Rarer Syndromes

Restricted Growth Association

Working to benefit people with restricted growth and their families

This booklet has been written to provide information and support for parents of children with a rare restricted growth condition, people with the condition, their families, friends, teachers and health care professionals.

Dr Will Christian is a paediatrician who has achondroplasia (restricted growth). The RGA would like to thank the medical specialists who have taken a special interest in reviewing this booklet: Prof Dian Donnai, Prof Norman Nevin and Dr Michael Wright.
The RGA acknowledges the help of the many members and their families who have contributed their experiences towards this booklet. Their contributions were compiled by the RGA Information Officer, Ros Smith.
The RGA would like to acknowledge the grants from the Department of Health and the National Lottery Charities Board which have made it possible to produce this booklet, together with the help of the Wellcome Trust Medical Photographic Library which has supplied many of the photographs for the series.

'Armed with the information in this booklet, help from RGA and support from other families in a similar situation, we, as a family, now have the confidence to face the world. We no longer feel isolated and we want to make the most of the opportunities for our child.'

The contents of this booklet are believed to be correct at the time of publication. However, knowledge about the range of conditions causing restricted growth is growing all the time, especially in the areas of genetics and orthopaedics. We encourage you to find out about new developments from the RGA and other sources, some of which are listed at the end of this booklet, or on the inserts on particular conditions. The RGA will endeavour to update the inserts on particular conditions as new information becomes available. We hope that members will feed back to the RGA any new information that they encounter.

Rarer Syndromes

by Will Christian MBBS, BSc

'When you have a condition which only two or three people in the whole world have, you can end up feeling like a guinea-pig – as though all the world is looking at you. You carry the responsibility as far as the medical condition is concerned, because you are viewed as a "living example of a condition that doctors have only read about in books". There can be a lot of intrusion into your life as doctors and researchers try to learn more about your condition. The best thing you can do is to find out as much as possible, become your own expert and then get on with your life.'

What is restricted growth?

'Restricted growth' is a term used to describe people whose adult height is under about 5ft – significantly less than the normal range for the general population. The commonest cause of short stature is 'constitutional' – small parents having small children, and there is nothing wrong with their pattern of growth. This booklet looks at the very rarest conditions that disrupt the usual growth pattern. Some types of restricted growth are characterised by disproportionate stature (eg shorter limbs with an average size body).

Most people of short stature are of normal intelligence and occupy positions in all sectors of society. There may be factors other than growth that are affected by a particular condition. These are dealt with either in the detailed information on particular conditions in the back pocket, or by literature from specific support groups to which we include reference information.

When parents become aware that their child has a restricted growth condition, they will naturally be anxious to know what the child's future will be. Although this may be impossible to predict, many people of short stature are able, with care, to live normal, happy lives although perhaps with some physical limitations.

Many practical difficulties can be overcome with a little imagination. Clothes can be altered and cars and bicycles can be adapted (see the RGA **Lifestyles** series). Many people with restricted growth can participate in most activities. Everyone will find their own limits and boundaries, but it is important that, within reason, these are not imposed by others or by society.

Conditions causing restricted growth may be inherited via parents' *genes** even if neither parent has signs of a growth disorder. They may appear 'out of the blue' due to a genetic fault at conception or there may be some environmental or social cause. Restricted growth may also result from pre-natal growth failure, chronic disease of an internal organ (heart, bowel, lungs, kidney, etc), or from drugs used in treatment of a chronic disease, or from hormone or enzyme deficiency.

This booklet (and the others in this series) is intended to provide information that may make life easier for people affected by some of the rarer restricted growth conditions. Most of these conditions have a genetic origin, which means they start at conception, developing while the baby is in the womb and continuing throughout life. All are extremely rare. Even the most common genetic condition causing restricted growth, achondroplasia, occurs in only (approximately) one in 25,000 people. The rarest syndromes occur in less than one in a million of the population. A few appear to be unique to the affected individual.

