A RELUCTANT ADVOCATE

A Reluctant Advocate

A brief history of the charity aHUSUK and one person's role in becoming a patient advocate.

By

Len Woodward

First published in 2020 by the aHUS Alliance Global Action

Revised and updated 28 February 2023

Image on front cover is of the author having completed the Great North Run in 2013 for Kidney Research UK.

CONTENTS

Preface

I have no natural inclination to write about myself, but I can see that in health advocacy these days it is not unusual for individuals to promote themselves and be identified with some cause or other they are promoting. Whatever organisation I am promoting I prefer to communicate in public as that organisation. I regard it as more important than myself. I prefer that anonymity. But here I am using the first-person pronoun seven times in the first paragraph of a book about my advocacy reluctance.

The book came out of a series of online blogs written for the website of the aHUS alliance Global Action during 2018/19. Taken together, the series was an attempt to capture the history of a charitable organisation called aHUSUK. The charity was set up in 2011 just to provide a patient voice for atypical Haemolytic Uremic Syndrome or aHUS patients in the UK. That voice was needed as part of an evaluation by the National Health Service of the drug eculizumab for English patients and then other nations in the UK.

There were others who became part of that aHUSUK journey, and some thought at the time that as the events that unfolded were so unusual, they might be worthy of a book some time. The blogs on the website attempted just that. The events in this book took place but are recalled from my perspective using records kept primarily on the legacy aHUSUK website.

It is not a complete history of the aHUSUK, but it tries to capture much of the story but interwoven with my family's personal aHUS story, both before, and during, my aHUSUK advocacy years.

It also includes an account of the start-up and early years of the only global aHUS patient advocacy organisation i.e. the aHUS alliance. The mission of the alliance includes supporting newly emerging aHUS patient organisations around the world. The UK example of organised patient advocacy could provide some insights and experiences for emerging aHUS groups to learn from.

Len Woodward

29 February 2020

Chapter 1

A change in gear for a Reluctant Advocate

“It’s a “no decision”. I said.

“They said “no?”” My wife asked.

“No, they said “yes””. I tried to explain.

“They said “yes””. She returned

“Yes” I confirmed “but the Minister cannot make a decision now as he wants it all done again, but this time by NICE, so it is a “no decision”

“They” were the Advisory Group for National Specialised Services “affectionately” known as AGNSS (“Agnes”). NICE was then the National Institute for Clinical Excellence. The Minister was The Right Honourable the Earl Howe, Parliamentary Under- Secretary of State for Health.

What they were saying “yes” or “no” to was whether a drug called Eculizumab, then reputedly the most expensive drug in the world, could be made available in the NHS England for the treatment of atypical Haemolytic Uraemic Syndrome (aHUS), a very rare disease.

It was the morning of 19th January 2013.

The conversation that morning was about something which had become a matter of life or death to our family and therefore marked a moment after which our family’s hitherto reticent involvement in patient advocacy went to a new level and would consume our lives for the next five years.

Chapter 2

Where the heck did that come from?

No one in our family had experience of kidney failure, or so we thought, on 19th January 1997 when our daughter went into respiratory and heart failure, in front of our eyes, in an old and almost derelict (through under investment) hospital in Manchester; now long pulled down to make way for housing development.

It was a Sunday. The hospital could not afford to open its dialysis unit on a Sunday and the fluid that builds up when your kidneys stop working cannot be expelled without an artificial kidney machine. The fluid builds up in the lungs like someone drowning and the heart struggles against the odds to continue to function.

“Well somebody got their figures wrong” said the Consultant in the Intensive Care Unit after the renal ward team acted professionally to undo the effects of the treatment which was killing her.

Too much fluid in (kidney patients are often treated for dehydration) not enough fluid out. The Intensive Care Consultant said, while showing us an X ray of our daughters’ lungs, “the errors in the sums had caused one lung to fill up completely and the other was half full”. Our daughter was now on dialysis to get the fluid out of her. It was the middle of the night but now Monday morning, so a dialysis machine could be brought into use to resolve something which earlier the previous day it could have prevented.

We were in the “car crash” scenario, which we now know would be familiar to many of those rare people who have experienced a catastrophic episode of atypical Haemolytic Uraemic Syndrome, or aHUS.

aHUS is very rare although no one knows how many people in the world have or have survived an encounter with it. Estimates vary between 15000 and 42000. Maybe around 4000 incidents around the

world each year. In the UK there will only be around 25 incidents of aHUS.

The terms “Haemolytic” and “Uraemic” are just describing the symptoms of the disease. aHUS patients will experience severe anaemia caused by their red blood cells being destroyed because of the uncontrolled clotting in the body’s capillaries leaving smaller and smaller gaps for the blood cells to squeeze through. The gaps gets so small that the cells explode like balloons. This is known as haemolysis.

This uncontrolled process seems to happen most frequently, but not exclusively, in the capillaries in the kidney. When it does, it causes the filtration system in the kidneys to become blocked. Once blocked the kidneys are not doing what they should be doing, there is, among many other effects, a build-up of uraemia in the blood a sign that the kidneys are failing to work.

aHUS is not the only disease in which this happens. HUS, the typical version, is more common. It is triggered by E. coli poisoning. The excessive haemolysis is the result of the toxins in the virus inflaming capillary walls which kicks of the same thrombotic process. There are very few incidents of HUS each year, yet it is ten times more likely to happen than the atypical version. Whilst HUS is the result of poor hygiene in food preparation or animal contact, aHUS can be triggered by other factors. An aHUS patient’s immune response is uncontrolled because of minute inherited defects in the aHUS patient’s own immune control system. The controls are needed to stop an excessive and unnecessary immune response to whatever has triggered it.

No one can be sure what triggered the illness in our daughter. At the time she was living in Glasgow and the news was full of a story about an E. coli outbreak in a nearby town in which poor hygiene practices by a local butcher had resulted in E. coli contaminated meat being served at a party causing partygoers to become ill. The youngest and

oldest of them dying from kidney failure. HUS was not necessarily something that would have been mentioned.

There were many people in the Glasgow area who were experiencing stomach upsets at the time, including our daughter. But unlike others who recovered quite quickly she did not. In the following six weeks or so her condition deteriorated until eventually a local doctor discovered from a simple blood test that she was in kidney failure.

It did not take long for the Renal Consultants in the hospital that she was hastily referred to, to see from the tell-tale signs in the blood that the cause of the kidney failure was HUS, although by then no evidence of E. coli could be found in any cultures that were taken.

Just what had hit us out of the blue? How could someone who had that summer toured the USA including universities in New York and Bloomington in perfect health now be laid so low and near to death?

Although we did not understand much at the time and had no idea then why the doctors were looking for other possible causes pregnancy, AIDS, drug use, there was a clue in our family history which we did not know was significant.

Chapter 3

Now where is my tutu?

With the family moto "*Non Offeres" ("Never Volunteer")* going through my thoughts, I entered the door of 1, Wimpole Street, London on 10 September 2011, little did I know how that day would change my life.

Wimpole Street is a well-known London street, and No 1 houses the Royal Society of Medicine in very prestigious surroundings. One of the changes I would experience was that I would now visit many such impressive, famous and historic venues over the coming years.

That day it was just to find out about the need for an aHUS patients organisation.

I had kept my head down when a volunteer was sought to be the first appointed Trustee of the patient organisation, which we had discussed and had agreed to form.

The first Trustee's role to be elected was that of Treasurer.

"He will do it" I heard as my family volunteered me. I had been a qualified accountant for over 30 years, and it was something that I could do easily, albeit with no previous experience of charity accounting.

So "Yeh I will do it" I said.

That was it, that was the start!

The meeting had been called by Professor Tim Goodship, the Doctor who we had first heard of when our daughter was first ill in that derelict hospital in Manchester, and when advice was being sought on the likely outcome of a transplant with a living donor.

Prof. Goodship, as he became, had undertaken genetic tests from our blood samples and had found that my daughter and I had a genetic predisposition to aHUS. That was important for the donor decision.

Now we were in the room with the families of another six aHUS patients who had experienced aHUS and who had answered Prof. Goodship's call and had been challenged to become a formal charity with objectives, rules and a constitution. To say there was a reluctance by all to do so would be an understatement.

As the meeting progressed it had become clear to us that such a group was essential to meet the National Health Service's criteria to be able to provide the patient case when its committee, AGNSS, met to evaluate the case for eculizumab to be used for aHUS in England. None of us had done anything like that before, but as our family came to realise that if a "box had to be ticked" then "tick it we would" if it meant that our daughter could have a successful transplant at last. Somebody said that "if they had to stand in a corner wearing a Tutu singing "God Save the Queen" to get access to a clinically effective treatment, then so be it".

