

Niemann-Pick type C disease: Journey to Diagnosis

A Patient Report



Introduction

Niemann-Pick type C disease (NP-C) is a rare genetic, progressive neurological disease. It is caused by the accumulation of certain lipids (fatty molecules) in several tissues in the body, for example, in nerve cells, particularly in the brain. The rarity of the disease, only one in 120,000 people is affected, along with the wide range and timing of symptoms means that NP-C can go undetected for many years. The lack of awareness of the condition and its symptoms means that the journey to diagnosis may involve many different specialists who may fail to link these symptoms together.

This report draws together the results of a much-needed piece of research among NP-C patients and their families. The interviews conducted with parents and carers of patients with NP-C provide an insight into their experience of the journey to diagnosis, the physical and emotional impact that this can have on families and the importance of support before, during and after receiving a diagnosis of NP-C.

A panel of healthcare and patient support professionals, all highly experienced in the field of NP-C, were consulted to guide the research contained within this report. Here, the panel introduce themselves and explain why they believe the findings from this report are so important and how these results could help improve future experiences for patients with NP-C.



Finally getting the right diagnosis was like sunshine, we have actually got that light at the end of the tunnel.

Parent, UK

Forewords



Hans Klünemann, MD PhD

Professor of Psychiatry, University of Regensburg School of Medicine, Germany

I saw my first patient with NP-C in a memory disorders clinic in 1996. She was in her mid-forties and was referred with a diagnosis of possible Alzheimer's disease. I am certain that NP-C is often undiagnosed in adult psychiatric patients. Educating physicians about NP-C will be extremely beneficial in terms of accessing treatments for these patients.



Frits Wijburg

Metabolic Pediatrician and Professor at the Academic Medical Center in Amsterdam, The Netherlands

During my career in metabolic diseases I have seen many patients with different metabolic disorders and I have learnt that NP-C is not only one of the more severe disorders but unfortunately also one of the most difficult to diagnose. Improving early clinical recognition is key and will decrease the often lengthy diagnostic odyssey by allowing for timely diagnosis. This report clearly shows the importance of this.



Jackie Imrie

Clinical Nurse Specialist, Niemann-Pick diseases (UK)

Having been actively involved with families with Niemann-Pick disease for over a decade I felt I had a lot of insight that I could offer the steering group. The survey results document what myself, other professionals and families have been saying for many years and hopefully we can act on these concrete findings. Not all families want contact with support groups but we need to be able to offer something to support them to suit their needs. We need to have professionals and families working together to raise awareness of Niemann-Pick disease and hopefully decrease the time to diagnosis for most families.



Bruno Bembi

Pediatrician and Geneticist, Director of Regional Coordinator Centre for Rare Diseases, University Hospital 'Santa Maria della Misericordia', Italy

Rare diseases are often under diagnosed and under managed. This is particularly the case in NP-C, where patient presentations are not homogenous. That is why it is so important to educate healthcare professionals and parents about the course of this disease and the impact on patients and families of a long journey to diagnosis. Hopefully this report will play an important role in educating and increasing understanding of NP-C.



Jim Green

*Chairman, Niemann-Pick Disease Group (UK), NPDG (UK)
Co-ordinator, International Niemann-Pick Disease Alliance, (INPDA)*

The collation and distribution of a patient survey for Niemann-Pick type C disease is something that has been needed for a long time. As someone who has been involved with this disease for 20 years I believe this report will help patients and their families feel less isolated by recognizing the issues they face. I believe too that it clearly outlines the reasons why professionals and support networks should explore all possible ways of working together in order to provide improved diagnosis, treatment and support. I am particularly pleased that the report recognizes that the issues raised are universal and unaffected by national boundaries. I hope that wherever the survey is read it will improve understanding and in so doing help those living with and managing this disease.



Sergio Vidal

Patron and member of the medical committee of the Spanish Niemann-Pick Foundation (Fundación Niemann Pick de España)

I wished to have the opportunity of sharing my personal experience as an active member of the support organization and primarily, as a father of a child with NP-C. NP-C affects patients worldwide with the same emotional and physical impact, as highlighted in the report. This survey is very important as it is the first time that the reality of the disease known by patient organizations, NP-C patients and relatives will be collated and presented as a report. Healthcare professionals need to use this knowledge to educate themselves and others about the disease, the symptoms of the disease, how we can achieve an early diagnosis and the benefit of an early diagnosis. For patient and carers this report highlights the importance of receiving a diagnosis and the role that the patient organization can play in supporting the patient and their family.

What is Niemann-Pick type C disease?

Niemann-Pick type C disease (NP-C) is a rare genetic disorder with progressive neurological symptoms caused by the accumulation of certain lipids (fatty molecules) in harmful quantities within cells throughout the body. This is particularly important within nerve cells, particularly in the brain, however, early symptoms generally only affect the liver and spleen (see Table 1).

