FREE

SPRING 2023 | ISSUE 98

Children's Cancer and Leukaemia Group | the EXPERTS in CHILDHOOD CANCER

contact

SUPPORTING FAMILIES THROUGH CHILDHOOD CANCER

MAGAZINE

Rare cancers

What are they? How are they diagnosed, treated and researched?

+

THE IMPORTANCE OF NATIONAL ADVISORY PANELS

+

WHAT IS INHERITED CANCER RISK?

Patient Story

Rugby player Will Jubb, who had retinoblastoma as a child, tells us about the challenges he overcame to become a professional athlete **Page 12**

BACK TO BASICS:

What are rare cancers and how are they treated?

Prof Bernadette Brennan tells us what rare childhood cancers are and how they are treated **Page 10**

WHEN LIFE TURNS FULL CIRCLE

Oscar Oglina, diagnosed with liver cancer as a four-year-old, tells us how his experiences inspired his life and medical career path

Page 6

INSIDE THIS ISSUE... ON RARE CANCERS

Spring 2023

EVERY ISSUE

ON THE COVER

Contact

is a free, quarterly magazine for families of children and young people with cancer.

Contact aims to reduce the sense of isolation many families feel following a diagnosis of childhood cancer.

Children's Cancer and Leukaemia Group brings together childhood cancer professionals to ensure all children receive the best possible treatment and care.

Contact magazine was founded by The Lisa Thaxter Trust and CCLG and first published in 1999.

Past issues of Contact: The wide variety of articles published during the year in Contact adds up to a valuable and informative reference archive. If you would like any back issues, please contact the Editor. Details of key articles in previous editions are listed on our website.

Children's Cancer and Leukaemia Group | the EXPERTS in CHILDHOOD CANCER

www.cclg.org.uk

ChildrensCLG CCLG_UK

KEEP IN TOUCH

Contact Letters,
CCLG, Century House, 24 De Montfort Street, Leicester LE1 7GB

Editor: Claire Shinfield
editor@cclg.org.uk

facebook.com/ChildrensCLG

twitter.com/CCLG_UK

instagram.com/CCLG_UK

Your messages...

From Contact's last edition:

Kind-hearted Ross receives support for plans to help young patients

"Well done, Ross – facing everything head-on and trying to help others in a similar situation. You should be so proud of yourself. Give yourself a pat on the back ⭐"

"Well done, Ross, I can see you being a great help to others."

Read the full story here ▶

CCLG's research webinars providing valuable insight into vital studies

"Great hearing an expert talk about this area in a way that is accessible to parents and survivors."

"Fascinating talk from @drbobphillips and @CCLG_UK about why we research childhood cancer."

"Really fascinating and thought provoking presentation."

Watch our webinars on our YouTube channel ▶

CCLG's research blog shines light on important research

"Excellent storytelling by **@EllieW_CCLG** about how Prof Maureen O'Sullivan's research into malignant rhabdoid tumours (MRT) is greatly improving our understanding of this rare form of childhood cancer."

Read the blog here ▼
www.cclg.org.uk/our-research/research-blog

If you would like to **SHARE YOUR STORY** in Contact or have an idea for a theme for us to cover, please let us know. **Email us at editor@cclg.org.uk**

Hello!

The types of cancers most commonly seen in children are all classed as less common or rare compared to, for example, the four types of cancer that account for almost half of all diagnoses in adults. Within the 1,645 cases of childhood cancer each year, over 900 children are diagnosed with leukaemia and brain & spinal tumours. So, what about the rest? These are broken down into less common cancer types which have far fewer cases per year. Some are even rarer meaning there may not be a proven method of treating them.

This Contact issue explores the implications and challenges of treating less common and rare cancers in children. It's an area where medical and scientific collaboration and knowledge-sharing, both nationally and internationally, play a key part in finding answers on the best way to treat patients.

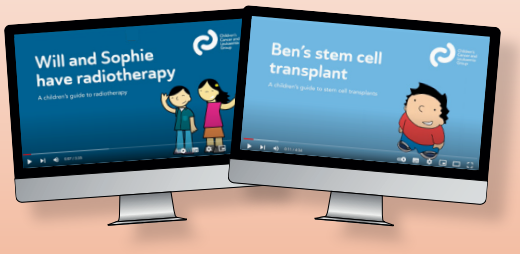
We also say goodbye to our amazing Medical Adviser, Dr Martin English, who is retiring this month. He has been an important part of Contact magazine since it began in 1999 and we will dearly miss his warm and kind manner, wisdom and guidance. Wishing you the very best in your next adventures, Martin!

Dr Martin English receiving a CCLG Member Award at the CCLG Annual Meeting 2023 for his outstanding contribution to Contact magazine and the childhood cancer community.

Claire editor@cclg.org.uk

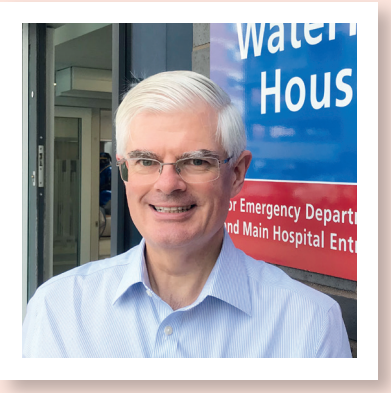
NEW FOR MARCH 2023

Our new animations **'Ben's stem cell transplant'** and **'Will and Sophie have radiotherapy'** have been made to help young children understand these treatments and what might happen.



The films are based on our storybook booklets which have been developed with input from families and our expert members.

www.youtube.com/@ChildCancerCCLG



MEDICAL ADVISER

Dr Martin English

Consultant Paediatric Oncologist at Birmingham Children's Hospital and CCLG member

This is my last column for Contact, as I'm retiring in the Spring. I'd only been a consultant for two years when I started contributing and no way envisaged I'd be involved for more than two decades! Contact has evolved, but it's still a great contemporary source of information: principally for parents of children with cancer and the wider family, but also for a much wider audience.

Looking back over the past 20-plus years, the biggest changes I've seen in paediatric oncology have been due to digitalisation - the internet, electronic notes, connectivity, and knowledge opened up to the many, rather than the few. Treatments have been evolving, and I sense that in the next 20 years new treatment that alters how the immune system interacts with cancer and the ability to identify specific genetic changes unique to each tumour will lead to more individualised care. Change is always happening. If I think back to between the period of me starting medical school and when I became a consultant 17 years later, one of the biggest impacts in children's cancer was the arrival of cross-sectional imaging with CT and MR scans, and evolution of ultrasound. Their impact has continued, but instead of having to send a patient 17 miles to the nearest big city for a CT scan, like when I qualified, most hospitals have CT and MR on site, and even in the middle of the night I can log in from home and look at a scan performed anywhere.