A charity was created but only members from five of the seven families attending were prepared to join in. There were estimated to be over 150 families in the UK affected by aHUS at that time and the burden fell to just five. It soon became four as one of those five families had second thoughts after the meeting and resigned, although the reasons for doing so seemed to be odd.

That is what it is like in charities, they are often run by a disparate group of strangers bound together with a common aim, which in our case was to convince the cash strapped NHS to fund treatment for aHUS patients with a drug reputed to be most expensive in the world. And there was less than a month to get started before the first meeting with the NHS was to be attended. If things were to be done that quickly, we thought it could all be over with by Christmas.

We also knew enough about each other to be aware that we lived in all corners of England and had no resources to do anything. To fund our ourselves we needed to be a legally registered charity.

The option of wearing a tutu and singing “God Save the Queen” seemed to be the much better alternative!

Chapter 4

Hurry up and wait

It did not take long to realise the meaning of the saying “Hurry up and wait” as far as the NHS is concerned. “To be done by” dates for third parties, which aHUSUK, the name of the charity formed in Wimpole St, had become, were set in stone, whilst dates for the NHS were flexible.

aHUSUK’s first meeting with the Advisory Group for National Specialised Services (AGNSS) was held on 31 October 2011 not early in October as was thought. Two trustees attended the meeting, the Chair of the charity and our daughter. The three-hour meeting was held to discuss the scope of the Eculizumab for aHUS evaluation and not to evaluate it. The evaluation meeting was now predicted to be held in June 2012. So much for it being over by Christmas 2011! Not only that, eight months would be needed just to get ready for the Group to receive evidence.

The meeting was also the first opportunity to meet some of the members of the Group as well as the people from the NHS who managed the whole process and on whom we became reliant as we learned about what was needed. None of us had done anything like this before.

It was also the first encounter with employees of Alexion and their consultant advisors.

My daughter’s recollection of the meeting was how welcoming and hospitable everyone was with refreshments laid on for early starting meeting finishing at lunchtime. As she was the only one who was living with aHUS on dialysis, she was asked to give a brief introduction of her experience. Perhaps the most telling illustration of what being on dialysis meant was that in front of her was a small cup of water which was still full. Although everyone had been kindly offering her drinks

before the meeting and in breaks, she said that that cup represented her total fluid intake allowance for the day. The food laid on had also contained too much salt and potassium for someone reliant on dialysis. These are the kind of day to day challenges that those not familiar with dialysis struggle to understand. In such simple ways the aHUS patients voice was already resonating.

Later, the Chair of AGNSS spoke to her and commented on how well she looked despite fourteen years of dialysis and asked whether she would wish to have an eculizumab supported transplant. “In a heartbeat” was her immediate response “…as it would mean “Freedom””.

The meeting also introduced the principles on which the decision-making frame had been designed with the patients’ needs out front and centre. It was a decision-making process that had been developed specifically for health technologies for those with rare and complex diseases diseases* which met pre-set criteria such as there had to be less than 500 patients affected in England. Although no one really knew the exact number, there were estimated to be fewer than 200 aHUS patients in England at that time.

The underpinning **principles** were:

- Societal value
- Best practice
- Sustainable Cost
- Health Gain

The **framework** which had developed from these principles required evidence to show:

- Does eculizumab work?
- Is it the best way of delivering the service?
- Is it a reasonable cost to the public?
- Does it add value to society?

For each of these, criteria were set, and each of the criteria elements would determine if they were met. In making its decision the Group would take a holistic view across all criteria.

aHUSUK believed most of the criteria would be met but the "reasonable cost ", when eculizumab was reputedly the most expensive drug in the world, was going to be a challenge even though every aHUS patient would think it was totally reasonable.

The trustees left the meeting with the task of providing a "Patient Submission" by 30th January 2012. No firm format was given for it as the Group were still consulting organisations who had previously gone through the process in the past to come up with a novel way of doing it. Given the lack of resources and experience that aHUSUK had, it was likely that we would be given access to consultants to help with the submission.

The time it was going to take depended on the NHS, so the completion date was going to slip!

This was just the start.

Chapter 5

Much ado to do nothing

The AGNSS journey had begun and it was to be aHUSUK's key task and focus for several months.

At the same time the demands of being a charitable organisation with objectives were also to be addressed.

None of the trustees had any knowledge or experience of running a charity although the trustee board possessed a range of skills and professional backgrounds. The charity had to be registered with the Charity Commission if it needed funds, and for that it needed a bank account.

It also needed members, the charity was an association (the membership decide what is done) not a Foundation (Trustees Decide). We needed to hold an inaugural meeting and soon. Members were also needed to make the AGNSS review more inclusive and informed, and for that the charity needed to be known about. It was too simple to expect the NHS to let us know who the aHUS patients were, and we soon got to know that the rights to personal anonymity superseded the right to know how their illness could be treated and to help with getting it.

At this point most aHUS patients knew nothing about what was happening to help them. Sadly, neither did many of those whose job it was to care for them.

Not all patients wanted to be treated either and we soon found out that not everyone shared the desire to leave a life of dialysis. One of the trustees thought just that and resigned as he could not support an application for aHUS patients to receive eculizumab. Charities for health action are frequently created by disparate strangers with varying views. We went our separate ways.

aHUSUK objectives, as all health charities seemed to do, included raising **awareness** of aHUS and getting better **understanding** of the disease (something individually even we needed to do rapidly) as well as provide **support** and **help** to those affected by aHUS. For the latter we saw having unfettered access to eculizumab as the main way we could support and help. Juggle the key words "**a**wareness **h**elp **u**nderstanding and **s**upport" around and the result is aHUS and that becomes the underlying theme for an aHUSUK website. Online visibility was almost mandatory for a charity. Our online presence was in the process being developed by me, iT and the finance functions often went hand in hand back in the day! Computer skills had to be quickly learned.

We needed a logo. We did not have professional design skills, nor could we afford to go to design consultants. It had to be home made and it needed thought as it had to represent our disease and purpose. It was left to me. The logo I developed was based on a double twisted "mobius band" which resulted in three sections representing the triad of aHUS symptoms, anaemia, clotting and kidney failure. The band was also given the colours of the rainbow to symbolise our optimism for the future. The website had a backdrop of blue sky to conclude the feeling of "hope" that aHUSUK was to give. That exhausted my design capability! It would have to do.

Although we were beginning to think as a large charity; and, with a website creating an image and perception of aHUSUK to back it up, who would really know what was behind it all?

The key difference for us was that although large charities were governed by unpaid trustees, which we were, they also had paid employees to do the work. In aHUSUK, trustees did the governance and all the work for no payment. No wonder a reluctance.

Years later a blog appeared on aHUSUK's website which contrasted what we had to do compared to other established charities

"Very few people would know about *Naglazyme****, $485,747 annual cost per patient, used to treat mucopolysaccharidosis type VI, which is better known as Maroteaux-Lamy Syndrome. In the UK the patients are represented by the MPS Society which has 12 trustees, interesting to see they are funded among others, by three pharmaceutical companies and employ 13 staff in dedicated office accommodation. MPS patients require the third most expensive drug too.***

aHUSUK has four unpaid trustees who have had to do much the same as the MPS Society with some of their out of pocket expenses for conferences and meetings found from an unconditional grant from Alexion."

I will come to funding of aHUS charities later.

With the splendid efforts of our Secretary we became a registered charity and I got it a bank account. Now we not only had to comply with registration rules and responsibilities but the job of accounting for expenses and complying with financial reporting regulations was to begin. All required time, whether the charity was doing things or not. As it happened there was much left to do and we had only got to Christmas 2011.

Chapter 6

"It's BLOODY scary!" An authentic aHUS Patient's Voice

By Christmas 2011 nothing had been heard from the NHS about what format the patient group evidence would take. But work had begun.

There were two strands of research already taking place.

Although some of the aHUSUK trustees had not seen another aHUS patient until the first aHUS patients conference which had been held in Newcastle upon Tyne back in June 2011 (and which led to the creation of aHUSUK) it was evident from those attending that conference that there was not a "typical" aHUS patient, there was a "spectrum" to describe.

Similarly, there were treatment outcomes which were different and more extensive than just being on dialysis. Dialysis itself would not come alone and those living with it would encounter complications and debilitating conditions in time, particularly as they were not likely to get relief from dialysis with an opportunity of a kidney transplant.