Non-neurological symptoms	Neurological symptoms
Enlarged liver (hepatomegaly)	Eye movement problems (vertical supranuclear gaze palsy)
Jaundice in newborns	Balance disorders (ataxia)
Enlarged spleen (splenomegaly)	Problems with information processing or memory (cognitive dysfunction)
	Difficulty swallowing (dysphagia)
	Slurred and irregular speech (dysarthria)
	Sustained muscle contraction (dystonia)
	Episodes of sudden muscular weakness (gelastic cataplexy)

Table 1. Understanding the technical terms for symptoms of NP-C^{1,2}

NP-C is a condition that is characterized by a wide range of neurological symptoms that increase in both severity and effect on quality of life in the late stages of the disease. The rate at which the disease develops varies greatly from patient to patient. Symptoms vary and may include some or all of the following: eye movement problems, slurred and irregular speech, balance disorders, difficulty swallowing, involuntary sustained muscle contraction, seizures, problems with memory or processing information which finally may lead to full dementia.^{1,2} It is an inherited disease that may appear in young infants or not until late adulthood. Typically, it presents in mid-to-late childhood, with a child appearing clumsy and experiencing frequent falls.^{1,2}

Who is affected by NP-C?

It is estimated that NP-C affects approximately 1 in 120,000 people in Western Europe;³ however, this is likely to be an underestimate due to the wide range of symptoms meaning the disease can often go undetected.¹

What are the causes of NP-C?

NP-C is an inherited condition, which occurs when both parents are carriers of a defective NP-C gene (autosomal recessive inheritance*). Carriers have one 'normal' and one defective NP-C gene and are symptom-free. With this type of inherited disease, there is a 25% chance that each child of parents who both carry the defective NP-C gene will develop NP-C and display the symptoms. There is a 50% chance that a child will be unaffected by the disease but be a carrier of a defective gene and possibly pass that gene (not the disease) on to their children in the future (see Figure 1 on page 5).

How is NP-C diagnosed?

Diagnosis of NP-C is not straightforward. The disease is rare and there is a wide range of symptoms; in some patients, initially there are only a few, mild symptoms. As a result, NP-C can often be misdiagnosed or may go unnoticed for many years.¹ A definite diagnosis of NP-C requires complicated tests and these can only be carried out at a limited number of specialist centers. Fortunately, there are new diagnostic tests in development which could make it easier to diagnose NP-C in the future. Current laboratory tests used to confirm a diagnosis of NP-C may include:¹

- A skin biopsy to obtain tissue cells that are then cultivated for several weeks to demonstrate the accumulation of fatty molecules within a cell
- DNA tests to look for affected genes (mutations), that cause NP-C

**Autosomal recessive inheritance is a pattern of genetic inheritance where two defective genes are needed to cause the disease*

How is NP-C managed?

There is no cure for NP-C and, until recently, management has focused on the treatment of individual symptoms and supportive care. For example, anti-epilepsy medication for seizures, anti-cholinergic medication for problems with muscle movement, antidepressants for sudden weakness or muscular collapse and physical therapy to help maintain mobility.^{1,2} Patients and their carers also need to be aware of the possibility of secondary complications, such as chest infections or severe constipation developing, so that they can help to prevent them.² There is now also an NP-C specific treatment available to help manage neurological symptoms of the disease.⁴

How does NP-C affect quality of life?

NP-C has an enormous impact on the quality of life of patients and their families and carers. For patients, NP-C can affect both schooling and work.¹ The progressive nature of the disease (gradual decline) means that children increasingly perform poorly at school and eventually experience difficulties joining in with recreational and social activities. For adults, the ability to work or drive will eventually be severely restricted and, as they lose their independence, their reliance on family members for support greatly increases.

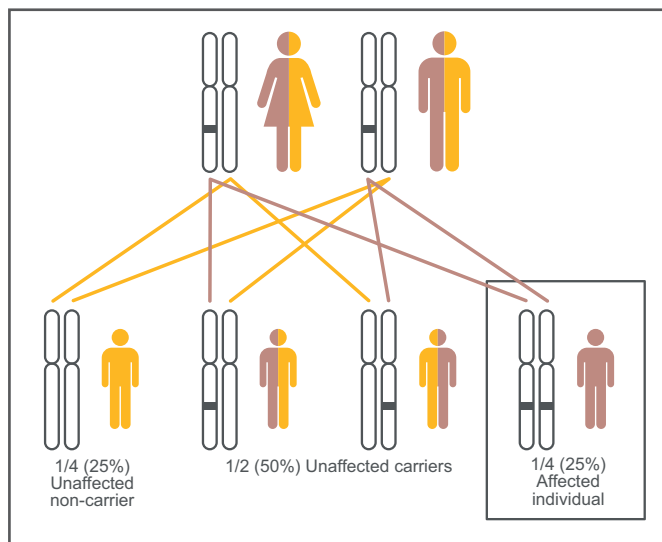


Figure 1: Inheritance of NP-C



What is the NP-C patient survey?

The NP-C patient survey provides new insight into the complexities of NP-C diagnosis from the patient perspective. Parents and carers in six countries shared their experience of the journey to diagnosis, its emotional impact on the family and the importance of ongoing support in order to help raise awareness of NP-C.