I think we will continue to need the stethoscope, tendon hammer and pen torch even in another 20 years (although I wouldn't be surprised if they could all function as part of a smart phone). However, I'm sure that the most important diagnostic tools and skills will still be listening and observing. Whatever new drugs, operations and treatments may arrive, empathy, compassion and communication, will remain essential.

I was lucky enough to have supportive and helpful senior consultants during my training and similarly fortunate to have had colleagues who are also friends, which meant working in some tremendous teams. I'm heartened by the knowledge that after I retire there will be new colleagues continuing to care - and improve the outcomes - for children with cancer. My thanks go to them all, but most of all to my patients and their families who gave me the privilege of being able to be involved in their care.

NEWS IN BRIEF

Circulating tumour DNA could help inform treatment for Wilms' tumour

Circulating tumour DNA could be used to help decide how high risk a case of Wilms' tumour is, according to Finnish researchers. In Wilms' tumour, circulating tumour DNA is DNA that has come from the cancer cells or tumour, and can be found in blood or urine samples. The research found that most patients had this DNA present, and that it could identify different tumour variants. As this test does not involve surgery, testing for circulating tumour DNA could be a good, non-invasive tool to diagnose and assess patients.

Source: Journal of Clinical Oncology

ADHD medicine could help improve quality of life for childhood brain tumour survivors

Doctors in Newcastle have trialled using an ADHD medicine to treat childhood brain tumour survivors who may face long-term issues with their memory, attention span and processing speed. They found that methylphenidate improved patients' attention and speed of response in tests and had few side effects.

Source: Taylor & Francis Online

Fatigue after cancer treatment could be predicted by tiredness during treatment

Dutch researchers have found that patients who experience fatigue or extreme tiredness during treatment for acute lymphoblastic leukaemia (ALL) are more likely to have cancer-related fatigue at follow-ups post-treatment. The research team wanted to find out what risk factors for ALL patients during treatment were, such as treatment intensity, gender, or age. They found that the only predictive factor was fatigue during treatment, and this knowledge will help highlight children that will require more support when treatment ends.

Source: Springer Link

Essential medicines for childhood cancer in Europe decided

The European Society for Paediatric Oncology (SIOPE) has created a list of medicines used to treat cancer that should be considered essential. This work was needed because across Europe, there are variations in which medicines are available for children due to shortages and unequal access to resources. They defined 66 medicines as essential, which they hope will be used to improve access to them through stakeholders and policymakers.

Source: The Lancet Oncology

Ten brains are better than one – what are national advisory panels?

*National advisory panels (NAPs) advise teams on the best treatments for complicated cancers. **Dr Jessica Bate**, a consultant paediatric oncologist at University Hospital Southampton, explains more and tells us about her recent research evaluating their impact.*

In the UK, multidisciplinary teams (MDTs) are a central part of children's cancer care and are included in the NHS Cancer Plan. All children with a cancer diagnosis have their care reviewed by an MDT at a principal treatment centre, with the team typically including oncologists, surgeons, radiologists and nurses. MDTs can help to make evidence-based treatment decisions, coordinate care and education for team members, improve patient outcomes and increase clinical trial recruitment.

National advisory panels (NAPs)

Over recent years, national advisory panels have arisen, made up of national experts for a specific cancer type. These panels are different from local MDTs. A child's consultant can request personalised advice from these panels - for example, in patients with rare cancers or who have relapsed. There is increasing demand for patients to be discussed at NAPs with more being referred year on year. National guidelines for certain cancer types recommend referral to panels.

NAPs are run on the dedication and goodwill of the NAP chair and panel members, who can include different cancer care professionals. The meetings are attended by the patient's referring consultant, to present their case and relevant clinical information. The patient is then discussed, with recommendations made and shared with the patient's family. The final decisions on how to proceed with treatments are always decided by the referring clinician, in discussion with patients and families.

> "MDTs can help to make evidence-based treatment decisions, coordinate care and education for team members, improve patient outcomes and increase clinical trial recruitment."

Our research

While NAPs clearly fulfil an important role, their remit and impact on patients haven't previously been studied. Based in Southampton, Dr Sarah Brown and I have worked on a CCLG-funded project to formally evaluate these panels and recommend best practice guidelines.

We looked at 920 existing referrals made to six NAPs, who have all discussed hundreds of cases. The evaluation highlighted the time and effort that NAP panel membership entails and the impact the panels have on the management of patients.

We found that doctors followed NAP advice around 90% of the time and, if they didn't, it was usually due to the patient's family and their wishes. Parents don't attend the NAP meetings but do play a huge part in a child's treatment. One of our goals was to help families understand panels' decision-making processes and to find out how best to involve parents in these decisions.

As part of this project, Sarah developed guidelines which set out ways the panels could improve and streamline their process. As part of this, she worked with parent and patient groups, to suggest ways to involve the family in NAP decisions. This included adding fields to the referral form, like whether the patient or their parents were hoping for a particular result, or to avoid a certain treatment.

Other recommendations for NAP best practice included making sure enough members attend meetings to give a fully debated treatment plan, being clear about how and why a recommendation was made and making sure that the referring doctor can represent the patient's views and wishes accurately.

What's next?

For NAPs to be sustainable, there needs to be a strategy to provide support and formal recognition of panel work within job plans. Prior to our project, there were no formal guidelines or standards against which to benchmark the NAPs and no currently established system for review of practice. By producing best practice guidelines, we hope that both existing and new NAPs will utilise them to assess their performance and to drive improvement in children's cancer care.

ON THE COVER

When life turns full circle: Using my experiences to help others

***Dr Oscar Oglina** was diagnosed with stage three liver cancer aged four. Now 24, he tells us how his experiences shaped his life and career path.*

I was diagnosed with cancer back in 2001. My mum had felt a hard lump on my stomach and some abdominal swelling. Unsure about what was going on, she sent me to the GP. A series of referrals sent me from GP to local hospital to Great Ormond Street Hospital (GOSH), where in just 24 hours I was given my cancer diagnosis. My parents were told I had cancer of the liver, hepatoblastoma, that was stage 3 and to be treated as stage 4.

GOSH became my home for the next year as I went through chemotherapy to shrink the size of my cancer, to prepare for a big operation to remove the cancer from my liver. The team there were fantastic. From the doctors and nurses to the surgeons and play specialists, every member of the multi disciplinary team was brilliant, and my parents particularly remember Professor Spitz as my surgeon, who was one of the best surgeons in the world at that time.

Everyone at GOSH was so caring and thoughtful, and brilliant at not only putting me at ease, but my family as well. It's important to remember that as well as myself going through this experience, my wonderful parents were too, and I want to thank them for their support and for being my rocks during this time.