There is a wide spectrum of restricted growth conditions of genetic origin. The main categories are:

- conditions where growth is affected evenly over the entire body – the affected person is small, but in proportion
- conditions where only the skeleton is affected, which usually results in short limbs or a short trunk or, occasionally, both – these are often referred to collectively as skeletal dysplasias.

* See later section on Genetic Inheritance

Most people with restricted growth have normal intelligence, but a few conditions may be associated with a degree of mental impairment.

The main body of this booklet explains general medical aspects of restricted growth conditions and gives practical and emotional support to individuals and their families. Information on a specific condition is included at the back of this booklet or else there is reference to a specific support group that can provide comprehensive medical information about that condition.

If you have a baby with any restricted growth condition, we strongly recommend that you read the RGA's booklet *Babies and the Early Years* in the **Lifestyles** series.

Diagnosing rarer syndromes

It can be extremely difficult to make a correct diagnosis as rarer syndromes are seldom seen and relatively little is known about them. Most family doctors will not have seen a similar condition before and often experts have difficulty in making a correct diagnosis. Some people, especially in the past when very little was known about these conditions, have not wished to seek a diagnosis, and have just taken life as it comes. With the recent very rapid increase in knowledge and the consequent rise in expectation, many people are now driven to find the cause of their (or their child's) condition.

Diagnosis of these very rare conditions is seldom confirmed by your local hospital medical staff, eg consultant paediatrician. They will usually refer you to a Regional Genetic Centre where there are specialist geneticists who are in contact with the network of Centres around the UK and also with world experts. If you are not offered a referral, you are entitled to ask for one. Your own GP or hospital paediatrician should be able to do this for you.

It is in your and/or your child's best interest to have a correct diagnosis. Informed guidance may then be

given about appropriate treatments and the early recognition of possible complications that may cause significant impairments such as those affecting the eyes or the nervous system.

If an inherited condition is diagnosed, it may affect future children born to the family or to the individual. Genetic counselling should be offered; again if it is not, you may ask for a referral yourself. Genetic counselling involves identifying the inheritance patterns of the condition from which an estimate of the risks of further occurrence can be made. This will allow you to make informed decisions about having more children. These patterns are explained in a later section.

In some cases, it may not be possible to make a precise diagnosis before the age of around five years, when the child's features may be more evident. As parents, you may feel 'fobbed off' when a doctor just seems to want to monitor your child's growth without offering any attempt at a diagnosis. You need to distinguish whether the doctor is looking for certain features to become more obvious or is covering up a lack of knowledge while being reluctant to make a referral. In adults, it is sometimes not possible to make a specific diagnosis as the causes of changes in the bones may not be identifiable after growth has stopped.

'Our local doctor just kept measuring Andrew without offering any possible diagnosis other than that he was small for his age. We knew that already, so in the end I found the name of a growth specialist at Great Ormond Street and got a private appointment. He recognised my son's condition straight away. We felt so relieved.'

Living without a diagnosis

Uncertainty about a diagnosis may be very frustrating, although there are still a number of practical steps that may be taken to make life

easier. People describe a sense of being unable to move forward in their lives until they know the name of their child's condition. Many people feel better if they have as much information as possible; this also makes it possible to know what to expect and to plan for the future. If you are struggling to achieve a diagnosis, you may find the fact sheet which is produced by Contact a Family*, *Living without a Diagnosis*, helpful.

'Bethany is now three years old and she is very tiny. We knew she had restricted growth before she was born as they could see it on the scan, but none of the experts we have seen have been able to give us a precise diagnosis. It is very frustrating as we would like to have more children, but until we know our daughter's condition, we do not know the chances of having another child with the same condition.'

Prenatal diagnosis

Tests in pregnancy can now detect some of the more serious growth disorders, but a precise diagnosis is seldom possible even at a late stage in pregnancy.