Videos of the June aHUS conference were online and would be viewed and reviewed to get a better understanding of aHUS, its impact on aHUS patients and families. To get the orchestrated voice we needed adults and children (or their parents), males and females, those speaking for patients who died, those on dialysis and /or plasma exchange, in remission and those few on eculizumab. We also needed family members. The search was on, articles were written for kidney patient organisation magazines, posting were made about aHUSUK on the EURORDIS social medium Rare Connect and the USA's Foundation for children with atypical HUS website. Letters were written to those who had attended the Newcastle Conference but who had not come to Wimpole St. After several weeks we had candidates for each of the categories we had decided upon, except male adult patients. We knew

of a handful of male patients by then, but all were reluctant to participate.

It was evident that, whilst Alexion knew about their drug and aHUS, it was weaker in its understanding of dialysis in its various forms and their co morbidities. Comparing eculizumab costs with a dialysis costs, plus plasma exchange, although the latter by normal treatment standards were expensive, they were nowhere near the cost of eculizumab. But the cost of treating the comorbidities, which, although they would not be experienced by all patients each year would be experienced by most at some time, some more than once. The search was on to provide such a list. Clearly our “patient voice candidates” would provide some of these, particularly those on dialysis for decades. But there was another source. Those from around the world who had told their stories on Rare Connect or the Foundation for children with atypical HUS websites. Each provided considerable evidence and experience, some were the same, some were different. I began reading those websites and making notes of the additional treatments for comorbidities reported by people in the public domain. The aHUS social media is full of such data for research but it is rarely harvested.

Eventually as months passed by, the NHS got in touch with our “trustee for the patient voice” the role given to my daughter. AGNSS had decided that the patient group’s submission should take the form of a piece of a written qualitative research. The NHS would provide qualified resource to do the leg work but the topics to be covered were left to aHUSUK to decide. Another month passed, and some consultants Toucan Associates were appointed. Working with my daughter, a range of key questions were chosen to be used in structured interviews with our “patient voice panel”. The interviews would be held either face to face or over the phone. The responses would be recorded and transcribed into written notes. Key themes

from the responses would be identified and, in some case, illustrated with quotes from the interviewees.

Meanwhile a list of comorbidities was being drawn up to put in the research paper. Sadly, there was no time to research the costs of the comorbidity treatments. We had hoped the pharmaceutical company would do that.

Eventually a draft report was produced. At an all-day meeting of trustees in Manchester, it was read, amended and approved. It was mid-May 2012, the AGNSS meeting was to be held on 14 June.

aHUSUK had got its written evidence done on time for the AGNSS Committee to read before the meeting.

If it achieved no more, what aHUSUK had produced had fully justified the creation of the charity. It was an acclaimed and unique example of qualitative aHUS research. If it had not been held "in strictest confidence" for the whole time that eculizumab was to be evaluated it would have been an excellent standalone publication about aHUS. (A version of it including more interviews with Welsh aHUS patients can be read at Appendix A).

However, there was more to be done to ensure the aHUS patient voice resonated so that AGNSS saw, and understood, what it is was like living with aHUS.

Chapter 7

Don’t rain on our parade!

14 June 2012 London – AGNSS Meeting to Evaluate Eculizumab for aHUS.

This was it. This was what we had been preparing for. The aHUSUK Trustee for the Patient’s Voice was the only representative for patients allowed to attend. The only one allowed to speak and was allotted only 5 minutes to present to the Committee Members.

Alexion Pharmaceuticals were there, the bulk of the evidence submission had been its to do. The case for clinical effectiveness and safety, the cost effectiveness, and for how eculizumab was priced was for them to make.

As participants, aHUSUK had been given rights to look at all of the written evidence presented to the Committee Members. There was over 700 pages of evidence, including around 30 pages for the patient voice research paper which aHUSUK had submitted. There were reports on the eculizumab trials, there were estimates of patient numbers projected forward five years, there were the costs of eculizumab, there were the costs of dialysis and plasma exchange, but no mention of costs related to damage done by years on dialysis. There were life expectancy estimates, with or without eculizumab. There was research on the quality of life of dialysis patients. There was even a “cost per QALY”.

The Cost per Quality Adjusted Life Year was a health service indicator of the cost effectiveness of new medicines and technologies compared with existing treatments. It involved estimates of costs of each technology. The life expectancy in years depending on treatment used, and the quality of those year assessed on a scale between 0 and 1, where 1 was excellent health and 0 was no life.

The difference in the quality of life for those on each treatment option say 0.9 for one and 0.2 for another, i.e. 0.7 was multiplied by the difference in the number of life years to give the quality adjusted life years. The result would be divided into the difference in the costs of each treatment to produce a "cost per QALY". There is a little bit more *jiggery pokery* using accounting techniques to get to the figure, but that essentially is what it involves.

Normally for medicines looked at elsewhere in the health service the cost effectiveness result would have to be less than £30,000 per QALY. AGNSS was not bound by that threshold as it was created to look at technologies for rare diseases. Just as well as based on the evidence given to Committee the Cost of QALY was many times that figure. In a way the calculation just demonstrated that Eculizumab was an ultra-orphan drug. But was it reasonably priced?

aHUSUK's job was to show how debilitating and life-threatening aHUS was and that Eculizumab offered benefits "beyond price". We had our Patient Voice Report, but we also had five minutes to get the point across too. It was important that every second of the 5 minutes was used and no more. Every word had to count. Three trustees and their families met and spent eight hours designing and developing the talk and its supporting visuals. Run through after run through, words were changed, and times were cut until the optimum was reached. A five-minute talk emerged which said all that needed to be said.

"One of the best presentations we have ever had" said the Chair of AGNSS after the Trustee for patient voice sat down after delivering the talk. A few questions followed and aHUSUK's job was done and from around the room there was a sense that a good case had been made. So much so that when the next speaker got up to speak even, he had to apologise for "raining on our parade". aHUS patients had felt the deluge of their illness, so one drop more made little effect. His talk was about critiquing the evidence, he read his presentation aloud and sat down

We could do no more. The stakeholders including Alexion Pharmaceuticals representatives and Prof. Goodship, left the room. AGNSS went into a closed discussion during which they could call on stakeholders to return for further questions. We did not know what had been said nor decided; we would not know because whatever they recommended would need to be given to Minister of Health, who then was The Earl Howe, to decide on whether to accept their recommendation. We were told it would be put into a metaphorical "black box" until the Minister opened it and made his decision on whether to accept the recommendation or not. We would then know what the fate of aHUS patients would be.

The meeting ended. It was 14 June 2012. We waited.

Chapter 8

The higher you build your barriers

Then came the announcement and the “No decision” conversation in Chapter 1.

To say aHUSUK trustees were incandescent would be an understatement. To keep us waiting for seven months on a decision that AGNSS had made and it had recommended that aHUS patients should receive eculizumab; and to say it was all to be done again because AGNSS was disappearing and to be replaced in April by NICE was deplorable. Appalling.

We were thwarted as there was no right of appeal. A great injustice had been foisted on to aHUS patients in England all because the NHS was to be re-organised and the Health Minister wanted a review on what eculizumab’s “affordability” was and he would use aHUS patients to find out. Another set of hurdles for an unfortunate cohort of people with a rare disease.

The Minister said that aHUS patients who needed Eculizumab could seek “Individual Funding Requests” (IFR). This was the process that had failed aHUS patients to date as it sought uniqueness within a rare aHUS cohort, so it could not be for all. It had created a postcode lottery and much discrimination, even within families. It was why a National Specialised Service was needed and had been applied for and which AGNSS had agreed should be given. Indeed, under the "new” NHS rules, if four patients got IFRs approved for a single therapy it would trigger an application for a National Specialised Service to be considered and approved. That is precisely what going through AGNSS had been about. A suitable plot for a Gilbert & Sullivan comic opera or “Catch 22” type novel.

Furthermore, a bit of news that we had heard a few days before the announcement made us scratch our heads. The NHS had approved a national service for a specialised treatment for a rare disease. A rare

cohort of those suffering from Cystic Fibrosis. We knew that the Cystic Fibrosis Trust was raising awareness for a drug at the same time as us. I had even signed a petition that the Cystic Fibrosis Trust had set up for the drug to be made available, such was our support for rare diseases by then. They were not in AGNSS' programme at that time and so were "behind us in the queue"

Except, once AGNSS had ended, and before they would need to go to NICE, Cystic Fibrosis clinicians, the pharmaceutical company, the patient group and the NHS conspired to develop a bespoke evaluation and funding process while aHUS patients were waiting for the outcome of AGNSS. Within three months it delivered a Specialised Service to be delivered Nationally, but not a National Specialised Service which, of course, it could not be. Good luck to Cystic Fibrosis patients for getting it approved though. It is an awful disease, as bad as aHUS, though perhaps not as immediately life threatening at onset. It did not seem that their drug was as clinically effective as eculizumab would be for aHUS patients, who could now die during their wait. It had been predicted that over 10 could die in the coming 12 months, while waiting for NICE to get ready.

aHUSUK needed to act and would have to campaign, not for the drug to be approved, we did not need to campaign for that because our Patient Voice had done its job, now it was the injustice of a decision-making process for which we had no right of appeal. Our campaign would be our appeal.