How was the research carried out?

In-depth interviews were carried out in the home environment with representatives, either parents or carers, of 26 families with one or more family members diagnosed with NP-C. A total of 28 NP-C patients aged between 3 and 36 years were involved; 11 males and 17 females. Two families had more than one family member with NP-C and their interviews focused on the first member diagnosed as, in the majority of cases, diagnosis of the second member was usually made easier due to the family history and previous experience. To provide a view of as many different experiences as possible, families from the UK, France, Germany, Italy, Spain and The Netherlands took part in the research. The research was conducted by Insight Research Group in January and February 2010.

- Whether parent or carer experiences of the journey to diagnosis could help raise awareness of NP-C and so reduce the time it takes to reach a diagnosis and start effective management of the condition
- The emotional impact of NP-C from a patient or carer perspective and the benefits of finally achieving a diagnosis of the condition and access to support
- Whether any differences exist in terms of the journey to diagnosis and its emotional impact and benefits in different countries to determine if experiences and practices can be shared

The aim of conducting the research was to understand the following aspects of diagnosis:

Results: Understanding the symptoms of NP-C

The three types of NP-C patient

Interviews with parents and carers confirmed the journey to NP-C diagnosis as lengthy and challenging. Symptoms are variable, not specific to the disease and they often appear and are recognized at different times. The average time from onset of noticeable symptoms to diagnosis for the families interviewed was slightly over five years. However, the patient research identified three specific patient types* and classified them according to the symptoms that patients experience and the time taken to diagnosis (see Table 2 on page 7).

**Naming based on respondent terminology and analysis/interpretation*

	Visceral (classic) symptoms	Learning difficulties	Psychiatric symptoms
Typical symptoms experienced	Child is born with 'classic symptoms' of NP-C, such as an enlarged liver or spleen and/or suffering from jaundice	Child starts to have difficulties in coordination, frequent falls and can struggle at school	Patient develops 'psychiatric symptoms', such as hallucinations, aggressive behavior or paranoia, often in their teens
Typical diagnosis journey	Usually diagnosed quickly after birth, particularly if the symptoms are severe	Often misdiagnosed as having dyslexia (problems with reading) or dyspraxia (difficulties planning or coordinating movement)	Often misdiagnosed with schizophrenia, autism or bipolar disorder
Possible reason for delay in diagnosis	The classic symptoms are not specific to NP-C disease, may not be recognized or may not followed up as they subside by themselves over time so it can often be many years before other symptoms develop and the opportunity to diagnose NP-C is missed	The family may see a series of specialists (such as neurologists, metabolic specialists, liver specialists, psychiatrists or educational psychologists) over a period of years before NP-C is identified	Absence of physical symptoms means that they can remain in psychiatric care either permanently or until physical symptoms start to appear and the original diagnosis becomes doubtful

Table 2: The three types of NP-C patient

Visceral (classic) symptoms

The patient research found that time to diagnosis for those exhibiting 'classic symptoms' is approximately nine months. An enlarged liver or spleen and/or jaundice at birth are usually recognized as a problem, especially if

they are severe, and the family is immediately referred to a liver specialist. Diagnosis of NP-C may be confirmed when the specialist has ruled out other conditions. Occasionally it is confirmed immediately using biochemical or genetic tests.



When my child was born she had another condition cytomegalovirus. She looked like she had jaundice but she didn't. We were sent home despite her being underweight, but her tummy was very swollen. I was very unsure, but another doctor said it was fine and that it was just because she was very thin. I took her back to the hospital when she was three and a half months old and was told that she needed to be hospitalized because they didn't know what was wrong. She was hospitalized for two months, on oxygen therapy for a long time until she recovered and the cytomegalovirus was cured. They decided to operate on her and to remove her spleen because it wasn't any good and this was when they noticed but at least the diagnosis was made early.

Parent, Germany

Learning difficulties

Not all symptoms are recognized in infancy. A physical problem may go unnoticed until the child experiences 'learning difficulties' at school, often aged between four and eight years, but sometimes later. These symptoms are similar to dyslexia and dyspraxia or general school difficulties and the gradual decline can often be difficult to see, especially in a family environment. A parent or teacher may notice memory and learning difficulties, lack of coordination, exhaustion or frequent falls but the problem is usually only flagged when the child falls far behind his or her peers or acquired skills are lost.



There were things that we didn't even notice as parents; for example, he could no longer hold the fork properly or hold his own cup, and whilst others would take note of that, we thought that perhaps he was simply mimicking his baby brother in order to attract attention.

Parent, Germany

Psychiatric symptoms

Patients presenting with psychiatric symptoms experience the longest journey to diagnosis, some involving up to 19 years of generalist and specialist psychological or psychiatric care before NP-C is confirmed. Some patients spend years enduring tutoring and counseling by psychologists for learning difficulties. Psychiatric symptoms, such as psychosis (for example hallucinations or delusions) often emerge in the teenage years before other, physical symptoms are noticed and are commonly misdiagnosed as schizophrenia, autism with psychotic features or bipolar disorder.