Prenatal diagnosis at an early stage may be possible in families that have a high risk of having a child with a restricted growth condition, where, for example, one or both parents is affected or there is already a child with a condition that indicates a high risk of recurrence.

Routine ultrasound scanning may reveal that a baby is not growing normally, and a condition that is associated with restricted growth may be suspected. From these scans it is often not possible to tell much about the nature of the condition, or whether restricted growth is the only feature or whether it is a minor part of the condition. You will usually be referred to a centre where more sophisticated ultrasound equipment is available for a special

* See *Sources of information*

scan, which may or may not confirm the original suspicions. An atlas of normal skeletal radiography throughout fetal life has been published along with examples of various skeletal disorders (dysplasias). This serves as a reference guide for specialists for the diagnosis of those dysplasias that have an effect on growth within the womb. The most severe forms may be detected by measuring the length of the baby's femur (thigh bone) on the ultrasound image at about 18 weeks of gestation and comparing it with standard measurements, and putting this information together with other features that may be seen on the ultrasound image.

Confirmation of some specific conditions can only be made by testing cells from the baby either by amniocentesis or chorionic villi test. (*Your maternity unit should have further written information about these tests.*) These tests can only be used to diagnose restricted growth conditions for which the genetic cause is precisely known and laboratory tests are available – in practice at the moment this is only for the more common conditions such as achondroplasia. Genetic advances are being made at such a pace that in the future tests may be available for rarer conditions. Conditions that are caused by chromosome defects such as Down syndrome and Turner syndrome that have associated short stature are also identifiable by these prenatal tests, as are conditions caused by enzyme abnormalities such as Morquio disease.

'We were told that our baby had restricted growth at about 28 weeks of gestation. We found the knowledge rather a double-edged sword as no-one could tell us anything about what restricted growth meant. They told us it could be Down's syndrome or achondroplasia or something else, but we were not offered a diagnostic test. We began to view Jessica as a kind of alien being rather than our baby. We were so grateful for the information from the RGA which helped us to cope.'

How a diagnosis is made

A diagnosis is made on the basis of information provided by the individual, his or her family and the results of certain tests. Unless there is a precise genetic test, the diagnosis cannot always be conclusive and sometimes a child's growth and development have to be monitored for some time. However, you should be made aware of the sort of things that the doctor is looking for if long-term monitoring is thought to be necessary.

A detailed family history is needed, especially if there are already family members with restricted growth. Information from the individual such as when the restricted growth was first noticed and other symptoms or abnormalities will be requested. This information is very useful as different skeletal dysplasias become apparent at different ages and it is helpful to know whether the effect on growth was seen at birth. The doctor will make a physical examination including the heart and chest, abdomen, limbs and spine, together with a neurological examination including testing reflexes. Measurements such as standing height, sitting height, weight, and head circumference are compared with standard charts. Do not be afraid to ask the doctor what he or she is looking for and to add your own observations if they are relevant. You should feel that you can enter into a dialogue with your doctor. After all, he or she is trying to help you and/or your child.

X-rays will usually be needed to look at the shape and structure of the bones to identify the skeletal dysplasias – conditions that specifically affect bone growth. As explained earlier, a series of X-rays showing development over time may be needed to differentiate between similar conditions.

Blood tests may be taken to examine aspects of body chemistry that may be associated with different conditions. Genetic information may also be found in blood cells. A blood sample may be

used to test for a specific chromosome or gene fault if there is sufficient knowledge about the genetic cause of the suspected condition. It could also be used to eliminate various possible disorders, which may be helpful.

Urine tests are also helpful for investigating body chemistry, especially in relation to conditions caused by enzyme deficiency. Occasionally skin, bone or bone marrow samples could also aid diagnosis. Try to ensure that you understand what the doctor is looking for and why these tests are necessary.