There was no right of appeal and the Minister making the decision had refused to meet and talk to us.

Oddly, at around the same time, we heard the results of an application we had made to a large kidney patient organisation, the BKPA. It had turned down our request for financial support because it considered us to be a campaign group for patients, not a patient support group. We were doing both, we had not been political but were advocating for aHUS patients, an extremely small group of

people because of its rarity. Something this industrial size charity could not get its head around at that time.

BKPA would continue to keep large sums of money in its bank account for which reputedly it was getting criticism from the Charity Commission. We needed funds though as publicity for our cause could cost us. One of our members donated to the charity to be used for awareness projects. Along with that came excellent advice because this member had also had experience of campaigning for a specialised service for another rare disease **Pulmonary Hypertension** which affected her family as aHUS had too.

aHUS people were going to die but had no rights to life, and others surviving would be destroyed through injustice.

They had been treated wrong. So wrong

Something inside was getting so strong.

The higher they build their barriers the taller we became....

Chapter 9

Good will come, together?

Before continuing with the UK front, there had been an international development worth a mention which would transform aHUS advocacy not only in the UK but internationally, for all aHUS patients and organizations around the world.

aHUSUK had accepted an invitation from AIRG France to attend its national aHUS Patients Conference two days after the AGNSS meeting on 16 June 2012. Although not as comprehensive as was to be the case in future when reporting about aHUS conferences which I attended, I wrote briefly on the Rare Connect website about the experience:

"*I would like to say thank you for my daughter and me. We too attended the 2nd Conference on aHUS in Paris.*

Professor Hubert Nivet, who made clear issues (about Complement) with his clever analogies and humour, Dr Veronique Fremeaux -Baachi whose enthusiasm and passion for understanding aHUS through research shone though, and Professor Chantal Loire's authoritative knowledge on matters aHUS is plainly evident. So were the other professors and doctors who talked about the treatment of children and adults, as well as the successes of transplants supported by eculizumab. All added to what is a positive and hopeful future for aHUS patients in France and indeed everywhere.

We shall therefore have the same questions, issues, concerns and stoicism in living with aHUS.

Thanks to Daniel (Renault) and Nicolas (Mullier) for organizing a worthwhile and successful conference at this impressive venue that is the Hopital European George Pompidou."

Little did we know then what would come of it but the aHUS patient organisation representatives who attended the meeting from France,

Belgium and Spain as well as the U.K. began to talk about a collaboration between countries. From those preliminary talks a momentum began building in the aHUS social media about some form of international group, culminating in the first meeting of the aHUS alliance in Barcelona eight months later.

A couple of weeks after the AGNSS announcement the first meeting was held of what was intended to be the **Alliance SHUa European,** a subgroup of the fledgling organisation FEDERG. By then aHUS organisations from Italy and Russia had been added to its number.

The meeting took place in the Hotel America in Barcelona. After introducing each other, our organisations and what the status of aHUS was in our countries at that time, a debate took place on what kind of activities could be done better together and whether a European organisation should be formed to do them. Those attending said that such an organisation, a loose affiliation (i.e. not a formal legal entity) should be formed (later amended), and it should not be confined to Europe and that it should be called the **aHUS alliance**. The group was to be associated with RareConnect (a EURORDIS project) whose representative also attended the meeting and whose on-line platform would be used for communication because no alliance website was intended to be constructed. It was on Rare Connect's website that the formation of the aHUS alliance was announced on Rare Disease Day - 28 February 2013.

But could good come from being together?

Chapter 10

What do we need? When do we need it?

Back to the UK and just putting the rhetoric aside for a while, aHUSUK was facing another hurdle but just what could it do about it?

aHUSUK was by then a rare disease organisation with the families of about 15 or so aHUS patients as members. It knew of another 15 or so aHUS patients at least; but they were not prepared to join with us. There could have been the families of another 150 aHUS patients, but they probably did not know what was happening for them, and about them.

aHUSUK had to decide what it wanted, and then have plans to act which would not overwhelm a small, and, it must be remembered, still ill group of people, with little or no resources.

It could not be political; aHUS people are from all sides of the political spectrum. It would be too easy to go to a newspaper which supports an opposition political party to have a go at the political party in power. That be would wrong.

On the day of the Government's announcement about the AGNSS outcome, the aHUSUK Secretary was in the Houses of Parliament attending and talking to a meeting called by the Opposition Health Minister about Rare Disease treatment access. This politician had been banging on for months in debates about how the implementation of Government reforms of the NHS would present high risks to patients. On that day the aHUSUK Secretary was able to give him a newsworthy example of how Government changes had put a small group of patients at grave risk. He did nothing.

Neither did the Health Minister who made the unjust decision and who was not even prepared to meet and discuss his decision with the aHUSUK.

A media campaign was out of the question. We sought advice and were told it would cost us over £100,000 to use media consultants and aHUSUK trustees would have to do a lot of the work. aHUSUK could not afford that.

aHUSUK would have to find a way that reporters and journalists would come to us for free but remembering that the Government and its agencies had public relations budgets of millions of pounds. It would be an unfair competition. Our strength was that we were the victims in more ways than could be imagined.

But what would be our message be about what we wanted?

We wanted AGNSS recommendation implemented

We wanted it done quickly

We wanted aHUS dialysis patients in scope

We wanted to influence NICE from the outset.

With the latter we were conceding then that aHUS patients would be the "guinea pigs" for NICE's new process but in return for that, aHUSUK wanted aHUS patients, there and then, to be treated equitably while the review took place.

We also wanted equity built into what NICE did.

SO, **JUSTICE** and **EQUITY.**

So, our aim was "to get eculizumab right then for aHUS patients who needed it for as long as they needed it"

So then

"What do we need.....?"

"**ECULIZUMAB"**

“When do we need it? "

“NOW"

Repeat!

Chapter 11

The finest hour of the few.

aHUSUK now had a message and had a target audience in mind and some plans for how it would be delivered.

But what started as a four hours a month task at the start had rapidly passed four hours a week and was now four hours a day for most aHUSUK trustees and would now move to 2 to 3 times that for some. We were doing what Public Relations professionals would do but in our case for no pay but just because it mattered very much. (Probably a key test for patient advocacy if it does not matter that much, do not do it).

Members of Parliament (MPs) were our first key audience. Earlier, aHUS patients and their families had been asked to write to them to tell them about aHUS and the AGNSS evaluation of eculizumab. Patients were advised to do that because MPs would have to write to the Health Minister who would have to reply. That correspondence would all go into a "file" at the Department of Health. The replies from MPs fell into the pattern "The treatment is being considered by AGNSS, so they would have to see the outcome before taking further action".

AGNSS recommendation was now known and aHUS patients had been treated unfairly so we asked them to take up the case once more. They did but now there were more than twice the number of letters sent and the Health Minister had to justify why the health reforms were punishing this small group. The "file" had grown considerably, and this was just for a very rare disease patient cohort.

There was another way to make MPs aware and that was through an 'Early Day Motion" which if sufficiently supported could permit the matter to be discussed in Parliament but, if not, would raise some awareness. A motion was put forward by a supportive MP and was supported by some notable MPs. Sadly, EDMs area much discredited

element of parliamentary democracy because ours was in competition with nonsense motions about support for football teams which had been promoted or won a cup competition.

There was one other way to get it into Parliament and one which would be a major challenge and a very high mountain to climb. The petition.

There were two types of petition - written and online

The online petition or e-petition was a formal process run by parliament itself which offered a formal response from the relevant Health Minister, if at least 10, 000 people signed it. It would also be debated in Parliament if 100,000 people supported it. We had supported an e-petition previously submitted by an organisation of aHUS clinicians to raise awareness and which was expected to raise a few hundred supporters. aHUSUK got involved and raised over 2,500 signatures. Not enough but we were told that it was someone's job at the Department of Health to monitor emerging issues and we had got aHUS on to the first page of Health issues and into view.

This time it would be aHUSUK that would be the petitioners and we would need to get many more people involved and get many more to support us. We wanted visibility but moreover we wanted a response from the Health Minister.

The written petition was the traditional democratic process. It could be delivered directly to the Prime Minister to get the Health Minister to act or could be handed over to the Speaker in Parliament by an MP or MPs to go to the Health Minister to respond. We applied for it to be done both ways.

All very well but we had to get signatures. Firstly, we created a call to action portal on our website. Anyone wishing to support the e-petition could be taken directly through to the "signing page" by clicking on the portal button. But we also needed to get people to come to the

site and this was going to take more than newsletters to our members. We also created Facebook and Twitter Accounts.