...finally the year 3 teacher recommended that we see a specialist so we went to a center and we saw a psychologist. He was diagnosed as a child with learning difficulties. We went to a psychiatrist, the psychiatrist treated him for anxiety, then when we realized that the medication for anxiety was having no effect and if anything he was much less receptive and much slower...

Parent, Spain



Results: The journey to diagnosis

The cycle of generalist care

The first medical contact for patients whose symptoms have been missed at birth is often a general practitioner (GP) or pediatrician who has little or no experience of NP-C. Their symptoms are difficult to distinguish from those of typical 'slow' or 'clumsy' students and so are rarely viewed as serious. Often, parents worry that they may be over-reacting, especially if it is a first child. Some interviewees said that these feelings may be made worse by the general medical community who, when unable to identify a physical illness to explain the symptoms, may dismiss the parent as over-anxious or neurotic. These experiences are traumatic for families and lead to feelings of anger and distrust of the medical profession.

It isn't until severe physical symptoms, such as seizures or cataplexy (an episode of sudden muscular weakness triggered by strong emotions such as laughter, anger or surprise) appear that a patient is referred to a specialist. This all creates a generalist cycle of care that is only broken either when the symptoms become more severe, when there is another major episode, or if the patient encounters a physician informed about metabolic disease, often completely by chance.

In those patients with mainly psychiatric symptoms, the underlying physical symptoms of NP-C may be masked. The patient's behavior may be mistaken for attention-seeking or family issues may be seen as the cause of the symptoms. The generalist or pediatrician may then refer the patient for counseling for mental illness or emotional disorders. Symptoms such as hallucinations, aggressive behavior, or incoherent speech usually result in a relatively rapid referral to a psychiatrist and initiation of treatment for schizophrenia or bipolar disorder.

Accessing specialist care

The findings from the patient research confirmed that the timing and nature of specialist care varies enormously for patients with NP-C. Each patient may see several different specialists before they are tested for the disease. For the patient with classic symptoms, recognition at birth leads to referral to a liver specialist who may diagnose NP-C very quickly. Where these symptoms are missed, patients remain in generalist care, only achieving referral for treatment of individual symptoms as they become severe. In some cases, patients are cared for by several specialists at the same time, most of whom have little understanding of the implications of the symptoms outside their specialty. The bigger picture of the patient's health is lost as there is no sharing of background information between departments and parents fail to volunteer seemingly unrelated symptoms. The absence of a checklist of symptoms for identifying metabolic disease often means that patients have a lengthy wait before receiving a diagnosis.



...it felt as if no-one was taking me seriously. I really had to bang my fist on the table to get some recognition. I insisted that my son needed support for his feet, and then others refuted that. I mean, as a mother I simply knew whether his feet were getting worse or not. I could see it. And it did get worse. So I really had to make fierce demands. I even threatened to put his feet into plaster myself if they didn't help me.

Parent, Germany

Patients in psychiatric care already have a 'diagnosis' accounting for a variety of symptoms. As a result, the patient can be hidden in psychiatric care, seeing a series of specialists in mental illness who have little reason to suspect misdiagnosis. It isn't until physical symptoms emerge that cast doubt on the early diagnosis that the possibility of serious physical illness is considered.

In general, an early diagnosis of NP-C depends on individual symptoms, which occur sequentially, to be linked together and then linked to the possibility of NP-C. Amongst specialists, it appears that neurologists are key, most often picking up on triggers and confirming NP-C through laboratory testing i.e. genetic testing or histological and biochemical testing in skin biopsy.



There is always a need for earlier diagnosis, because of progression and early death. If this could be shortened it would be much better. Optimal window for treatment would increase. This is a problem with diagnosis, but because symptoms are so various, and often specialists have never seen a patient with such symptoms, they have not got a clue for diagnosis. You need very specific research to find it.

Healthcare professional

Seven years to diagnosis and no support was available

Mary** was diagnosed with NP-C when she was 19 years old. Although she first showed symptoms of carelessness and dropping things when she was 12, they were attributed to cerebral atrophy. It wasn't until a relative was diagnosed with NP-C five years later that the family sought genetic testing and found the true cause of Mary's symptoms. By then, she was too old for pediatric care and there was no specialist center available. Lack of awareness of the disease meant that Mary received no treatment and there was no support offered for her or the family.

Mary is now 28 and unable to manage any activity by herself; she has problems sleeping and eating and requires 24-hour care. Although her parents were able to organize some home care, they couldn't continue with it once they managed to access a day center, and they now provide every aspect of their daughter's care themselves.

"Before she started going to that center, someone used to come to our place and give her therapy – physiotherapy and logopedics... and then she started attending that center so she lost her rights to home support, so we had to choose: either one thing or the other."