Having experienced all that I had done with my cancer journey, I felt passionately about pursuing a career in healthcare. I knew that I possessed a level of empathy that I could give to patients that I wouldn't have done had I not been through what I had, and this spurred me on throughout school to work hard and earn a place at medical school.

Starting university

In 2016, I was offered a place to study medicine at Bristol University, where I spent the next six years studying and working on placement. My university experience was a fantastic journey and one I'll always cherish. Bristol itself is an incredible city and allowed me to explore the best art, food and music the UK has to offer. It also has much history, and so much to explore.

Academically, my university experience was challenging. My pre-clinical years saw me sit through 30+ hours a week of lectures and labs, a timetable that was drastically unfavourable when compared to that of my non-medic colleagues. I also spent my early medical school years doing classes I never thought I'd do like anatomy class working with cadavers (dead bodies donated to science), which was a crazy thing to become a 'normal' part of your day.

After my pre-clinical preparatory years, I moved into my clinical years going into placement. This period really tested my commitment to medicine as I was on 'outplacement' living out of the city in faraway hospitals, away from friends, but it gave me the opportunity to practise and learn from real-life patients. Despite the challenging times, this was all a sacrifice I was ready to take on when applying myself to this intense course.

Outside of university, I really enjoyed hanging out with friends, keeping active and charity work. One of the biggest things I got involved in was the medical school's charity show that raises money for Young Lives vs Cancer. I started watching the production as a fresher, but left university running the show with my friends, which saw us raise over £60,000 for young people with cancer. This was the most ever raised across the 30-year history of the show, and as someone who had gone through cancer, it felt rewarding to help sick people beyond the remits of a doctor.

My first job in medicine

The summer of 2021 saw me graduate medical school and move to Essex where I was fortunate enough to have a competitive academic job alongside being a clinical doctor. Everyone told me being a doctor is a rollercoaster - it brings the highest of highs and sometimes the lowest of lows and, reflecting on the last eight months, I've so far found that to be true. Despite times of long and unsocial

hours, and days where I'm mentally, physically and emotionally challenged, it's offset by the rewarding moments where I've been able to help people and actively make a difference to someone's life.

I'll always be so grateful to all those at GOSH and I'm fortunate to now work with them on a professional level for various projects and campaigns. Recently, I was lucky enough to pay a visit to the hospital and my old ward. It was surreal returning to a place I was once a patient, as a doctor. It was a true 'full-circle' moment and really reminded me why I'm doing what I'm doing.

My time at GOSH had a really big influence on my thought process and on just how I want to go about life and the things I want to do and, looking back, I think it was there that the seeds of wanting to become a doctor were first really sown. I knew from very early on that I wanted to give back to the NHS and help other children like me, knowing first-hand the difference that can be made.

In sharing my story, I want other young patients to know there is so much to life beyond cancer, and I want children and their families to be empowered in the knowledge that ambitions can be realised, and dreams can be reached!

"My time at GOSH had a really big influence on my thought process and on just how I want to go about life and the things I want to do. Looking back, I think it was there that the seeds of wanting to become a doctor were first really sown."

Overcoming barriers to researching rare tumours

Dr Sara Stoneham is a paediatric oncology consultant at University College London Hospitals. Here, she explains some of the barriers to researching rare tumours and what can be done to overcome them.

Research is the best way to improve outcomes for all children with cancer, but the rate of progress for children with rare cancers is much slower than for more common cancers. For some cancers, there might be fewer than 20 children diagnosed per year in the UK. Not only does this make it difficult to carry out research, but it also makes it difficult to find a funder willing to support a project that may only help a few patients.

The challenge

Rare cancers have less scientific consideration and less financial support to develop better, kinder treatments. For clinical trials to show that a new treatment is effective, it needs to be tested in many patients, to show that any improvement is not down to chance. This is much more difficult when a cancer is rare as there are so many fewer patients that not only have the disease, but also meet the trial's eligibility criteria.

Access to clinical trials is only part of the problem - progress is hampered at almost every stage of research for rare cancers. It can be slowed by drug companies that can be indifferent to developing new drugs for a rare cancer. There is also a shortage of storage facilities for leftover diagnostic samples for future research, meaning we learn less about how these rare cancers behave and what new treatments may be useful to try in the future.

How can we learn to speak the same language and design effective treatment options?

Current initiatives like biobanks, which store cancer tissue and cells left over from diagnostic tests, are an important way to support rare cancer research. By increasing the amount of cancer samples that a researcher can work with, they allow better quality research to be conducted. Biobanks can store samples indefinitely, and research has shown that frozen samples can still be useful over eight years after being stored. However, a more widespread change in the way research is conducted is needed to take treatments from laboratories to patients. Bringing international experts together is an important first step. By thinking differently and taking away barriers that exist between countries and clinical teams, we can re-examine what we think we know.

Sharing data to create an international 'super-database' can create large enough numbers to answer questions that no single country was able to answer before, leading to meaningful change. This may require joint international lobbying of national trial institutions and regulators to help overcome the differences in international law and national ethical frameworks, so we can ensure that all patients' data can be kept confidential, but still put to best use.

If we have consent from patients across the world to use leftover diagnostic samples, combined with cancer genomic data, we can start to answer the questions that have been prioritised jointly by patients, families and researchers.

By designing international trials together, we can identify barriers for each country and learn how to avoid these pitfalls. We can use novel statistical methods that allow us to answer important treatment questions quicker, but while still ensuring robust scientific methods are followed.

International collaborations are more likely to persuade research funders it is worthwhile to support rare cancer research. These collaborations can also increase access to rare cancer expertise by developing expert advisory panels that can make a difference for patients right now by offering specialist advice and most importantly, they can create a forum of like-minded experts, patients and families who share a common goal to improve rare cancer outcomes through meaningful, impactful research.

What happens when doctors find it difficult to diagnose a child's cancer?

***Dr Ren Manias**, Consultant Paediatric Oncologist at Southampton General Hospital, explains what happens and why when doctors find it difficult to diagnose a child's cancer.*

When a child develops cancer, it's important to make an accurate diagnosis so the right treatment can be planned, and to help families understand what to expect from the journey they're about to undertake. In most cases, the history and examination findings, imaging, blood tests and biopsy results fit together to give a clear diagnosis.

However, even straightforward cases can take a few weeks to diagnose and stage accurately, and sometimes diagnosing a child's cancer can be even more difficult, perhaps because the cancer itself is rare, or because some features don't fit the usual pattern we expect to see in certain cancer types. In these cases, making a definitive diagnosis can take time. This can be very stressful for parents and can raise all sorts of questions about treatment and what to expect in the future.