The social media is a very powerful tool when it comes to gaining on line support. Posts and tweets to primary followers need to be shared and retweeted by them to their followers and so on to other followers if the petition was getting the outreach to get the e-petition signed. It happened on some posts as a reach of 20,000 or more was achieved, not all led to signatures but if 5% or 10% did it would boost numbers greatly. It was also a good thing if someone with a high profile with lots of followers was to support you. The lead singer of Dr Hook (songs: “Sylvia’s Mother” and “If you’re in love with a beautiful woman") Dennis Locorriere gave his support and asked his fans to sign our e-petition.

The e petition began on 26 February and by Rare Disease Day 48 hours later we had already got 1000 signatures. We set ourselves a target to get 10,000 signatures by St George’s Day, 23 April, and “By George we got it!”.

Our petition was in the top three health topics matching topics affecting 100,000 or more people.

The written petition demanded a different approach. It could include those not on line and was easier for all signatories to do. Families were galvanised asked all and sundry to sign the petition, neighbours, parents in school yards, window cleaners and so on. Some grandparents also stood in town squares and asked passers-by and others stood outside football grounds and got 1000s of support signatures.

By 25 March we were booked to present the first tranche of the petition containing 15000 signatures to 10 Downing Street. 6 members of aHUSUK were allowed into Downing St to hand it over. It was filmed and featured on national and regional TV.

aHUS patient Maya knocking on the door of 10 Downing St, London

The second tranche was to be handed over in the House of Commons and split between two MPs who had been asked and had agreed to support us. So another 20,000 to 30000 signature petition was duly handed over some six weeks after the Downing Street handover.

In addition to this, some aHUSUK members had appeared on national and local radio and TV, as well as in national and local newspapers. A small number of aHUSUK members had created considerable noise, all of which was being noted at the Department of Health. It was now May 2013.

It had mattered to aHUS patients and so the few had done it for each other, even for the benefit of those aHUS patients yet to come, even for those who had chosen not to join in the battle.

The aHUS few's finest hour.

Chapter 12

If you want our help, help patients

By May 2013, after nearly three months of campaigning by the "few" and getting the issue to the attention of the Health Minister and Department of Health, two notable events happened.

In April NICE had taken on responsibility for evaluating eculizumab for aHUS but was not ready to do so and it expected to begin its work on eculizumab in December that year.

The e petition response from the Department of Health confirmed this, but also said that in the meantime another NHS group would look at the service to be given as a priority in the interim period.

The NHS had shifted its position and was now prepared for an interim policy to be implemented ahead of NICE. Starting with all new onsets. A newly created Clinical Priorities Advisory Group decided at its first meeting that new onset aHUS patients were a priority for treatment. The first sign of a change of mind but we also wanted to bring aHUS dialysis patients in scope for a transplant. NHS now had to do it via this new group which had been set up in the NHS reforms. Whilst yet another hurdle for aHUS patients to get over there would be no more discriminatory individual funding requests in a post code lottery.

By July 2013 CPAG held its second meeting which aHUSUK Trustee for Patient Voice, along with Alexion and Prof. Goodship were invited to attend and present to the Group (our research document was the basis of the patient's voice, it had been added to and improved upon since the AGNSS meeting, so we were confident it would do the job.)

Immediately after the meeting we were told that an interim aHUS Service had been approved for all aHUS patients, and it would be included in the NHS Specialised Services list for 2013/14. The service would be an interim one pending the review of eculizumab by NICE.

The CPAG meeting was the day after the first formal meeting by NICE to define the scope of the evaluation of eculizumab for aHUS. So, with that we were back to the stage we had reached with AGNSS in October 2011 but with some progress made for existing patients.

It can never be discovered what went on behind the scenes, but this shift was announced following the aHUSUK campaign and the noise created by tens of thousands of people who felt ahus patients had been poorly treated. Even the Health Minister invited aHUSUK to visit him finally (Sylwia an aHUSUK member had telephoned a radio programme which had the Deputy Prime Minister as a guest, and he agreed to arrange a meeting with the Health Minister) and he welcomed our intention to help NICE develop its new Highly Specialised Technology evaluation process providing existing aHUS patients were treated.

aHUSUK would be doing it in the knowledge that aHUS patients known about there and then would have access to eculizumab even those who were trialists and those who needed a transplant.

If NICE turned down eculizumab for aHUS at the end of its review, future aHUS patients, including those on dialysis who could not be transplanted in that time, would not be treated.

Our job now was to help NICE make the right decision that eculizumab should be given when needed for as long as is needed.

Chapter 13

Affordable means able to afford

The evaluation of eculizumab for aHUS was now needing to be carried out by NICE, even though it had already been evaluated and recommended by another group. This was called for by the Health Minister because he wanted a view on whether eculizumab was “affordable” by the NHS for the treatment of a small number of rare disease patients.

Eculizumab had already been deemed an approved highly specialised technology for the treatment for patients affected by Paroxysmal Nocturnal Haemoglobinuria, or PNH; so, the question now really was “was it affordable for aHUS too?”. What had happened for PNH patients was irrelevant. Neither could support to our cause from those PNH patients be expected.

However, it could be said that what was going to happen to us was going to have a bearing on those rare disease patients who were going to follow us in the NICE process. There was a great responsibility on our shoulders.

Affordability. Eculizumab came at a price and NHS England had resources from taxation etc. of over £100 billion, £2 billion a week and rising some might put it. The cost for a small number of rare disease patients was well within its means. So that could not be the test of what affordable means.

The finances and economics of health are both complex and confusing subjects, with inconsistencies throughout, so to get a simple answer for the Health Minister was not going to be straight forward. That was aHUSUK’s worry. An unanswerable question being posed for debate when patients were suffering.

It is at this point that awareness grows that there is no human right to life when it comes to decision processes about providing treatment to

patients. This does not mean that those making the decisions do not care about people, it just means that they are protected from any action against their decision on the grounds of abusing human rights to life, because it is ruled not an abuse. Not many people know that.

Another issue which emerges is the lack of clear thinking on financial and economic terms used. In the time aHUSUK had been involved, and particularly in communications supporting the Minister's decision, we had heard about need for cost effectiveness, reasonable price, wise use of NHS resources, a cash strapped NHS, value for money, value-based pricing. All of which mean different things and are mostly subjective in nature with rarely an acceptable established methodology to arrive at an indisputable conclusion. Cost effectiveness in health economics "science" means lower incremental cost per QALY. QALY has been mentioned before and is a difficult concept to understand. Those defending using cost per QALY as a methodology were apt to defend it from critics by saying "that if you cannot find three flaws in the QALY process you do not understand it".

Hardly a ringing endorsement for using it but the flaws apply equally to all. It is the comparative result between treatments which is important.

But cost effectiveness as determined by the QALY assessment, although egalitarian, does not necessarily mean affordable. Neither would it be equitable, it would only apply to a small fraction of total NHS spend and would be institutionally discriminatory against those needing ultra-orphan drugs. In QALY assessments for aHUS patients their quality of life after treating would need to be 1 on scale of 0 to 1, having been 0.1; or with eculizumab they would have to live in perfect health for 300 years or more. Not going to happen.

aHUSUK would focus on affordability being what the "cost" of treating the aHUS patient cohort would be. That would be determined by the number of aHUS patients there were and what the average cost of

eculizumab doses needed would be. Quantity x Doses x Price. The drug budget.

Following that our focus was on the cost of other uses of NHS resources using the principle that “when escaping from a lion you do not have to run fast, but just need to run faster than others running away”. That is how NICE would be looking at it effectively, in a cash strapped NHS are there other treatments that are less beneficial that could be given up affording the treatment of aHUS patients? The **opportunity cost** as the experts call it i.e. the cost of the foregone alternative.

Thirdly aHUSUK would look deeper into the price of eculizumab and what elements make up its price because for all the academic nature of such health evaluations, the main concern remained “was Alexion's price for eculizumab a “rip off” of ultimately the tax payers who fund the NHS?”. Making profit was acceptable for the sustained availability of eculizumab, but as the market sales grew and costs of sales reduced, and overhead costs fixed, where was that sales growth dividend going?

aHUSUK had come a long way since it was formed with barely anything but a personal knowledge of a family member’s encounter with aHUS. The trustees were now learning about concepts and methodologies used by experts, but without the training and experience of these experts. Armed with common sense and a growing confidence in what to challenge and how to do so, we still needed to punch way above our weight, but do it now in a high-profile formal evaluation process which was being developed in front of our eyes.

Affordable clearly means a lot more than simply an ability to afford.