** Patient name has been changed for confidentiality reasons

Results: The emotional impact of receiving a diagnosis of NP-C

According to parents and carers interviewed, receiving a confirmed diagnosis of NP-C has a huge emotional impact on the patient's family. They experience a wide spectrum of emotions, often compounded by the length and nature of the journey to diagnosis and ongoing lack of support. Timelines drawn by the parents and carers participating in the research show the emotional roller-coaster that families endure trying to achieve a diagnosis. Parents and carers describe the process as a series of obstacles along a journey. In the example shown in Figure 2, access to a full support team and care package at the time of diagnosis was the only real positive factor.

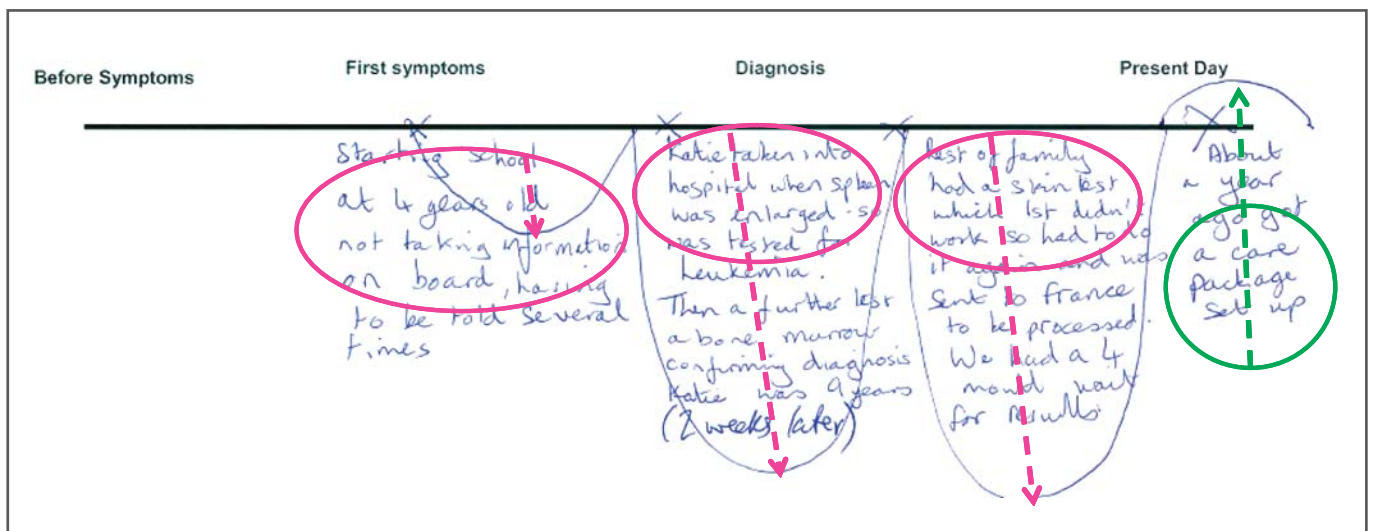


Figure 2: The emotional rollercoaster of the path to diagnosis

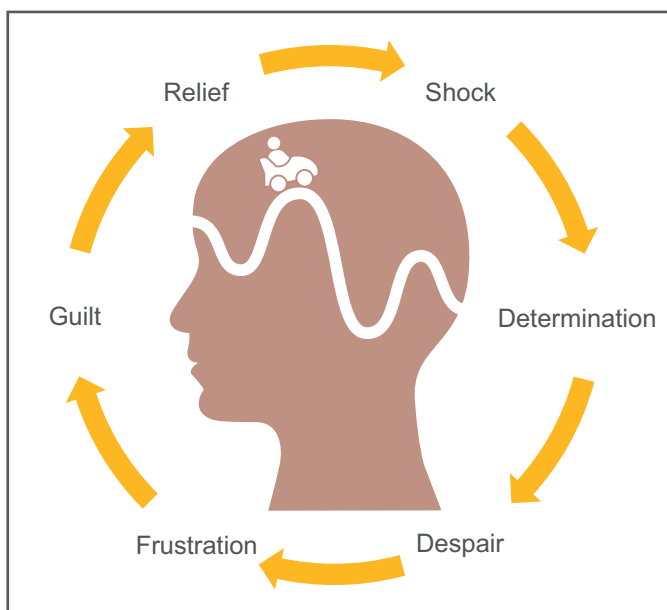


Figure 3: The emotional impact of a diagnosis of NP-C

Once diagnosed, parents and carers experience a number of strong emotions (see Figure 3). Even if diagnosis removes the uncertainty, it is always a huge emotional blow and can lead to feelings of devastation and despair at the loss of a child and many future dreams.

For some, there is a sense of relief that their child's illness is no longer a mystery. The stigma of the 'naughty' child or 'pushy' mother disappears and they can finally access any support or services on offer. However, for those parents whose child has only shown mild symptoms or where less severe diagnoses have been discussed, the diagnosis of NP-C comes as a complete shock.



My stomach was in absolute knots and I was devastated that one of my children had such a disease.

Parent, UK

Finally finding out what is wrong can lead to incredible feelings of frustration with the experts who have missed the child's illness. Such feelings are aggravated when support is not immediately available or complex information is provided too quickly or insensitively, leaving parents confused about where to turn for more information and help.