Children's cancer diagnosis has become increasingly sophisticated in recent years. In the past, cancer was simply diagnosed based on imaging, blood tests and histopathology (viewing the tissue down a microscope). But now, other elements are incorporated to further refine the diagnosis and assign specific treatments according to cancer sub-type. These include:

- molecular diagnostics (which analyses the genetic code found in our cells to identify disease)
- cytogenetics (the testing of tissue or blood samples to look for changes in chromosomes that may be a sign of a genetic disease or a type of cancer)
- immunophenotyping (using antibodies to identify cells based on the types of antigens or markers on the surface of the cells to help diagnose certain diseases)

Some types of cancer are diagnosed and sub-classified following central review, which means that biopsies and imaging are sent to national laboratories and panels for expert analysis. This has advantages: treatment can be much more personalised, risk-stratified and targeted, translating to improved survival outcomes with fewer long-term side effects. But it also means it takes longer to gather all the information to form a definitive integrated diagnosis. Sometimes the original diagnosis and treatment plan can even change when all the new information is available.

What happens when a diagnosis takes time?

Your child's consultant oncologist and treatment team will weigh up the benefits and disadvantages of starting treatment based on the most likely diagnosis, while waiting for all the results to come back. This decision will be based on a number of factors. These include:

- how unwell your child is
- whether the cancer is causing problems such as breathing difficulties or compression of vital organs
- how quickly it seems to be growing
- how confident they are that they're right about the type of cancer it's expected to be

In these cases, doctors start 'empirical treatment', based on broad principles about how different cancers tend to respond. The idea is that a broad type of treatment can be given to shrink the tumour (or slow its growth), helping the child to feel better. Then, when the diagnosis is confirmed, this treatment can be refined accordingly, and a definitive specific protocol can be decided.

Diagnosing and treating rare cancers

Sometimes, diagnosis is difficult because a cancer is very rare. Rare cancers are treated with the same treatments used for other childhood cancers, including surgery, radiotherapy and chemotherapy, or these in combination. There are now groups of experts in rare childhood cancers who meet to discuss difficult cases and provide guidance on treatment. Doctors also communicate with colleagues in other countries to develop new forms of treatment and promote research in rare cancers.

National and international collaboration has resulted in significant improvements in care in recent years. However, specific treatment protocols or clinical research trials may not be available for a child's particular tumour due to the small number of children with rare cancers. In this case, oncologists will offer the most appropriate treatment using guidelines agreed by experts, such as CCLG.

Every diagnosis of cancer is different, and it can be especially hard when there's a long journey to reach a diagnosis. Your child's health team will do their best to answer your questions and support you while they determine the best treatment.

What are rare cancers and how are they treated?

Professor Bernadette Brennan, *Consultant Paediatric Oncologist, tells us what rare childhood cancers are and how they are treated.*

What is a rare cancer?

Firstly, we need to put into context what we mean by a 'rare cancer' in childhood. This is because childhood cancers can be seen as rare in the general population accounting for less than 1% of cancers across all ages. The incidence of cancer in children (0–14-year-olds) is currently 1,645 cases per year compared with 375,000 cases per year of all cancers in the UK.

The most common cancers in children are leukaemia, brain tumours and lymphomas, and these have long-established trials and treatment guidance which have evolved over many decades through research and clinical practice. This level of focus has not been available for many rare childhood cancers, therefore there is very little information from prospective trials or collected patient data.

However, we are now seeing more international effort in producing treatment guidance and new registries for rare cancers based on the best available evidence. Therefore, there are now many more resources on how to best treat these cancers.

Types of rare cancers in children

Rare cancers in children can broadly be grouped as:

- rare cancers that only affect children, such as pancreatoblastoma, malignant rhabdoid tumours and melanotic neuroectodermal tumours of infancy
- cancers that usually only affect adults, such as cancers of the digestive system, the thyroid and the adrenal gland
- rare cancers in the head and neck area, such as nasopharyngeal cancer
- rare hormonal or endocrine cancers, such as phaeochromocytoma
- rare brain tumours, such as meningioma
- rare skin cancers, such as melanomas

Causes

The causes of most rare childhood cancers are unknown. But, if other family members have had particular types of cancer, this may sometimes suggest there is an inherited faulty gene within the family.

Rare cancers that only occur in childhood

Some rare cancers only occur in childhood, a good example of which are malignant rhabdoid tumours. Much work has been done in this cancer over the last 10 years to find out more about its specific cells, pattern of disease and tumour site. By collaborating internationally, more prospective trials and establishment of international guidance and registries have developed. Patients have also benefited from drug trials with specific targeted drugs with remarkable responses giving hope for

future trials and better outcomes.

This particular type of rare cancer lends itself to the concept of 'ask an expert'. This means that if a medical team is unsure on how to manage a patient with a rare tumour, there is always a wide network of UK and international experts who can be consulted. CCLG has led the national effort to produce clinical treatment guidelines for the diagnosis and management of over 20 rare cancers, which are regularly reviewed and updated. This network of experts has much clinical experience in the management of these rare cancers and indeed providing guidance in their management.

Importantly, in the UK we have the National Cancer and Registration and Analysis Service (NCRAS) which records the incidence, survival, prevalence and mortality for all cancers in childhood, and hence provides the baseline data for building these CCLG consensus guidelines. It also gives encouraging data so that the survival of children with melanoma, as an example, is over 90%. Internationally, the EXPeRT group of European countries including the UK has produced consensus guidelines for rare cancers, implemented a website (raretumours-children.eu) and have established a virtual tumour board (VTB) to help medical teams discuss the best management of patients with a rare cancer. This VTB has been established in an international setting that includes experts with outstanding expertise. Lastly, they have produced patient information which is freely available about rare cancers on their website so parents and patients can understand better.

Rare childhood cancers that commonly occur in adults

Many adult cancers occur very infrequently in children as these are often related to age and lifestyle factors such as diet, smoking and sun exposure. Good examples are bowel cancer and a type of skin cancer called melanoma. If a child is diagnosed with a cancer usually seen in adults, the management of these tumours is often guided by adult clinical practice and evidence. However, these cancers are biologically different in children, behave differently and, while environmental factors play a definite role in the development of these cancers in adults, the timelines are too short in children so genetic factors may be important – not necessarily inherited but a new genetic change within the cells of the child with cancer.

Like other cancers in childhood, if a child is diagnosed with a particular type of rare cancer then this can be a defining indicator of a genetic condition, either inherited or only happening in the child. A good example is a type of adrenal gland cancer called 'phaeochromocytoma' which, even if there is no family history of other cancers in family members, indicates a referral to the genetics team. This is important as if an underlying genetic cause is found, this could lead to a set of screening studies to detect other cancers at an early stage and hence successful treatment.