Chapter 14

One step at a time

NICE was not ready to begin its work on eculizumab when it took over responsibility for the job as part of the NHS reorganisation. It had done no preliminary preparation because the organisation itself was going through change and the outgoing Chair of NICE, who had known about taking on this responsibility for at least 7 months, decided to leave the management of its implementation to his replacement. The replacement would take over from 1 April 2013. No joking.

However, there were several people who had been given the job of communicating the change decision. A meeting had been called with potential stakeholders to explain the implications. aHUSUK had not been invited to attend. This did not auger well as a start.

Having complained about NICE's snub to aHUS patients aHUSUK was invited to meet them in their London office.

Understandably aHUSUK trustees told them that they did not believe aHUS patients should be going through this evaluation again having gone through it with AGNSS. aHUSUK was not happy to do so. The trustees said that aHUSUK did not think NICE would come to a different conclusion. Trustees argued that to remove any doubt it needed to build equity into its process and properly address the affordability question. aHUSUK insisted that getting the NHS to let it be known how many aHUS patients there were and who needed treatment and for how long was imperative. aHUSUK did not believe there was as many patients as estimated which had raised the doubts about affordability.

By then aHUSUK had found out the work on treatment adjustment taking place in a Milan clinic in Italy, having heard about it from the aHUS alliance affiliate from Italy but this was not just what we meant. Just the mix of patients on different doses levels for weight would have a bearing on the actual average cost per patient. Similarly, we

did not believe the projected number of patients within five years needing eculizumab for life was right. Neither was the estimate of existing numbers of patients. If that basic budget forecast was flawed how could affordability be assessed!

We were told NICE would try to devise a methodology for comparing resources on an opportunity cost basis as part of its decision making. However, there was a feeling that this would not be robust. aHUSUK did not believe that the relative societal costs would be adequately reflected. aHUSUK had contacted a Professor Jennifer Roberts of the London School of Hygiene and Tropical Diseases (now deceased). Prof Roberts along with Professor Jennifer Busby of the USA were eminent authorities on the true cost to society of E. coli outbreaks, from their research on typical HUS and its implications. The costs of the alternatives to eculizumab they found were higher than those used in the AGNSS process, including the impact on society. The morbidity and outcome for aHUS patients not transplantable would be higher still. aHUSUK thought that NICE should look at that too. Professor Roberts wanted to challenge NICE but sadly she was seriously ill and died later that year. But we knew what she thought, and it would help.

Finally, aHUSUK asserted that this whole process would be improved if the NICE committee had a qualified accountant on board to give a professional opinion on the profitability of the price of the drug because that was a key determinant in the decision. Health economics was not enough.

So, before aHUSUK got into the process, it had made clear that unless changes were made a similar non-conclusive outcome would be likely due to incomplete evidence.

Another example of aHUSUK's advocacy going beyond just giving the patient voice about the disease. However, for the process it would initially be giving evidence about the illness again. aHUSUK would have to bide its time on the finance and economics.

We will get there just one step at a time.

Chapter 15

NICE Process begins it will soon be Christmas

NICE manages each evaluation as a project. Each evaluation is assigned a Project Manager. A Project Management Methodology is used to plan and control the operation in a logical manner.

The evaluation is broken down into stages and each stage results in a “product”, such as a document which defines the outcome and decisions made.

Each stage has a gathering evidence step, evaluating and decision step and documenting and communicating the decision step and followed by a consultation or quality assurance review step (or steps as the latter can be repeated) before the stage is complete and the project moves on to the next stage.

In April 2013 we heard that NICE would not get to the evaluating and decision step until December 2013, which would be over two years since aHUSUK had been created. None of the trustee advocates had expected that.

Although aHUSUK was also preoccupied with the Clinical Priorities Advisory Group, we began the NICE process by responding to a request to comment on the scope of the “eculizumab” project. We answered the questions posed and then attended a meeting on 13 July at NICE’s office. We were shocked by the numbers attending the meeting; NICE tended to make its consultations public affairs. Anyway, it seemed that aHUSUK had responded with the most detail and the conversation mostly addressed our views.

The initial stage of the NICE evaluation began with this scoping stage -where it establishes and defines what they are going to examine and how they will do it.

They decided: -

- they were reviewing eculizumab;
- to be used for treating atypical Haemolytic Uraemic Syndrome;
- and compare it with other treatments including plasma exchange and dialysis and combined liver/kidney transplants;
- they will gather clinical and economic evidence from the manufacturer;
- they will gather patient impact data from the patient organisations;
- the evidence will be gathered in a format they have devised for the Evaluation Group led by Prof. Jackson;
- evidence will be gathered over the next eight to eleven weeks;
- NICE will only meet with evidence suppliers if they need to test understanding or seek more data;
- Otherwise the next meeting will be on 11 December 2013 when the NICE HST Committee meets to make its decision.

So aHUSUK now had to complete its Patient Voice Submission in less than two months, which in effect meant improving the original AGNSS submission by adding the Welsh Patients testimonies, the data gathered from a Survey Monkey and for other meetings, including CPAG. It was hoped that members, including those from Scotland, would continue to feed into the process and make it a very compelling document.

The meeting was a very positive experience because the NICE staff were keen to develop an ultra-orphan evaluation methodology, and so many clinical experts, who attended, were very supportive of eculizumab for their patients.

Looking back, it seemed that despite how much we had developed as a patient group, our understanding of aHUS within the context of all thrombotic microangiopathies was just beginning. Such knowledge would have benefited the trustees more in understanding potential patient numbers for inclusion in the scope for treatment. aHUSUK

would know now that it was only those TMAs that were “Complement mediated" which should be in scope, not other secondary causes of aHUS, thereby reducing the costs to be afforded. Although there are overlaps between categories that could extend scope.

With the scope defined, the next step would be supplying evidence of what it is like for those affected by aHUS, that evidence was called for in late July and had to be completed by 9th September. Less than two months. Fortunately, aHUSUK already had its evidence. Indeed, it had improved it with interviews of 4 Welsh patients/ carers. Doing it ourselves revealed how hard a job it was to interview and record participants. Then transcribe the interview word for word before analysing the thread of the discussion to determine unique or confirming comments to use, and specific "sound bites" to make the point in a memorable way.

Except NICE had decided to use an on-line questionnaire for patient organisations, but when aHUSUK tried to copy and paste the content of our evidence research into the relevant questions, the system crashed. aHUSUK was providing "too much" evidence but to precis it would ruin and diminish the work it had done. aHUSUK was going through an unprecedented third evaluation process which was not of its making. The trustees complained to NICE and it was agreed that aHUSUK would map and cross reference relevant questions in their form to the sections of our research document, and we would append our full report to read. That plus some administrative details and closing comments was our submission and it was provided on time.

The next step in the evaluation process would be the holding of a meeting of the Evaluation Committee. aHUSUK would be expected to attend. Indeed, two representatives were allowed, and it was decided that I and another trustee, who had been an eculizumab trialist, would provide any additional answers for the Committee at this meeting.

NICE, unlike AGNSS, did not want a presentation, so aHUSUK had no control over what its representatives would expect to say. A list of

possible points needed to be got across when an anticipated relevant question was posed. Its representatives would answer the closest question prepared for but not necessarily the question asked! All the contact with politicians was now rubbing off on us!

Eventually we were advised that the Committee would hold its meeting in public, unlike the AGNSS meeting at which only stakeholders attended along with the Committee.

It was scheduled for 11th December 2013 and the result would not be known until 2014, but with an intention to complete the project by July 2014. A year on from the scoping meeting and nearly three years since aHUSUK was created.

In that time an additional 75 English patients were likely to have onset with aHUS most of whom would not have known about the illness they had. At least now they had the safety net of the interim service.

Another Christmas was to pass before aHUS patients would see the outcome of what some had come together to achieve.

It was not be a foregone conclusion and our anxiety about having to do this again was evident in this extract from a press release by the charity.

aHUSUK GOES TO NICE: Press Release

Ahead of its appearance at NICE when eculizumab will be evaluated again, aHUSUK has released the following statement.

PRESS RELEASE FROM aHUSUK (www.ahusuk.org)

Anxious Patient Group calls on NICE to approve only drug treatment for ultra -rare disease

Fight for treatment over three years – NICE Committee in the spotlight as it evaluates first ultra-orphan drug

On 11th December the National Institute for Health and Care Excellence's (NICE) First Appraisal meeting is taking place to judge whether eculizumab should be recommended in England as a treatment for the ultra-rare disease atypical Haemolytic Uraemic Syndrome (aHUS). National commissioning of this drug for the treatment of aHUS was recommended in June 2012 by the Advisory Group for National Specialised Services (AGNSS) which stated, "It is clear that eculizumab is an effective treatment for aHUS and gives a much better quality of life than the alternative treatments". Patients' elation turned to horror when, following this recommendation Health Minister, Earl Howe, unilaterally decided that the drug should not be made available to sufferers, but must undergo a further evaluation by NICE, the first time NICE has ever had to approve an ultra- orphan drug for a rare disease. Eculizumab has already been approved for treatment of aHUS in forty other countries and is even commissioned nationally for another rare disease in England.