The atomic bomb is the announcement of the news that your child has NP-C.

Parent, France

Feelings of guilt are also common amongst parents and carers, as they express regret over lost time with their child or maybe realize that they may have been disciplining the child unnecessarily or he or she may have been made to struggle in mainstream education. They may also feel that in some way that they are responsible because it is an inherited disease.

Overwhelmingly, parents and carers feel a sense of determination in achieving the best possible quality of life for their child or family members, gathering information and accessing support wherever they can. For many, sheer determination got them to a diagnosis in the first place; so now they feel they can't give up.



It [diagnosis] is like your house of cards collapses. Especially once you type 'Niemann-Pick C' into the search engine. You find out what it is and you think: My God, why did this have to happen to me?

Parent, Germany

Years to diagnosis and misdiagnosis meant a long and difficult journey

Michael** was a low birth weight baby with a large tummy but this went unnoticed at the time. Despite his mother expressing concern about his progress when he was three years old, it wasn't until he was a teenager that he and his family started the route to diagnosis. Between the age of 15 and 24, Michael was treated in psychiatric care for delusions and fears and eventually diagnosed with schizophrenia. He spent four years being cared for in a center for autistic children 300 km from the family home but, when his symptoms worsened and he became reliant on a wheelchair, he was unable to continue there. Michael was finally diagnosed with NP-C at 24, following a chance recommendation by a psychiatrist to see a neurologist. He is now 30 and his parents provide full-time palliative care at home. His mother feels that his diagnosis has been a long and difficult journey and has felt quite isolated in her struggle.

"When he was 3 yrs old I thought he was not well, not serious, but it did not feel normal to me. And when he was 5 yrs old, we saw a psychologist because I was worried. They said I was a mummy who worried too much. It was mummy's fault. Even our friends, even though some were psychologists, re-educators, some in psychiatry just told me, "All is well, leave him alone". It was like that for a long time and it created real tensions. He wasn't diagnosed until he was 24."

** Patient name has been changed for confidentiality reasons

Results: The value of having a diagnosis

All families interviewed, whether experiencing prompt or delayed diagnosis of NP-C, emphasized that early diagnosis not only helps families access support, advocacy and appropriate treatment earlier but also helps prepare them emotionally and physically for their child's future. They can spend more quality time with their child before the disease progresses for example, prioritize holidays, and plan for the future.

Struggles of caring for a patient with NP-C

Looking after a seriously ill child/adult puts a great deal of physical and emotional strain on the families of patients. Mothers usually take on the full-time care, finding out about available services, making the case for eligibility, and coordinating efforts across a variety of healthcare teams. Many report of the struggles in providing 24 hour care as symptoms become progressively worse and their child becomes older and heavier. It is also emotionally draining, both in terms of marital relationships and in the care of and interaction with other children. Siblings have to become more independent and in some families, become regular carers.

The importance of support

Support upon diagnosis varies both across, and within, the countries included in the research. The general level of support appears to be best overall in the UK, where it is usually available immediately, even when NP-C is only suspected. Parents are provided with information and given access to specialized nursing services. In other countries, it is usual for parents or carers to be connected to a patient organization at diagnosis although they often have to seek out support and information on their own. Few families have access to social workers, in-home care, home alterations or respite care and highlight that, without regular contact with patient organizations or their own support network, they would have to do everything themselves.

Support networks help carers to cope

Simon** is 18 years old and was diagnosed with NP-C about 4 years ago. His symptoms first appeared when he was 5 or 6 years old. The family GP referred him to a pediatrician and he was diagnosed with ataxia. Following a number of seizures at 11, he was diagnosed with epilepsy and received medication which controlled the seizures for 3 years. At 14, following hospital admission because the seizures had re-started, a pediatrician noticed Simon had eye movement problems and the journey to confirmation of NP-C began. Although frustrated by the lack of support and length of time it took to reach a diagnosis, his mother, who is his full-time carer, has managed to build a strong support network involving regular, local respite and hospice care, a community nurse, a social worker and a carer's support group. She also managed to secure funding for adaptations to the home. The support network works well together; there is good communication with the family and with each other in providing support. As a result, Simon's mother has been able to cope with providing his care.

"... I am really happy with the hospice, because they do a bit with him and he is comfortable there... It gives me valuable time with the younger children really. And allows me to catch up on sleep."

** Patient name has been changed for confidentiality reasons

Results: The value of having a diagnosis

The role of patient organizations

Contact with patient organizations varies according to the specific needs of patients and carers; some have rare contact, others access them frequently; only a minority actively avoid them. For some patients, there is an awareness of the organization and initial contact but then a reluctance to pursue it further. Reasons include lack of online access, living too far away to be able to attend meetings, feelings of anxiety when seeing more severe patients or discomfort when discussing their child with strangers. However, some parents become extensively involved with patient organizations, attending conferences, joining online forums and accessing advocacy services or offers of practical help. Some have eventually gone on to become central members of the organization and its activities are at the center of their family life.