Terminology

The language used to describe and discuss restricted growth conditions can be confusing and intimidating. Beware that descriptions of the condition in medical literature or on the Internet are likely to include all the possible features and complications of the condition which are seldom experienced by any one individual. To add to the confusion, one condition may have a variety of names.

Many of the rarer syndromes are named after the person who first identified them, for example Kniest dysplasia, which is also known as metatrophic dysplasia type II. There will also be a medical name, almost always in Greek, which describes the condition in terms that health professionals (and Greek scholars!) can understand. Sometimes the name refers to physical features of the condition, sometimes it is an attempt to explain the cause of the condition or, most commonly, the name refers to features seen on X-rays. Various attempts have been made to group conditions together on the basis of the visible and X-ray features (hence metatrophic type II in the example above) and/or on the mode of inheritance. As more research is carried out on the genetics of these conditions, so the root causes will become known and the similarities and differences will be better understood.

The word *dysplasia* is one you will encounter frequently and refers to growth abnormalities. Thus *skeletal dysplasia* refers to abnormalities of bone growth.

Living with restricted growth

There is a great deal you can do to make it easier to live with a rare restricted growth condition – don't feel that you are entirely in the hands of doctors and health professionals. There are plenty of practical steps you can take that really do make a difference. Some are described in the RGA's **Lifestyles** booklets and the RGA actively seeks to enable members to exchange ideas to save re-inventing the wheel.

There may be some difficulties associated with having shorter arms and legs and back problems. Extender sticks and steps can help with reaching, while 'bottom wipers' can be contrived or purchased to aid personal hygiene (there is more information in the **Lifestyles** booklet on *Personal Hygiene*).

Children may need a bit of time in the morning to limber up before they are able to undertake activities that require them to twist, bend and reach. You can contact the RGA Office for information on a wide range of gadgets, sources of clothing and help with obtaining benefits.

Take the lead

One of the greatest problems for many people with restricted growth is overcoming the prejudice of people who are frightened by anybody who is different.

Parents need to take the lead in discussing their child's height. Children and adults need to learn that the huge diversity that exists amongst people's appearances is a good thing, and that variation in height is just one part of the richness of humanity. Grandparents and other family members, teachers, doctors and friends will take their lead from parents. If parents are able to discuss the issues that their child may face, other people will become more knowledgeable and better able to

offer the right kind of support at the right time. It may also help to discuss possible strategies for dealing with inquisitive or insensitive people at school or in the future and to anticipate the questions or comments that may arise.

One of the most important things parents can do to overcome the problems we have considered here is simply to accept their children for who they are and realise that they are unique, with the same individuality and capacity for giving and receiving love as any other child. All the attributes of good parenting apply, such as listening, education, love, setting a good example and appropriate discipline.

It is just as important not to be over-protective. Children need to develop good self-esteem on the basis of their relationships with parents and with other children. Young people should be encouraged to develop friendships, become involved in school activities (including sport, within appropriate limits) and gain a good all-round education that will help them in the future. There is more on these issues in several **Lifestyles** booklets, but especially *Going to School* and *The Teenage Years*.

'We have learnt that it's what's inside that counts. Our son does look a bit different, but he is his own person and ready and willing to meet life's challenges.'

Parents also need to take the lead in obtaining the most appropriate help and advice for their child. GPs may need to have things explained to them – restricted growth conditions are rare and many doctors may not have encountered them before. Parents may need to ask for referral to appropriate specialists, such as an orthopaedic surgeon, chest physician, ENT surgeon, speech therapist, physiotherapist or other specialist clinics. But remember, these specialists do not necessarily have any experience of the overall effects

of your child's condition. You need to help them by sharing your knowledge or by referring them to the RGA. It is difficult to find someone that has any previous experience of these rare conditions. The RGA is assembling the names of specialists with appropriate experience. Parents need to know who to ask and what to ask for. You must become the expert.

