagnosed. This should include a heart ultrasound scan.

Colds and throat infections are common in babies with RTS.

If a baby has repeated chest infections, a doctor should check to see if they have acid reflux or are inhaling a little when they swallow. This can be the cause.

If reflux, or inhaling when swallowing is not the cause of chest infections, the doctor should check to see if the child has poorer immunity than normal (this is not generally the case).

Lung disease with inflammation and scarring of the lungs (fibrosis) can come on in childhood or in adults. This isn't common in RTS, but can be serious. Treatment in RTS is no different than for anyone else.

Breathing problems in RTS can be caused by curvature of the spine (scoliosis) restricting the expanding of the chest. Or by interrupted breathing during sleep (sleep apnoea).

Eyes and Sight

Everyone should have an eye examination with a specialist (ophthalmologist) when they are diagnosed. Eye problems are common and may need prompt treatment.

Some eye problems can come at any age, so individuals should have eye exams regularly throughout life.

Watery eye can be caused by a blockage in the tear duct, where it joins the nose. This affects up to 1 in 2 people, usually only on one side.

Glaucoma is an eye disease that happens in just over 1 in 10 people with RTS. It causes increased pressure inside the eye. All babies with RTS should be checked for this, as it can damage sight if not treated. It can also come on later in life.

Cataracts are a clouding of the lens of the eye, making it difficult to see properly. These affect up to 1 in 4 people with RTS, usually from birth. They can develop later in life. Treatment is important to prevent blindness. Babies are usually treated in the first few months after birth.

Short or long sight is common in RTS and people often need glasses. Children may also have a squint.

If children with RTS need glasses, they should be introduced gradually. This gives the child a chance to get used to them and makes it more likely that they'll wear them in the long run.

Sensitivity to light is also common. Sunglasses, tinted lenses in glasses or hats with brims may help.

Hearing

People with RTS are prone to ear infections. Repeated infections can damage hearing. So people with RTS should have their hearing checked regularly.

Sleep

Many children, and 2 out of 3 adults with RTS, have **difficulty breathing during sleep**. This is because of smaller airways, the structure of the nose and tendency to have less muscle tone in the throat.

There are sleep questionnaires designed for people with learning disabilities and these can help to diagnose and manage sleep problems.

In some children and 1 in 4 adults, breathing stops and starts during sleep. This is called **obstructive sleep apnoea** (OSA). Signs are snoring and daytime sleepiness.

Doctors should always investigate and treat OSA, as it can lead to other health problems.

Anaesthetics

Because they are at risk of various health conditions, nearly half of those with RTS need at least one anaesthetic for surgery during their lifetime. Many need more than one. As with sleep, the structure of the face and throat can make giving an anaesthetic more difficult.

It's important for people with RTS to have an anaesthetist that knows about the possible difficulties and how to manage them during and after surgery.

Unless it's an emergency, it's best to try and group procedures together, so the person has as few anaesthetics as possible.

Skin Problems

It's normal for scar tissue to form after an injury. But about 1 in 4 people with RTS have thick, raised scars called **keloids**. These are more common in type 1 RTS, but can also happen in type 2. They're also more likely as you get older.

Keloids can be painful and itchy, so they do affect quality of life. They are difficult to manage and your doctor will choose a way to manage them that is best for you.

About 1 in 6 people also have skin growths called **pilomatricomas**. These are hard lumps that tend to form on the head and neck.

Pilomatricomas that are uncomfortable can be removed with surgery.

Ingrown nails are common, particularly in the thumbs and big toes.

It's important to cut nails carefully and have well fitting shoes to help prevent ingrown nails. They are managed as for anyone else.

Kidneys

There are several possible kidney problems with RTS. Kidney problems can also cause **high blood pressure**.

Everyone diagnosed with RTS should have at least one kidney ultrasound scan. This is usually done in newborn babies. If a baby has a kidney problem or high blood pressure, they should see a kidney specialist (paediatric nephrologist or urologist).

The Sex and Reproductive Organs

Undescended testicles are very common in men with RTS. A doctor should check for this when RTS is diagnosed. This helps doctors to check for testicular cancer when they are older. It also improves fertility, if desired.

Women with RTS may have frequent or very heavy periods. This can usually be managed by taking the pill (hormonal contraceptive).

Muscles and Bones

Differences in bone structure are common in RTS, but vary a lot between people. They're a little more common in type 1 RTS.

Outward bending thumbs and big toes may cause problems with using the hands or walking.

It's best to wait and see how a child is managing before thinking about surgery for thumbs or toes. If needed, surgery should be done by a specialist.

A doctor should regularly examine people with RTS to check for any mobility problems that may need treating, particularly in the knees and hips.

Older children and teenagers may develop a curvature of the spine (scoliosis). Everyone should see a specialist to check for this, in late childhood or early teens.

People with RTS often have **loose joints**, with a wider than normal range of movement. If this is the case in the hips and knees, it can cause stiffness and a type of waddling walk.

Both children and adults are more at risk of fractures and adults may have thinning of the bones (**osteoporosis**).

If someone with RTS keeps having fractures, they should have a bone density scan to check for osteoporosis.

The Mouth and Teeth

A doctor should examine all babies diagnosed with RTS to make sure there isn't a gap in the roof of the mouth (a cleft palate).

Both baby and adult teeth may come in later than usual. There may not be the normal number of teeth and they can be overcrowded or discoloured.

An unusual shape, called talon cusps are common, particularly in adult teeth. This is an extra growth on the inside of the front teeth, which looks a bit like a bird's claw.

If talon cusps are causing tooth decay or stop the mouth closing properly, they should be treated, especially in adult teeth.

Children and adults with RTS need good care of their teeth and to see a dentist regularly to try and prevent tooth decay. They may need a sedative or anaesthetic if they need treatment. It's best to see a dentist who has experience with people with special needs.

Infections

Apart from colds and ear infections, people with RTS are just as resistant to infection as anyone else. They should have vaccinations at the same times as anyone else.

A child with RTS, who has repeated unexplained infections, should have blood tests to check their immune system. If these are abnormal, they should see a specialist (immunologist).

Nervous System

Unless there are symptoms, such as **seizures**, there's no special need for brain or spinal MRI scans in RTS. Some people have epilepsy, which is treated as for anyone else.

Learning Disability and Behaviour

This varies a great deal. It's generally milder in type 2 RTS.

Children with RTS need to have their abilities assessed early in life so that they can get the care and services they need. This can include physiotherapy and speech therapy. They should also have regular reassessment at significant points, such as when starting school or at puberty.

Early and ongoing help with communication helps to improve social development in RTS.

Specific care and treatment for RTS is not well developed.

People with RTS tend to be friendly and trusting of others.

Screening for anxiety and for autism can help people with RTS access appropriate support and care.

Programmes that teach skills for managing social situations can help to stop them being taken advantage of and acting on impulse.

High Pain Threshold

People with RTS tend not to show obvious signs that they've been injured or are in pain. It's important for parents to let teachers and other carers know this. Doctors should be prepared to take parents' views on board and investigate even if they think there's nothing wrong.