Sufferers of aHUS have been living in a state of limbo. Some have been able to access the drug, through interim funding measures and clinical trials, and are waiting anxiously to hear if they will be able to continue to take the drug and lead a normal life, or whether they will have to revert to previous treatments such as plasma exchange or much worse, be condemned to renal dialysis for the rest of their much- shortened lives. The fight to get any access to this life changing treatment has been hard – in March and May of this year we delivered petitions to Downing Street and the House of Commons calling for everyone to be able to have access to this miracle drug.

"Eculizumab is the only treatment for aHUS. Everyone, including ministers, NICE, AGNSS, CPAG and clinicians in the field, agrees that it is clinically effective. Dialysis and plasma exchange are ways to manage the disease but with this management strategy aHUS

sufferers cannot work, cannot travel far from hospital and must endure horrendous treatment side effects. Eculizumab allows sufferers to live a normal life, to work and contribute to the economy. We urge NICE to think differently when it comes to payment for and commissioning of treatments for very rare diseases that have devastating effects on a few sufferers. We trust that its Evaluation Committee will show it can make well-rounded decisions for rare diseases, like its highly regarded predecessor, AGNSS, and will not condemn all aHUS patients to horrific and foreshortened lives,". Ian Mackersie, Secretary of aHUSUK Patient Group.

"Our lack of confidence in the process of approval for this drug, given it has already been approved by two previous evaluations [AGNNS and CPAG], has meant we have had to fight publicly to try to ensure NICE does the right thing. The treatment is life transforming. aHUS patients previously had no light at the end of the tunnel, now they do. Surely, they too deserve the right to get the very best care available today. NICE can take that bright horizon away from us and we cannot let that happen. This is a heavy burden for aHUS sufferers and their families to shoulder in addition to coping with living with this terrible disease". Emma Woodward, Trustee, aHUSUK Patient Group.

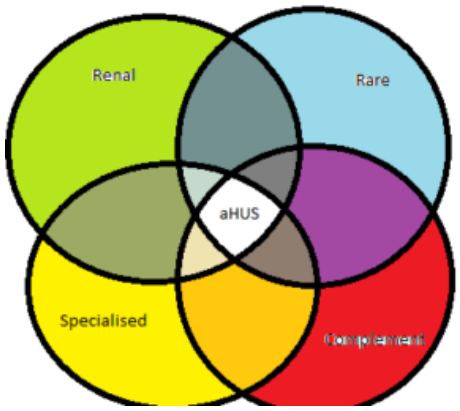
Chapter 16

And keep those plates spinning while you are at it

Our NICE evidence was submitted on 9 September 2013. The day after that it was the second anniversary of the forming of aHUSUK. That day we heard that the interim aHUS service recommended by CPAG had been ratified by the NHS Board. It would be three months until the next NICE meeting.

Time for a rest. Not so.

Two years after its creation aHUSUK was very active in the communities relevant to aHUS - Renal- Rare/Genetic -Complement- Specialised Health Services. The reports on aHUSUK's website in that period reflect that.



-The charity was invited by the Bio Industries Association, or BIA, for a "breakfast meeting" in the House of Commons with politicians, pharmaceutical industry and health organisation representatives. aHUSUK, uniquely, able to comment on an experience of going through two evaluation processes for a treatment for our illness AGNSS and NICE. It was interesting to hear the industry's side of matters and their commitment to and investment in research; and one statistic was very surprising. Of the €70 billion invested in research into developing medicines for rare diseases, €60 billion is invested by

the US government and its Pharmaceutical Companies in almost equal measures and a creditable €5 billion by academia/patient-based charities. Leaving just €5 billion to be spent by the governments and others in the rest of the world. If true, rare disease patients depend a lot on the USA. Makes you think.

-We attended the first public meeting of a new major project for cancer and rare diseases. ***The 100,000 Genomes Project.*** Its aim was to undertake full genome testing of 100,000 patients in England. This was being done to find possible genetic causes of their diseases. aHUS was just one such diseases that had a genetic cause. However not all genetic reasons had been discovered. Nearly 40% of those tested were found to have no known genetic mutation. The meeting was held in the Great Hall of St Bart's Hospital, London. Its walls were covered with 18th century murals painted by William Hogarth, another historic and impressive building visited as a patient advocate. aHUSUK was fully supportive of this project even though aHUS patients would be a very small number of potential participants.

- aHUSUK had been asked to join the Rare Disease Group for aHUS. This was an initiative led by the UK renal professional body "The Renal Association" and funded by major renal charity organisations like Kidney Research UK. The group's task was to set guidelines for the diagnosis and treatment of aHUS.

It also provided encouragement for research into the disease. It was chaired by Professor Tim Goodship.

- We also attended the annual meeting of Complement UK, an organisation set up to develop knowledge and understanding of the Complement system and its impact on diseases such as aHUS. That meeting was an eye opener in so many ways not just from the presentation on aHUS but also how different mutations in different components of Complement led to it having too little or too much activity which results in a spectrum of diseases. Complement plays a part on its own or in conjunction with other parts of the immune

system in diseases such Alzheimer's, Multiple Sclerosis, Parkinson's, Antiphospholipid Syndrome, Age Macular Degeneration, as well as renal diseases like Lupus, MPGN and aHUS. ***Complementology*** could be an important specialism in the future!

- Soon after aHUSUK attended a meeting about all Renal Rare Disease Groups in Peterborough to develop a cross group understanding and support. Inspired by one patient representative attending that meeting it led to an aHUSUK research fund raising project. But that was one for the future.

- aHUSUK thoughts were also turning to the next Rare Disease Day, to a project to create an artwork to be revealed on that day, the "Raise Your Hand" was seeking the names of 2,000 patients to be a "named hand " and aHUSUK was encouraging as many aHUS patients and carers as possible to join in and show support.

- aHUSUK had given evidence to the Scottish Government about how health technologies for cancers and rare diseases were evaluated. The work of the Scottish Medicines Consortium, a sort of NICE for Scotland, had been studied by a Government Committee which had been set up following petitioning by the Rare Disease Community. Most drugs for rare diseases had been turned down by SMC, unlike those for common diseases. That Committee had submitted its report. The Scottish Government was consulting stakeholders on its proposal for change. aHUSUK provided its views.

- As was the case in England and Scotland, NHS Wales was also re-evaluating its processes for highly specialised technologies undertaken by the Welsh Strategic Health. aHUSUK were invited to attend a focus group meeting to provide feedback to the task group which would be reporting its recommendations to the Welsh Government. It did begin to seem more than coincidence that all UK health authorities (Northern Ireland would follow what was happening to NICE) were suspending, reviewing and changing their

process just as Eculizumab for aHUS had entered or were about to enter evaluation.

-Genetic Alliance UK were working with the NHS and NICE to design a "Patient's Charter for the appraisal of rare disease treatments" As aHUSUK had experiences of AGNSS and uniquely NICE too we could contribute a lot to the discussion, although with great care as we were in the NICE process.

-three trustees attended the Annual General meeting and Conference of the National Kidney Federation and stood a table in the exhibition area to raise awareness about aHUS and its kidney patients.

-Of course, the charity itself had to be administered and the third general meeting was held in Solihull in the centre of England to make travel more equidistant for those in all regions. Apart from the administrative part of the day, including the "Treasurers Report", a role I had been volunteered for. Part of the day was given over to a conference about aHUS. Prof Goodship continued to give his support with updates about developments in aHUS. The conference was also addressed by Phyllis Talbot a director of the USA's not for profit patient group, ***The Foundation for Children with atypical HUS***. She did it while driving with her family from her home in Atlanta to Baltimore for Thanksgiving and it was via Skype, projected on to a large screen. A technical feat only spoiled by a hitch when the connection was lost at the end and before she could see the standing ovation she received. aHUS was a small world and aHUSUK's outreach to other countries' patient groups was growing.

Indeed, there was much to do still, and this period illustrates how running a charity made more and more demands on its volunteers and their time

Keeping plates spinning just while we were at it.

It being the main aHUSUK objective to get eculizumab approved free for all patients when they needed it for as long as they needed it.

Why would anyone be reluctant to do all that?