Treatment

There is currently no single treatment that will result in a baby with a rare restricted growth condition attaining a 'normal' physique or appearance by the time he or she is fully grown. Some treatments may be required to avoid or reduce possible complications, such as bone or joint surgery, which improve body function, while others may be a matter of choice (such as limb lengthening). Trials with growth hormones indicate some success in improving initial growth rate, but the increase in final height may not be significant.

Although it is natural to search for a 'cure', some treatments (such as growth hormone, except where the condition is caused by a hormone deficiency) may succeed only in giving false hope. It is important to be realistic. Knowing what questions to ask is a great help in determining the most appropriate form of treatment for the specific condition. Read as much as you can (starting with this booklet), talk to as many people as possible and find out about all possible options before deciding on a course of action. Be prepared to be flexible as knowledge, attitudes and relationships develop.

The best possible treatment for anyone with a restricted growth condition consists of a sensible diet, regular gentle exercise and routine check-ups with the paediatrician throughout childhood to identify any complications associated with the condition as soon as they arise (please see the sheet containing information specific to particular conditions at the end of this booklet).

Surgery may be used to lengthen the arms and legs in some individuals, although this is a controversial issue among people affected by restricted growth. On the one hand is the joy and satisfaction resulting from a possible gain of several inches in reach and height. On the other hand, the process is long and painful and not without complications.

Surgery is no magic wand and should be considered only when the affected child has had an opportunity to develop good self-esteem and a positive self-image and is old enough to make an informed choice. This is one reason why the RGA encourages young people to socialise together and develop positive attitudes. Unfortunately, this surgical procedure is sometimes offered by doctors who have no concept of the psycho-social issues facing the young person or the complications associated with the procedure.

Determining whether or not limb lengthening is appropriate may also depend on the specific condition (if a diagnosis has been made) or particular characteristics. Further information can be found in the **Lifestyles** booklet *Limb Surgery*.

Genetic inheritance

All aspects of a person are influenced by genes. Genetic material (DNA) provides a blueprint for each person and is contained in almost all cells in the body. Genes govern very obvious features like hair and skin colour and the shape of the nose and ears, but also extend to the attributes and traits we can't see, such as the rate of growth, personality characteristics, tendencies to certain diseases and conditions.

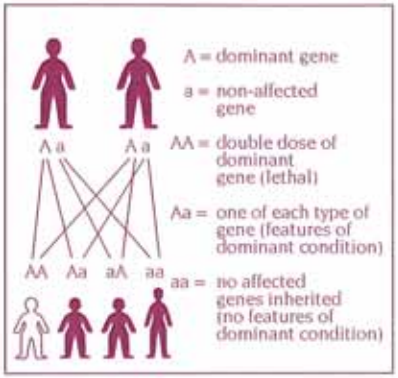
Nearly everyone (including those with restricted growth conditions) carries two copies of every gene: one from their mother and one from their father. Restricted growth conditions that have a genetic origin are caused by a fault in one or both genes that control particular aspects of the body that

are connected with growth.

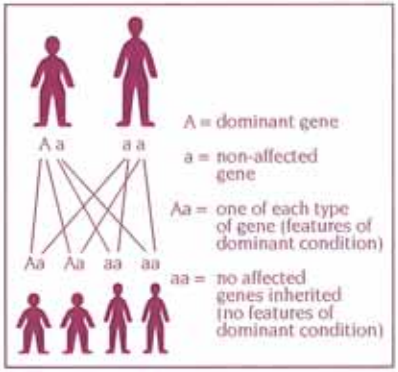
There are three main types of inheritance in restricted growth conditions:

- **dominant inheritance**

Only one copy of a gene (from either parent) need have a fault to cause the condition. If one parent has restricted growth, there is a 50% (one in two) risk for each child that he or she will have the condition. The child will either inherit the normal copy of the gene and be unaffected, or the faulty copy of the gene and be affected. If both parents have the same dominant condition, then there is a two in four chance that the child will inherit the faulty copy from one parent and have the condition. There is a one in four chance that the child will inherit the normal gene from each parent and thus be unaffected, and there is a one in four chance that the child will inherit the faulty copy from both parents and will have an extreme form of the condition and may not survive beyond birth (this is often referred to as a double dose).



