Introduction

In 1953 and 1954, Drs. Silver and Russell independently described groups of small-for- gestational-age [SGA] children whose pregnancies had been complicated by intrauterine growth retardation [IUGR]. Their common findings were short stature without catch-up growth, normal head size for age, a distinctive triangular face, low-set ears and incurving fifth fingers. These two groups of patients are now considered to have had variations of the same disorder that we now call Russell-Silver Syndrome [RSS] in the U.S. and Silver-Russell Syndrome [SRS] in Europe.

One interesting and important aspect of the Russell-Silver syndrome is its variation in phenotype. In this context, a phenotype is all the physical characteristics and abnormalities found in an individual patient that are attributed specifically to RSS. Some individuals with RSS have many traits, thus a severe phenotype, while others have very few traits, thus a mild phenotype.

When first described, RSS was NOT thought to be a genetic disorder because it recurred within families rarely, and when it did recur, its pattern of transmission failed to follow a consistent genetic mode of inheritance. More recent understandings of genetic mechanisms have led scientists to conclude that RSS is genetic, but its genetics are not simple. Scientists now believe that the RSS phenotype is associated with more than one genotype.

A genotype is the status of a specific gene at a specific location on a specific chromosome. Therefore, an abnormal genotype means there has been a specific alteration, such as a deletion, duplication, insertion, substitution or imprinting error within the code of a specific gene located at a specific site in an individual's genetic code.

Since our genotype is responsible for our phenotype, abnormal genotypes result in abnormal phenotypes. If we assume several genotypes for RSS, then we should not be surprised at a variety of phenotypes. We view this as one reason for the marked variability within the group of patients considered to have RSS. But deciding which child should be considered to have RSS is not always easy. When more is known about the genetics of RSS, we will find that some patients were incorrectly included while others were incorrectly excluded.

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Major Aspects of Growth In Children

The MAGIC Foundation is a national nonprofit organization created to provide support services for the families of children afflicted with a wide variety of chronic and/or critical disorders, syndromes and diseases that affect a child's growth. Some of the diagnoses are quite common while others are very rare.

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Russell-Silver Syndrome

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How is RSS Diagnosed?

The diagnosis of RSS is still a judgment call on a physician's part because there is no definitive laboratory test that can answer yes or no in a specific case. Doctors generally base their diagnosis on characteristic, clinical findings that make up the RSS phenotype. It is easy to diagnose the "textbook" RSS phenotype. An SGA child, however, who lacks catch-up growth, has low weight-for-height, normal head size for age, and few, if any, features that make him look different, is much more difficult to classify.

What is the Typical RSS Phenotype?

The RSS phenotype includes a number of physical and developmental characteristics. One of these, asymmetry, is unique to RSS, while others, like low birth weight and length, are shared by RSS and SGA children in general.

Characteristics Considered to distinguish RSS Children From Other SGA Children:

- body asymmetry -LARGE side is "normal" side
- inadequate catch-up growth in first 2 years
- persistently low weight-for-height
- lack of interest in eating
- lack of muscle mass and/or poor muscle tone
- broad forehead
- large head size for body size
- hypoplastic (underdeveloped) chin & midface
- downturned corners of mouth & thin upper lip
- high-arched palate
- small, crowded teeth
- low-set, posteriorly rotated &/or prominent ears
- unusually, high-pitched voice in early years
- clinodactly (inward curving) of the 5th finger
- syndactyly (webbing) of the 2nd and 3rd toes
- hypospadius - abnormal opening of the penis
- cryptorchidism - undescended testicles
- café-au-lait (coffee-with-milk) birth marks
- dimples in the posterior shoulders and hips
- narrow, flat feet
- scoliosis - curved spine, associated with spinal asymmetry & accentuated by a short leg

Characteristics of SGA Patients in General That Are Seen More Often in RSS Patients:

- fasting hypoglycemia & mild metabolic acidosis
- generalized intestinal movement abnormalities:
  a) esophageal reflux resulting in movement of food up from stomach into food tube
  b) delayed stomach emptying resulting in vomiting or frequent spitting up
  c) slow movement of the small intestine &/or large intestine (constipation)
- blue sclera (bluish tinge in white of eye)
- late closure of the anterior fontanel (soft spot)
- frequent ear infections or chronic fluid in ears
- congenital absence of the second premolars
- delay of gross and fine motor development
- delay of speech and oral motor development
- kidney abnormalities
- delayed bone age early, later fast advancement
- early pubic hair and underarm odor (adrenarche)
- early puberty or rarely true precocious puberty
- classical or neurosecretory growth hormone deficiency
- ADD and specific learning disabilities

What Should I Do If I Think My SGA Child Has RSS?