An example of an adult cancer rarely occurring in children is melanoma, which can happen in children with an abnormal mole and usually behaves less aggressively than melanomas occurring in adults. They are usually managed with surgery after which there is surveillance only. In adults, melanoma needs more invasive treatment as it spreads more easily.

Final message

A rare cancer diagnosis in a child can cause much distress for the child and family as there is often a perception that if it is rare then no one knows how to treat it, and the child will do badly. We now know this is untrue, and much effort and success has happened over the last 10 years to provide national and international consensus on their management.

This network of experts within the paediatric oncology community means we now have lots of advice and support on how to treat children with rare cancers.

> We are now seeing more international effort in producing treatment guidance and new registries for rare cancers based on the best available evidence. Therefore, there are now many more resources on how to best treat these cancers.

I want to inspire young people to reach for their dreams

Will Jubb

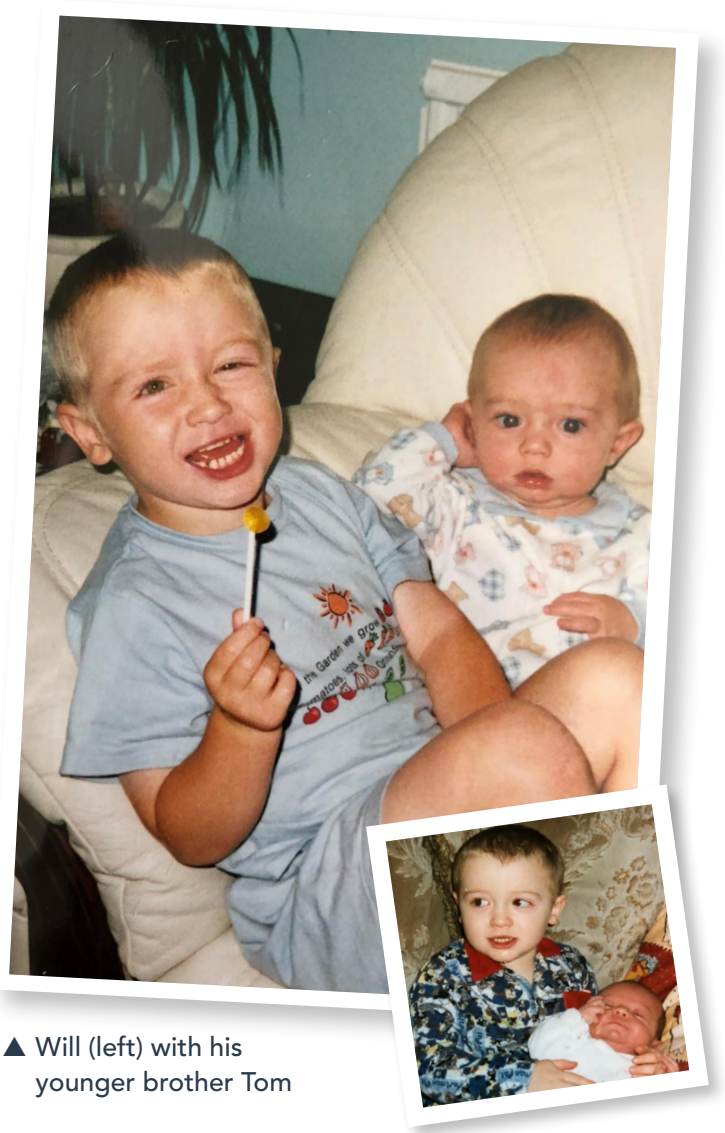
***Will Jubb** was two years old when diagnosed with eye cancer in 1999. Now 26, he tells us about the challenges he overcame to become a professional rugby player and how he hopes that he can inspire others.*

My cancer journey began when I was two years old, when my mum noticed that my right eye flashed white instead of red when having my picture taken. Worried that something wasn't right, she took me to the opticians and from there I was rushed to hospital for further checks, before being diagnosed with retinoblastoma. I subsequently had to have my right eye removed at St Bartholomew's Hospital in London and even after the operation I still had to return to London every month until I was five, to ensure that the cancer hadn't returned.

My younger brother, who was only two weeks old when I had my eye removed, also had to have checks at the same time as me to see whether he also had the cancer. This was obviously a very traumatic experience for me, my brother and the whole family, but especially my parents, as me and my brother were both so young that neither of us can really remember anything. Thankfully, all checks for both of us were clear and it was also found that the cancer wasn't hereditary.

Despite me only having one eye, my dad was adamant that it wouldn't hold me back and allowed me to do anything I wanted to. For as far back as I can remember, I was playing with different bats and balls with my dad and brother and have played every sport you can think of. I genuinely believe that doing this allowed me to adapt to having one eye and being so young at the time, I can't remember anything different, which also helped.

While trying all these different sports, it became increasingly apparent that rugby was my favourite. However, owing to the game's physical nature, my family had already been quite apprehensive about me playing it. I know they had a lot of difficult conversations, but I'm eternally grateful that they allowed me to try any sport or activity I wanted, and especially my dad for making sure I had the opportunity.



▲ Will (left) with his younger brother Tom

My journey to professional sports

I began playing rugby at Hull Wyke rugby league club when I was 10 years old. Having helped my dad when he was coaching my younger brother's team, I decided one day that I wanted to have a go myself. After a few years, I was selected for a scholarship with Hull Kingston Rovers and went on to represent the club's academy and first team. I made my debut for the first team in 2016 away at London Broncos and even managed to score. During my second year with them, I was sent out on loan to York City Knights to gain some more first team playing experience. From that first moment in 2017, I absolutely loved my time there and felt like it was the best place for me to develop and enjoy my time playing. I joined permanently in 2018 and have been at York ever since. I have had some fantastic experiences and gained many great memories throughout my time with the club, including playing at Wembley.

Learning to play rugby presented certain challenges, which meant I had to adapt in order to compete. This involved learning to turn my head more to one side to be able to see and how to protect myself in certain situations. This took time and some painful lessons, but as I progressed through the ages and ranks, I was able to pick things up from other players and learn from them, especially when I began playing with seasoned professionals. As I gained more experience, I had a better understanding of what I had to do to perform effectively and became better at protecting myself. I'm still always open to learning new skills and techniques, which I see as one of my best attributes. You never finish learning, and I'm always looking to better myself.

Giving back

Due to my association with York, I was lucky enough to be introduced to a Wilberforce Trust charity called Club Wilber, who had contacted the club after hearing my story. The charity supports children with visual impairments but is unique in that it provides activities for the whole family. As soon as I heard about the work it does, I was keen to get involved. I was honoured to be asked to be an ambassador for Club Wilber and first met with all the team at its launch night in early 2020. The COVID pandemic meant that I was unable to get involved too much until restrictions eased, but once that happened, I was able to meet the children and their families and help with activities.