Additional support

Access to other forms of day-to-day support varies significantly in all countries. For example, availability of financial support for alterations to the home, respite care or counseling services for the family often depends on the child's age and local policies. All families report that achieving support for their children is a draining task, requiring access to extensive information about both NP-C and local services.

An optimal support structure

Parents and carers interviewed have a clear idea of what an optimal support structure looks like. They describe a model with the mother, or parents, at the center but with layers of support around them performing different functions (see Figure 4). These layers comprise social workers, healthcare practitioners, local government, and charities; however, they acknowledge that this is rarely achieved.

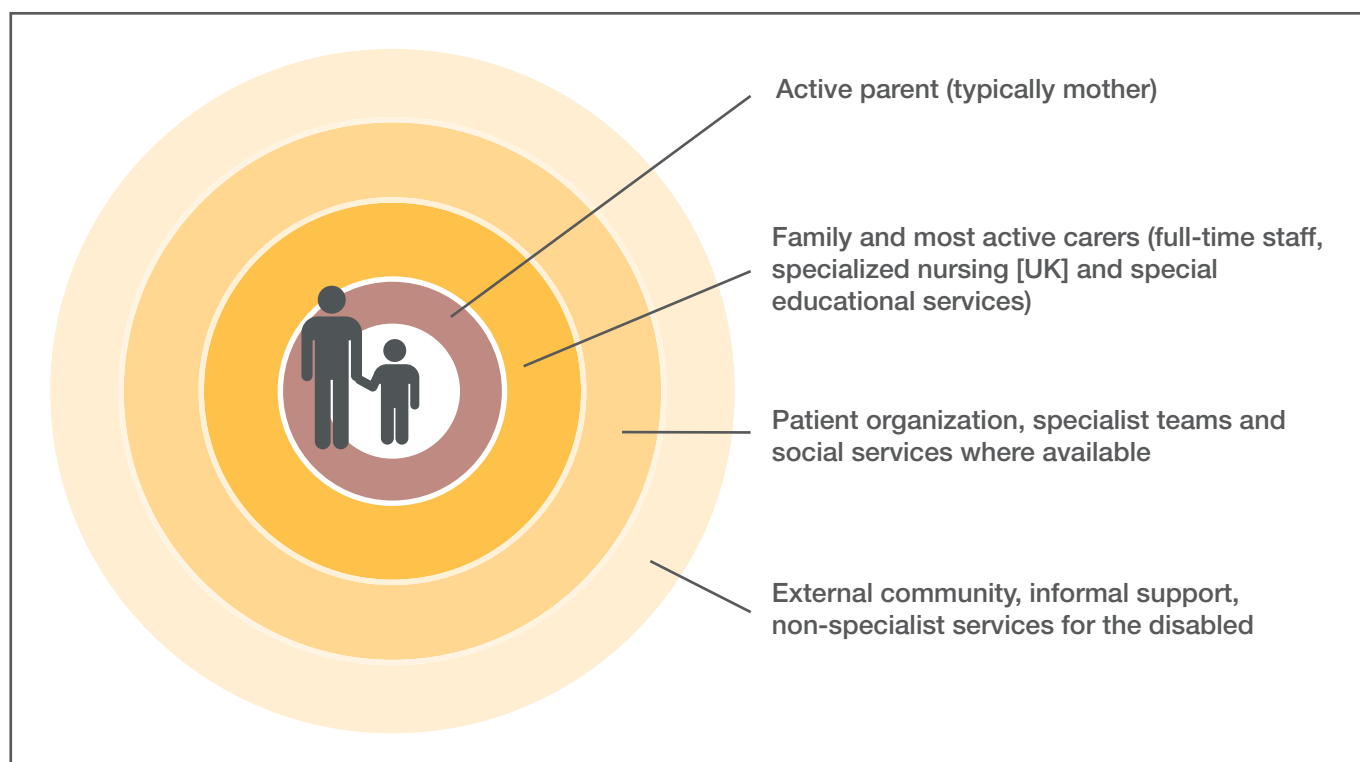


Figure 4: The optimal support structure for a family affected by NP-C

Even though the circumstances of the families interviewed differed extensively in terms of the support they receive, they were unanimous in their view of the most valuable elements of support:

- A voice on the phone – someone to talk to about a child's day-to-day symptoms
- A central point of coordination for advocacy – someone who knows what is available and can help them prepare all the necessary documentation
- Coordination of services – a team around the family to care for the child and ensure consistency of in-home services

A quick diagnosis allowed early treatment of NP-C

Jane** first showed symptoms of NP-C when she was eight years old. She had difficulty walking which prompted her parents to visit an orthopedic surgeon. Although she was later diagnosed with mononucleosis (glandular fever), her parents were not convinced that this was the problem and asked to see a neurologist, who noticed a problem with her gaze and sought confirmation of NP-C.

Jane was diagnosed very quickly and, as a result, was able to receive treatment for the various symptoms as they developed. She is now 21 and her disease has progressed very slowly since diagnosis and is receiving a specific NP-C treatment. Jane's parents believe that their daughter's early diagnosis was extremely beneficial in terms of accessing treatment.