- Have your child's diagnosis confirmed by a doctor who is familiar with RSS-SGA patients.
- Make sure your child is measured carefully & frequently. KEEP YOUR OWN RECORDS. Find an endocrinologist who knows how to treat SGA children's growth failure and discuss the options.
- Find a pediatrician who is willing to learn from experts about RSS-SGA children, and will coordinate care and opinions with consulting specialists.
- Get adequate calories into your child. Insufficient nutrition & low blood sugar damage the developing brain and compound the growth failure.
- Take necessary measures to prevent hypoglycemia in young RSS children. Pay special attention to the night when everyone is asleep, anytime your child is ill or not eating normally, and when your child is unusually active or stressed.
- Know clues that hypoglycemia is occurring:
  a) waking to feed at night past early infancy
  b) excessive sweating
  c) extreme crankiness improved by feeding
  d) difficulty waking up in the morning
  e) ketones in the urine
- Prevent hypoglycemia by:
  a) feeding frequently during the day & night
  b) keeping snacks with you at all time
  c) feeding through gastrostomy tube
  d) adding glucose polymer in infant's, & corn-starch in child's, bed- & night- time feeding
  e) keep glucose gel with you at all times
  f) making prior arrangements with your doctor and local ER to start IV glucose if feeding is impossible
  g) having urine ketone sticks at home
- Treat your child his age not his size. Arrange safe, age-appropriate activities; buy age-appropriate clothes; and expect age-appropriate behavior & responsibility.
- Watch your child's psychosocial and motor development. All states have developmental evaluation & intervention services for children less than 3. These programs are based on the child's needs not parental income. For children over 3 years, the school district becomes responsible for providing these services. Take advantage of this; intervention can make a world of difference for your child!
- Seek appropriate consultation for recurrent, ear infections, hypospadius, undescended testicles, leg length discrepancies, etc. But remember:
  a) Only emergency surgery should be done until the child is gaining weight well.
  b) A young SGA child should NEVER be fasted or kept NPO for more than 4 hours for ANY reason without glucose-running IV
  c) For surgery, IV glucose should be given during the procedure and continued in the recovery room.

Why Does My Child Have RSS?

It is not your fault! You could have done nothing to prevent it! RSS occurs through complicated genetic mechanisms and could never be caused by what you as parents did or did not do.

What Can I Expect Regarding My Child's Cognitive Abilities?

An infant with RSS is generally born with normal intelligence. Learning disabilities and Attention Deficit Disorder (ADD) appear to be increased in incidence in RSS. Autism and similar disorders like pervasive developmental disorder (PDD) may also be increased. It is unclear whether these problems just appear to be increased in RSS, are innate to RSS, or are acquired through early malnutrition and hypoglycemia, both of which are preventable.

Where can I meet other RSS families?

Coping with the time-consuming special attention and services necessary to care for an RSS-SGA child can be overwhelming, especially if you try to face it alone. Good physicians often have no experience with routine needs of RSS-SGA children. Day-to-day challenges such as feeding, formulas, fitting clothes, school issues and peer pressures can be less stressful if you are in contact with other families who "have been there and done that." Making connections between families with similar issues and facilitating sharing of information and experience is a major goal of the MAGIC Foundation's RSS Division. We can put you in touch with other people who have had, and have solved, problems similar to yours.

What Treatments are Available for RSS?

Treatment of RSS children's problems should be approached in a systematic and timely fashion. The major problems that require intervention in the various age periods are all different, but most all these problems can be solved or dealt with successfully if you get the help you need. It is beyond the scope of this brochure to go into treatment protocols. Be assured as parents, however, that you can find acceptable treatment options that will help your child's weight gain, increase your child's final adult height and improve your child's general quality of life. Please contact us at MAGIC-RSS for up-to-date information regarding research, treatment, current literature, Internet support groups and videos of past summer conferences.

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