They have such an amazing time and being able to help with that is priceless. It's also been a great honour to have some of those the charity supports at York City Knights games and allow them on the pitch afterwards for pictures. They're an inspiration to me and if knowing that I play rugby inspires them a fraction of how much they inspire me, then I'll be extremely happy.

If I could offer one piece of advice to anyone in a similar position to myself, it's possible to do anything you want to do and achieve what you set out to if you put your mind to it and work hard enough. I've never considered myself as any different to anybody else, and my competitive nature has meant that I have always wanted to be the best and endeavoured for perfection. I'm able to play a sport that I love and have achieved what I have wanted to achieve (I've also just completed a PhD in Fisheries Management) and hopefully others will be inspired by this to chase their own dreams, too.

How we tripled survival and reduced toxicity for children with liver cancer

Dr Peppy Brock is a retired consultant paediatric oncologist. She explains how a dedicated international group of medical professionals helped improve survival and reduce toxicity for a very rare type of childhood cancer.

Dr Peppy Brock

There are around 20 cases of liver cancer in children per year in the UK, the commonest type being hepatoblastoma (HB), localised to the liver. Children with localised HB have an average age of 13 months at diagnosis. Even though this cancer is rare, the rate of children now surviving this type of cancer is greater than 90% compared to around 30% during the 1970s. This is the result of international collaboration, clinical trials and knowledge-sharing over many years through an expert group called SIOPEL.

I was lucky enough to do a research fellowship at Great Ormond Street Hospital in the late 1980s to look at a new chemotherapy drug called cisplatin. It was being combined with another drug called doxorubicin and surgery to treat paediatric liver cancer. The initial results of this combination were so encouraging that a small, international group of medics met and formed SIOPEL – a specialist liver tumour group – in 1987.

What we wanted to do

We wanted to foster international collaboration, and to design and run clinical trials specifically for children with liver cancer. It was exciting as this collaboration enabled more children to enter clinical trials, bringing answers to research questions in a reasonable timeframe.

The introduction of the MRI scanner also brought in clearer images of the liver. I remember being called down to the radiology department to look at the first MRI images of a child with liver cancer. Using these highly defined scan images, we established the pre-treatment extent of disease - PRETEXT system - which described the extent of the tumour across the four surgical sectors of the liver. Depending on how many sectors were involved, we grouped the tumours into PRETEXT I, II, III and IV permitting an image defined accurate analysis of the tumour at diagnosis.

Our impact

Before SIOPEL, liver cancer was staged and treated with surgery alone and only around 30% of children survived. The first SIOPEL trial, which introduced initial chemotherapy, followed by surgery and then more chemotherapy, increased the survival rate to approximately 70% for children with all types of liver cancer. Around 40 countries worldwide participated in this trial, with the study being run from CCLG in Leicester and funded by Cancer Research UK. The PRETEXT analysis from SIOPEL 1 validated the PRETEXT system as being prognostic, where the lower the PRETEXT at diagnosis the better the survival chances of the child.

Further SIOPEL studies mainly focused on the commoner form of liver cancer, hepatoblastoma (HB). Patients were grouped according to PRETEXT – those with standard-risk disease (SR PRETEXT I, II and III) and those with high-risk disease (HR PRETEXT IV) and/or with disease that had spread to the lungs (metastatic). Children with high-risk (HR) disease were treated with more intense treatment. The survival rate for children with metastatic disease increased from 0% to more than 50%. In children with standard-risk (SR) disease the treatment was made less toxic. SIOPEL 3 eliminated doxorubicin which is toxic for the heart.

By SIOPEL 6, over 90% of children with SR-HB were being cured with cisplatin and surgery. However, approximately 60% of children were being left with permanent hearing loss in both ears from the cisplatin. The trial centre had moved to Birmingham, I had been appointed principal investigator and like other SIOPEL trials we had funding from Cancer Research UK. SIOPEL 6 trialled sodium thiosulfate (STS), a drug pre-clinically tested in Portland, Oregon, and showed that STS could reduce cisplatin-induced hearing loss by 50%. STS was subsequently licensed, as Pedmark®, in the US for all children with localised cancer. It will soon be licensed in Europe. STS is currently available in the UK on compassionate grounds.

Today, SIOPEL is still a thriving, pioneering research group and new breakthroughs are continuously being sought to help all children diagnosed with liver cancer.

▲ Peppy and SIOPEL colleagues

A parent's view...

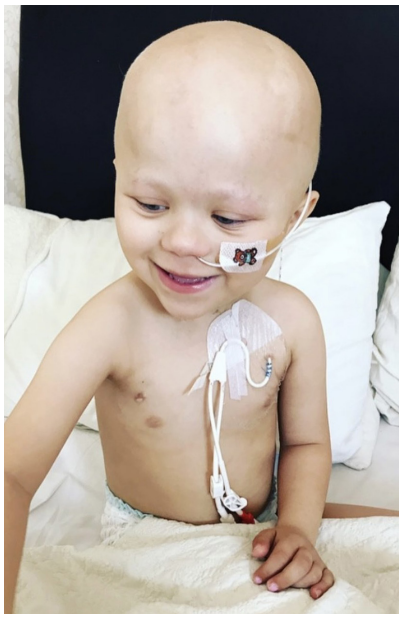
Holding on to hope after a cancer diagnosis

Jemma Smith's son **Freddie** was diagnosed with a germ cell tumour in September 2017. She tells us about the support they received and offers advice to other families after a cancer diagnosis.

Jemma, with her husband Gareth, Freddie (right) and Freddie's brother Buddy

Our little boy Freddie was born a healthy, happy baby boy, but when he reached his second birthday, things started to change. Freddie was checked out a few times, but each time it was put down to general childhood ailments, such as constipation. He then developed a limp and our local hospital referred Freddie for an MRI scan at Birmingham Children's Hospital.

Following the scan, it came as a crushing, heart-breaking shock to find out that Freddie had a 10cm tumour on the base of his spine, which had spread to his liver and bones. He was diagnosed with a stage 4 germ cell tumour and the following morning, his central line was inserted and chemotherapy began. It all happened so fast but, as frightened as we were, we were just so grateful for how quickly everyone at the hospital was acting. We were also hugely appreciative for the compassion and care that Freddie's medical team were providing, to both him and us as a family.



After six rounds of chemotherapy, Freddie needed surgery to remove the remaining tumour and take away his coccyx and several lymph nodes. He recovered quite quickly and was back home within four days. That same month, Freddie rang the end of treatment bell, something we had aimed for during those long, dark days of Freddie's treatment.

> "Keep looking to the next step and celebrate every achievement, no matter how small."