“Well, you know what it is about so can start with a medication, you can start taking a certain treatment pathway... When you do know, you have a starting point.”

** Patient name has been changed for confidentiality reasons

What does this research mean?

The NP-C patient survey highlights an overwhelming need for change. There is minimal knowledge and low awareness of metabolic storage diseases, of which NP-C is one of many, amongst generalist physicians, such as GPs and pediatricians.

This can lead to lack of acknowledgement of parental concern regarding physical illness. Not only does this delay diagnosis but it can also lead to feelings of anger and frustration amongst parents whose instincts tell them there is a problem.

As well as a combined effort to improve symptom recognition and creation of the opportunity for earlier diagnosis of NP-C, the survey also shows the desperate need for better provision of co-ordinated healthcare and social support to enable families to achieve the best quality of life possible for their child.

Taking action

The parents and carers interviewed highlighted the need for earlier diagnosis of NP-C. This will not only allow treatment to begin when it is at its most effective but also ensure that patients and families have earlier access to a support network. These families need the support of advocates who can help obtain the services needed, help access specialized clinics, hospices and respite care and in some cases, facilitate the connection with other NP-C families and patient organizations.

The variability in the type and timing of symptoms has made the path to diagnosis lengthy and challenging for many patients and their families.

So how can healthcare professionals help?

There is a need for improved education amongst healthcare professionals in order that they can recognize the link between the symptoms that lead to a diagnosis of NP-C. Whilst we want to avoid raising unnecessary concern, all healthcare professionals need to be encouraged to question what they see. For example, there needs to be a greater focus on raising awareness of the classic symptoms in infants and proactive testing of newborns with enlarged spleens and severe jaundice before symptoms subside.

For those patients whose first symptoms are that of 'learning difficulties', specialists and pediatricians need to recognize and link symptoms together, listen to parents and think of the wider picture to allow multi-specialty collaboration. In patients with psychiatric symptoms, healthcare professionals need to look outside those symptoms they are familiar with and look for others, usually physical, that do not fit their current diagnosis. With greater awareness, they may be able to ask themselves whether the patient's symptoms fit the profile of NP-C; whether there are symptoms that the parents have missed; whether the parents can share any other symptoms they are concerned about, even if they seem unrelated and whether they should ask a colleague about the patient.

The research provides extensive insight into the huge emotional, social and financial burden that families face when caring for a child with NP-C, emphasizing that more needs to be done to help these families cope. The research highlights the need for the provision of fully co-ordinated healthcare teams around the family in order to provide a support structure that enables them to achieve the best quality of life they can for their child both in the early stages of NP-C and as the disease progresses.

The research showed that many parents are dismissed as being over-anxious and little attention is paid to instinctive knowledge that something is wrong.

So how can parents and carers help themselves?

Persevere! Parents and carers should be encouraged to persist in discussing symptoms with their healthcare professionals even in the face of skepticism. Linking seemingly unrelated symptoms appears to facilitate the diagnosis of NP-C, therefore parents and carers should be encouraged to inform healthcare professionals of all symptoms, even if they seem irrelevant at the time. Parents and carers should be encouraged to look for support through patient organizations and family support networks, where they can listen to and share experiences; gain and give advice on how to speak to healthcare professionals and talk about coping and living with NP-C. Overall though, they should stay determined.



A call to action for everyone affected by NP-C

1. Increase awareness of NP-C symptoms amongst healthcare professionals:

- Better healthcare professional knowledge of the classic symptoms of NP-C would facilitate the earlier referral of infants for specialist care and those children who present in early school years with classic symptoms

2. Consider a diagnosis beyond the obvious:

- Specialists need to ensure that they are looking at all the symptoms a patient presents with and to link these symptoms together
- Encourage parents to share more background about their child's illness even if other symptoms seem irrelevant
- Encourage healthcare professionals to speak to colleagues if unsure of the symptoms presenting

3. Listen to parents and carers:

- Generalists, such as general practitioners and pediatricians, could listen more to parents and consider the possibility of and suggest ruling out a severe physical illness rather than dismissing them as over-anxious
- Parents and carers could seek the support of teachers or other social networks to gain extra evidence when presenting concerns to healthcare professionals

4. Seek support:

- Parents and carers should be proactive in seeking support from patient organizations, social services and family networks to ease the emotional impact of receiving a diagnosis of NP-C and to help manage challenges in coping with the condition

Further information

For more information on NP-C please visit the following websites:

- www.npc-info.com
- www.niemannpick.org.uk

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If she has had a good night, she gets up, she is quite happy, her speech and her eating are good. And you can actually get some interaction, in that you can actually make her laugh... If we can see a little chink of our old [daughter], which you do from time to time.

Parent, UK



...remain as calm as possible given the situation, and not to get overwhelmed any more than is necessary... take each day as it comes because not all the problems happen at once and you can resolve them one by one as they happen. You can't do any more than this.

Parent, Spain



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