Both parents with a dominant condition



One parent with a dominant condition

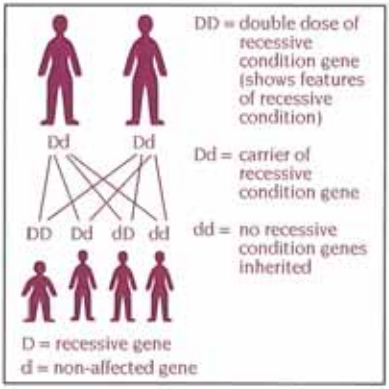
If neither parent has a restricted growth condition and they have a child with a condition that has dominant inheritance, the faulty gene causing the condition will have been due to a copying mistake

in the genetic material from one or other parent, probably the father, since millions of sperm are made throughout adult life in males, whereas females are born with all their eggs. This is a one-off occurrence and it is extremely unlikely that further children will be affected.

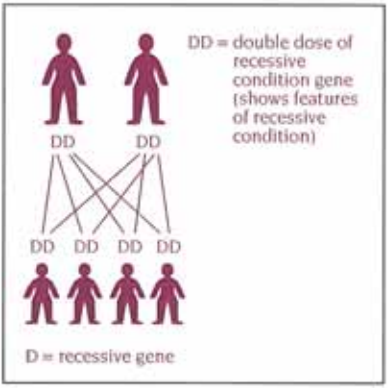
In the very rare circumstance in which unaffected parents have two children with a dominant condition, it is usually due to a situation affecting the occurrence of the faulty gene in the ovary of the mother or the testes of the father called *gonadal mosiacism*. This has only been documented for one or two conditions that cause restricted growth.

- **recessive inheritance**

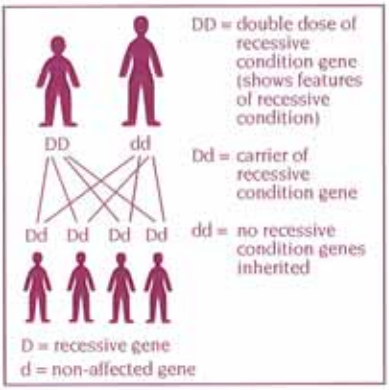
The person with a type of condition that has this pattern of inheritance will have received two copies of the faulty gene, one from each parent, in order to be affected by the condition. A person with only one copy of the faulty gene will not usually be affected by the condition and is called 'a carrier'. Parents of a child with a recessive condition will both be carriers and the chance of further children having the condition is one in four. This is one of the reasons why the diagnosis of the condition and



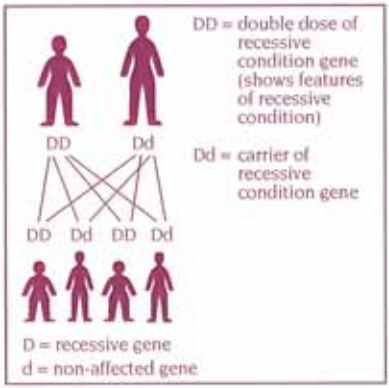
Both parents carriers of recessive condition



Both parents with recessive condition



One parent with recessive condition



One parent with recessive condition, one parent carrying one copy of the recessive gene

determination of its inheritance characteristics are important and why genetic counselling should be offered or sought.

If two parents with the same recessive condition have children, they will always be affected. If only one parent has the condition, it is extremely unlikely that their child will also have the same condition, but all their children will 'carry' the faulty gene and have a one in two chance of passing it on to a future generation.