Unfortunately, eight months after finishing treatment in January 2019, when he was three-and-a-half years old, Freddie relapsed to his lungs. This came as another huge blow. He went back into treatment and was given a harsher chemotherapy programme to follow. This was extremely tough on Freddie's body, and we felt so helpless. Thankfully, we were supported by the hospital, friends and family, who helped us through to the end of Freddie's treatment, when once again he rang the bell with pride.

Freddie is now aged seven-and-a-half and is three years on from his treatment. Unfortunately, due to where the tumour was situated on the spine, he has suffered from nerve damage. His mobility has been affected and he suffers with pain and needs daily medication. However, he's determined to live life to the max and doesn't let much get in his way.

He enjoys school, swimming lessons, going to friend's houses for tea - just 'normal' things that all children should experience. We don't take these things for granted anymore, but instead, they're all seen as a milestone in our house.

My advice to any family suffering a cancer diagnosis is to dig deep, keep looking to the next step and celebrate every achievement, no matter how small. Also take the help and support you are offered from loved ones - they may also feel helpless and want to help you in any way they can. And lastly, remember to hold on to hope.

Sharing knowledge and best practices: Starting blocks for progress and innovation

The European Society for Paediatric Oncology (SIOP Europe) is the only pan-European organisation representing all professionals working in the field of childhood cancers. ***Annika Strasser****, SIOP Europe Communication and Marketing Coordinator, tells us about how it fosters partnerships that are helping to push progress across international boundaries.*

With more than 2,500 members across 35 countries, SIOP Europe has been leading the way to ensure the best possible care and outcomes for all childhood cancer patients and survivors in Europe for the past 25 years. Our mission is to cure more children and to cure them better - and we won't stop until the job is done. Many of the issues at stake for SIOP Europe are similar to those of general rare disease organisations, such as:

- the development of new therapies and treatments
- difficulties finding clinical expertise & accessing appropriate treatments
- difficulties carrying out clinical studies due to the small number of patients
- insufficient medical training on each specific disease area
- the quality of survivorship due to late effects of treatment
- lack of information among the general public

Collaboration is key

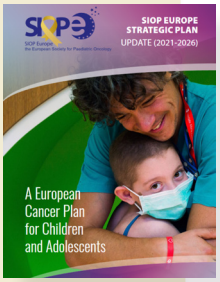
At SIOP Europe, we believe partnerships are fundamental for innovation and progress that will benefit both the professionals who deliver care as well as the childhood cancer patients and families who receive care. To identify and understand the most pressing issues, SIOP Europe collaborates with several rare disease advocates, using the information gleaned to raise awareness and engage in advocacy activities at European level. This is indispensable to placing the issue of rare cancers firmly on the European policy agenda, and to identify and promote appropriate solutions and exchange best practices. We also work closely with Childhood Cancer International - Europe, bridging any gaps between childhood cancer patients and professional communities.

As a result of these activities, SIOP Europe is involved in many projects, such as ERN PaedCan, EU Network of Youth Cancer Survivors, SmartCARE, QUARTET and the Access to Medicines Project, to name just a few. Together, these projects address specific needs covering the entire childhood cancer spectrum ranging from drug research and development to delivery of care and all the way up to patient-centred survivorship care to improve quality, effectiveness, cost-effectiveness and accessibility for survivors and caregivers.

The common denominators of our projects are fostering innovation and progress and sharing best practices and knowledge through collaboration and cooperation at an international level.

To further complement these activities, SIOP Europe also coordinates several working groups that address specific areas of care and research for the benefit of children and young people with cancer in Europe and works together with other organisations to offer continuing medical education to paediatric oncology professionals.

The SIOP Europe Strategic Plan Update (2021-2026) focuses on several key areas that will move us towards achieving our mission, including:



1) addressing inequalities
2) precision medicine and treatment innovation
3) tumour biology
4) teenagers and young adults
5) quality of survivorship
6) causes of cancer
7) big data and artificial intelligence

FOR MORE INFORMATION ABOUT SIOP EUROPE:

www.siope.eu/eu

office@siope.eu

Using super-fit immune cells to seek and destroy bone cancer

- **PROJECT TITLE:** Delivering γδ T cells (gamma delta T cells) for osteosarcoma immunotherapy
- **LEAD INVESTIGATOR:** Dr Jonathan Fisher
- **PROJECT TEAM MEMBER:** Alba Southern, PhD student
- **INSTITUTION:** University College London (UCL)
- **AMOUNT AWARDED:** Approx. £245,000 (funded by The Little Princess Trust in partnership with CCLG)

▲ Alba Southern and Dr Johnathan Fisher

Osteosarcoma is an aggressive cancer that usually affects bones in teenagers and young adults. Patients need gruelling chemotherapy, radiotherapy and surgery that can drastically affect quality of life, both during and after treatment. Current therapies don't only attack the osteosarcoma cells and so there are a lot of side effects which often require time out of school and studies, making a big impact to patients' lives. Sadly, even with current treatments, osteosarcoma often spreads to the lungs and comes back after treatment has finished.

Here at the Fisher Lab at UCL, we are trying to find a better treatment that specifically attacks osteosarcoma cells, to better fight the cancer and reduce the burden of side effects. We think that immunotherapy could be the right treatment because it trains cells from the immune system, called T cells, to fight cancer and has been very successful in other cancers.

However, immunotherapy doesn't currently work for osteosarcoma - we think this is because the immune cells can't find the tumour or are too worn out when they get to it. We want to make a new type of T cells that will seek out osteosarcoma and remain strong enough to fight it. My lab is focusing on immune cells called gamma delta T cells, which we're using to create a new type of immunotherapy.

Testing the treatment

It's important to test the new immunotherapy in a realistic setup. Researchers have found that 3D models of cancer show how the disease may behave much better than 2D layers of cells grown on plastic. Therefore, we needed to develop a 3D model of osteosarcoma that mimicked the cancer's normal environment inside bones.

In collaboration with researchers from UCL and the Italian Istituto Ortopedico Rizzoli, we created a 3D model similar to bone tissue, using osteosarcoma cells embedded in high-density collagen. This is more realistic and makes it much harder for immune cells to get to the cancer cells.

To see whether our T cells worked, we labelled the cancer cells and T cells with different colours that glow under fluorescent lights. Through the microscope, this showed that our T cells can not only penetrate the dense collagen surrounding osteosarcoma, but also can find and kill the cancer cells in the 3D models.

Presently, this 'seek and destroy' process requires extra medicines, but we want to enhance the T-cells so that they can work without additional drugs.

What's the impact?

This project also gives us a fantastic opportunity to share our knowledge, raise awareness of osteosarcoma and talk to young people about their research priorities. Through our Patient/Public Engagement group we have shared our results with osteosarcoma survivors.