- **X-linked inheritance**

Several restricted growth conditions are caused by faults in genes carried on the X chromosome (one of the two types of sex chromosome). Males have one X and one Y chromosome and females have two X and no Y chromosomes.

Affected men carry a faulty gene on their only X chromosome. Women who carry the faulty X chromosome will always have one completely normal X chromosome and do not, therefore, usually show features of the condition, but they can pass the faulty gene on to their male children. Sometimes females do show signs of the condition due to a process known as 'Lyonisation', whereby one of the two X chromosomes in each cell is non-randomly switched off.

If this leaves the more abnormal X chromosomes switched on, then a woman will show signs of the condition.

Genetic counselling

When a person with restricted growth is born into a family, it is natural to want to know the chances of the condition appearing in other members of the family. Genetic counselling provides information about the nature and recurrence of a disorder and offers help and support to affected people and their families. It involves:

- an accurate diagnosis
- determining the pattern of inheritance and calculating the risks of recurrence in future children
- providing clear, easily understandable information

Genetic counselling is available from one of the Regional Genetic Centres in the UK. A list of centres (many of which are based at major teaching hospitals) is available from the RGA Office. These specialists are there to help you with your concerns. It may be useful to make a list of questions you wish to ask. Do not hesitate to ask for a follow-up visit or information in writing if you find it difficult to absorb all the information at the first visit.

Becoming the expert

Many health professionals have limited knowledge of restricted growth conditions. These conditions are very rare and few health professionals will have come across them before. The RGA is seeking to address this problem through this series of booklets. As well as answering some of your own questions, you may wish to pass copies of this booklet (or other booklets in the series) to professionals who care for you or your child.

Research is ongoing into the genetic basis, the effects and treatment of restricted growth conditions.

Sources of information and support

In the UK the largest organisation for parents, their children and individuals of restricted growth is the Restricted Growth Association. The RGA is a self-help organisation concerned with the welfare of people of restricted growth. Members maintain contact through a magazine, meetings, conferences and social activities. There is a support network for families and medical and practical information is provided. The RGA is also compiling a list of specialists who have expertise in symptoms that are peculiar to restricted growth. Their address is:

Restricted Growth Association
PO Box 8919,
Birmingham, B27 6DQ
Tel & fax: 0121 707 4328
email: RGA1@talk21.com
website: *rgaonline.org.uk*

There are organisations that provide information and support for a particular condition or group of related conditions. These are listed on the insert sheet relevant to those conditions. Most such groups support conditions that are not bone dysplasias. They all provide medical information related to the condition and usually know of specialists with experience of people with the condition. Some groups are large and are able to offer their own social events as well, but many, due to the rarity of the condition, are small but are able to put families and individuals in touch with each other and often have a newsletter.
Other general sources of information are below.

Child Growth Foundation
2 *Mayfield Avenue*, *London* W4 1PW
Tel: 0208 995 0257

Skeletal Dysplasia Group for teaching and research (for medically or scientifically qualified people)
2 *Dale Close*, *Oxford* OX1 1TU

Dwarf Athletic Association
C/o 44 *Middlecroft Road*
Leeds LS10 4QZ
Tel: 01132 703791

Contact a Family
170 *Tottenham Court Road*
London W1T 7HA
Tel: 0207 383 3555
e-mail: *info@cafamily.org.uk*
website: *www.cafamily.org.uk*

Little People of America
website: *www.lpaonline.org* (includes online library and medical links)

List of publications available from the Restricted Growth Association

What is . . .?

Achondroplasia

Hypochondroplasia

Pseudoachondroplasia

SED

Diastrophic Dysplasia

Rarer Syndromes

Lifestyles

Babies and the Early Years

Going to School

Driving a Car

Bikes, Trikes and Ride-on Toys

The Teenage Years

Sporting Opportunities

What Shall I Wear?

Having a Baby

The Later Years

Adoption

Careers, Employment and Education

Limb Surgery

Personal Hygiene

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