Patient representative Melissa said: "Osteosarcoma patients have had the same treatments and the same survival statistics for decades. As patients, we want more tools in the fight against this disease, and this new treatment option could offer a better chance at long-term survival for those of us living with osteosarcoma."

We hope that, by continuing to improve the T cells' fitness and their ability to find cancer, they will be better at seeking out, and fighting, osteosarcoma.

The lessons learned from this project are not limited to osteosarcoma - we hope to apply them to other cancer types in the future.

www.cclg.org.uk/our-research-projects

www.fisher-labs.com

60 SECONDS WITH

Dr Madhumita Dandapani

Consultant Paediatric Oncologist at Queen's Medical Centre, Nottingham

Q: Tell us about your career so far?

A: I was born and raised in Chennai in South India, qualifying as a doctor from the Christian Medical College in Vellore, Tamil Nadu, before coming to the UK in 2002. I trained in hospitals in England, Wales and Scotland, and became a consultant in 2016. I also obtained a PhD in cancer metabolism from the University of Dundee in 2013 and have since done research alongside clinical work, spending half my time studying rare cancers.

Q: Tell us about your role?

A: As an oncologist, I lead and facilitate the care of children and young people with cancer from diagnosis and treatment to follow-up as well as long-term survivorship. I specialise in treating children with solid tumours and brain tumours.

Q: Did you always want to be involved in childhood cancer care?

A: I always wanted to be a paediatrician and as I went through training, I decided to train in a research-driven speciality. I spent six months on the oncology ward and realised that the team looking after children with cancer have a multi-disciplinary approach, guided by research, and deliver compassionate, holistic care centred around the young person. I haven't looked back since.

Q: What's the most rewarding thing about your job?

A: It's a privilege to be able to help and support the children and young people I look after and I really enjoy getting to know and find out more about them, whether that's their interests in sport, music or film, the games they like to play, or what their pets are called.

Q: What are the biggest challenges?

A: The biggest challenge in my opinion is striking a balance between cure and long-term side effects from treatments. We need more effective treatments for hard-to-treat cancers. At the same time, we also need kinder treatments so that children and young people live well, once cured.

Q: Why are rare and hard-to-treat cancers so important to you?

A: Some cancers are as rare as one in a million. It takes international collaboration to research and carry out clinical trials in rare disease. I believe that every child deserves the best available treatment driven by research and we mustn't use rarity as an excuse to not develop treatments for these children. And, understanding rare cancers could lead to new treatments that could be used in other cancers or diseases.

Q: What are your research interests, and what area of your work excites you most?

A: My research interest is in cancer metabolism, which is to understand what nutrients are specifically needed to help cancers grow and to develop treatments that selectively block these and therefore only kill the cancer cells. I'm particularly interested in liver and brain tumours as they're the two types of cells that are metabolically most active.

Q: What's the proudest moment of your career so far?

A: Establishing my own research group focused on cancer metabolism four years ago. Over the last few years, we've identified novel alterations in nutrient uptake by cancer cells, and we're in the process of testing the effects of interfering with these processes in the lab. If successful, some of these panels could be used to monitor response to treatment. We could also potentially develop new treatments in the future.

Q: Do you have a message for children and their families affected by childhood cancer?

A: Every child is unique and clinicians and researchers are continuously developing tailored treatments that can be personalised to improve outcomes. This work wouldn't be possible without the generosity and altruism that children and families show in donating tissue for research and participating in clinical trials.

ASK THE

Expert

Dr Ren Manias, Consultant Paediatric Oncologist at Southampton General Hospital, and Contact's medical adviser

What is inherited cancer risk?

Cancer predisposition syndromes are rare conditions that result from genetic mutations that increase the chance of developing cancer compared to the risk for the general population. In these conditions, genetic traits or mutations are passed from parents to children, so several close relatives may be affected. Depending on the specific mutation, hereditary cancer may increase a person's risk of developing a specific type of cancer, cancer at an early age, or multiple types of cancer.

How common are hereditary cancers?

About 10% of children with cancer have an inherited mutation that increases their risk of cancer. If your child's cancer is thought to be related to an inherited mutation, your consultant will talk to you about the gene it affects, what type of mutation it is, and whether there is a chance that other family members may also have that gene.

What are the most common cancer predisposition syndromes and what types of cancer do they cause?

- **Fanconi anaemia:** A disease that prevents bone marrow from making enough new blood cells. Fanconi anaemia increases a person's risk of developing several types of cancer, including acute myeloid leukaemia (AML) and squamous cell carcinoma
- **Xeroderma pigmentosum:** Causes extreme sensitivity to sunlight, leading to a high risk of developing skin cancer
- **Li-Fraumeni syndrome:** An inherited genetic predisposition to multiple types of cancer, which increases a person's risk of developing cancer at any age. This condition commonly leads to cancer in the brain, bones, soft tissue, blood and breasts
- **DICER1 syndrome**: A mutation in the DICER1 gene that increases a person's chance of developing tumours in the lungs, kidneys, ovaries and thyroid
- **Neurofibromatosis type 1:** Causes changes in skin colour, non-cancerous tumours and cancerous peripheral nerve sheath tumours. It also increases a person's risk of developing brain tumours and blood cancers
- **Down's syndrome:** Children with Down's syndrome have a higher risk of developing blood cancers like acute lymphoblastic leukaemia (ALL) and acute myeloid leukaemia (AML) but are less likely to develop solid tumours
- **Hereditary retinoblastoma:** Mutations in the RB1 gene lead to retinoblastoma (an eye cancer that usually develops in the first five years of life) and increased risk of other types of cancer in later life, including common adult cancers and sarcomas

What happens if there is a concern your child's cancer is inherited?

If there's a concern that your child's cancer is inherited, your consultant will talk to you about genetic testing and refer you to a geneticist for counselling. Genetic testing is usually done initially by testing the child who has cancer, by examining a sample of blood to see if there's a mutation.

We sometimes do something called multigene panel testing to look at the DNA of several related cancer genes at the same time. If a mutation is found, we can discuss the implications and offer to test other family members to see if they have it too.

Have a question to ask one of our experts?

Please get in touch by emailing **info@cclg.org.uk** or via DM on our social channels.

Teenagers and Young Adults with Cancer

HELP US FUND THE ANSWERS

Researching the important questions in young people's cancer

Find a fundraising event near you, or organise your own!

#FUNDTHEANSWERS

TYACancerOrg

TYACancerOrg TYACancerPro

www.tyac.org.uk

Children's Cancer and Leukaemia Group | the EXPERTS in CHILDHOOD CANCER

www.cclg.org.uk ChildrensCLG CCLG_UK

Century House, 24 De Montfort Street, Leicester LE1 7GB • 0333 050 7654 • Email: info@cclg.org.uk