Three months passed quickly and soon it would be the 11th December 2013

CHAPTER 17

11th December 2013 (Part 1)

It was a cold, crisp and frosty morning in Manchester in the north of England on 11th of December 2013. Above the sky was vivid blue when it could be glimpsed through the fog that shrouded much of the UK that day. Road conditions were poor as I set off to the city.

Once inside the NICE office in the centre of Manchester, we were taken to the 20th floor of the Tower and the view confirmed that, above the fog, the day was bright and clear into the distance; but all the well-known Manchester landmarks were invisible.

The Evaluation Committee meeting began with the Chair explaining how the meeting would run. After introductions and declarations of conflict of interests the witnesses were addressed in turn. Giving evidence, apart from ourselves, was Prof. Tim Goodship and a Dr Rodney Gilbert from Southampton Hospital, the NHS Specialised Services leaders (including Dr Edmund Jessop, 2019 Winner of EURORDIS' "Policy Maker Award"), and a team from Alexion. The academic guys from Sheffield University, who were expert in health economic evidence critique, were also there. The Evaluating Committee was made up of clinical experts from a range of medical roles, some lay members, and was supported by officials from NICE itself, some of whom we had already met.

No patient presentation had to be made, instead one of the Evaluation Committee's lay members summarised the case from our patient submission. His conclusion was the evidence was “rich and robust” and that “it made a compelling case for a call on NHS resources”.

WOW! The only issue now was that I and the other patient representative said nothing that would detract from that view! The only criticism of our report was that there not enough stories about patients who had received eculizumab. That was true, but few had

accessed it so far and only some of those who were trialists were known to us at the time.

It had been difficult to find aHUS patients, as we had told NICE at the outset. Eculizumab had not been approved so by definition such patients were few and far between. However, my aHUSUK patient expert colleague was a recipient of eculizumab but was not included in the report as it had been completed before she joined us. She was able to tell the Committee how ill she had been with loss of kidney function and needing dialysis after plasma exchange became less and less effective. She had been included in the eculizumab trial and was given doses of the drug. Soon her aHUS came under control and she recovered some kidney function. She came off dialysis and began to feel better. With better health she returned to work and got married. She was also starting a family. That is what eculizumab can do.

When asked for any concluding comments I remembered what my daughter had said at the first AGNSS meeting. Eculizumab for those on dialysis meant FREEDOM. *Freedom* from living a life around a dialysis machine, *Freedom* to eat and drink as we all do, *Freedom* to work and have a full life again. It goes without saying that those newly onseting would no longer need to know what that aHUS dialysis life would be like.

Unexpectedly the expert from Sheffield University in his critique mentioned an article on the aHUSUK website about a visit to Milan to find out more about the pioneering work of Dr Gianluigi Ardissino in adjusting and tapering the doses of eculizumab in his patients, and with some withdrawing from treatment once stable. This of course meant, unlike the “licensed full dose for life” on which the Committee had to consider the drug, that the average cost per patient would be much less. We could not have brought that up, it was not part of our evidence, but now it was part of the discussion and some doubt about the true treatment cost had crept in. Eculizumab when needed for as long as needed. It should not be wasted at that price.

The morning session went very quickly and there was a break for lunch. The meeting was going very well. In part of the afternoon session Alexion was asked to talk to the Committee without anyone else present; such was the commercially sensitive nature of the talk about its price for eculizumab.

It was a relief when the meeting ended and “witnesses were released”. I do not know if it had been the coldness of the day or the dryness of the air-conditioning, but by the beginning of the afternoon my voice was disappearing and became croaky! Maybe it was nature's way of saying “shut up and say no more, the patients' voice had already done its job”.

The Committee would spend the rest of meeting making its decision in private. Our main concern was about what Alexion had said during its closed session, it could be very detrimental.

We had been told that the next step would be the release of the Evaluation Decision document (the “product” of this stage). It was likely to be published sometime in late January 2014 (after our third Christmas as a charity).

Personally, none of that seemed to matter to me for now because during the lunch session a message had got to me (I was not one for mobile phones!). It was from my wife. The hospital had called. There could be a kidney for my daughter.

There was no rush!

CHAPTER 18

11th December 2013 (part 2)

It may seem odd that on the very same day that NICE was making its decision on whether eculizumab should be made available for aHUS patients throughout England that my daughter could be about to receive it to support a kidney transplant.

Some might say that this was because of the CPAG decision to extend scope of eculizumab to dialysis patients. That was a possibility.

Except my daughter had been called as a potential recipient twice before. Those calls came before the CPAG decision. On those occasions the kidneys were thought to be too marginal for her and they might have been donated to the "reserve patient" . Reserves are always called up and many are disappointed and stand down.

So why had this happened at all?

Our knowledge about eculizumab's existence went back to before 2004. We were not told its name but in passing in the hospital corridor her transplant surgeon from her first transplant mentioned to my daughter that something was coming which could be of help. In 2004 work began for a transplant listing but was stopped when a doctor said that he would seek Prof. Tim Goodship's advice. Nothing more was heard, but at every clinic she asked how the listing was going, only to be told that her notes said that this doctor was still looking into it.

My daughter had not been put on the transplant list before her first transplant, that same doctor from the near derelict hospital she was treated had failed to do so. So, her first transplant was with a kidney donated by her mother. That was on the Thanksgiving Day 1999. By Millennium Eve the decision was made to remove the failed graft. aHUS recurrence was the cause, but it was clear the clinicians treating her had no idea until we told them that it was a possibility and that she should be given plasma exchange. We were ignored and

dismissed. But we continued and eventually she was given fresh frozen plasma, and not PEX, to treat the TMA. Although they now, looking back, very recklessly, zapped her whole immune system for rejection, putting her at risk of infection, it was too late. It then emerged that the promised management of her transplant between the derelict hospital and the one where the transplant took place had failed because of politics between two organisations which were going through a managerial change.

Had she been on the transplant list the fact that the graft failed within six months, it did not last 6 days, would have meant she would have retained her waiting time credit, which would be important in a future allocation decision, all other things being equal.

Even if she had been put on the transplant list in 2004, she would have accrued 7 years waiting time credit. When we asked Prof Goodship at the Wimpole Street meeting in 2011 what would happen to aHUS patients who had not been on the transplant list. He said they would go to the bottom of the list. So even if a decision was made to provide eculizumab my daughter could be looking at a further five year wait. That seemed unjust as those aHUS dialysis patients who had been listed but suspended and not transplanted (which was protocol) could have accrued enough time to be top of the list when their temporary suspension was lifted. What should be a fair and just system of allocation was, in practice, flawed.

So, when we left that first aHUSUK meeting in London we were determined to address that injustice. For that we had to switch to private patient engagement advocacy.

We began by writing to the hospital quoting the six-month rule. We were told with some certainty that would only apply if someone had been on the kidney donor list. Correspondence continued until we asked whether it was accidental (negligence) or deliberate (wilful) she had not been treated fairly by that Doctor. The correspondence continued and escalated through 2012 so by the end we were having

to write through the Chief Executive of the hospital such was the nature of the "complaint" it had become.

The hospital was saying that it was my daughter's fault she had not been listed because someone had written in her notes that she had said that "she had not wished to go **BACK ON** the list". It was that "note" on which the hospital was defending its position. But when we pointed out she could not have said that " because she had never been **ON** the list" the Hospital relented and agreed to approach the donor list authorities to put right her waiting time and it did.

Private patient advocacy can work but it is not easy. It takes an enormous amount of time to do (and we were also active in public advocacy). There can be much resistance to your view, however right you may be. It also emerged that the doctor who everyone thought had been reviewing the advice for now eight years had not been at all but had neglected to tell anyone. All this could have been sorted out years before if communication had been to professional standard. The precedent of relisting, with waiting days credit, having been set would change the policy and benefit all aHUS similarly affected.

The other factor that may have had a bearing on the call up before eculizumab was approved for dialysis patients, was that during the correspondence with the hospital one doctor said that we should apply for an Individual Funding Request, IFR, for eculizumab. No IFR had been approved for an adult aHUS patient, and certainly not one for an adult aHUS dialysis patient. But we agreed to try and were asked to make the case so the hospital could make the request. I remember it took two days of research and draft rewriting to produce a two-page case of why an IFR should be made in my daughter's case. We were confident after we gave it to the hospital when the hospital staff told us that "no one at the hospital could have made the case as well as we had done", but the application went ahead.

This was all happening concurrently with the "reorganisation" of the NHS which was taking place in 2013 and decision-making committee

structures were changing. The same reorganisation which had forced eculizumab to go to NICE for re-evaluation. We waited and waited. Our MP had become involved and was prompting the decision-making group for a decision. Finally, it was approved in May 2013 and with my daughter's waiting time credit given too, the transplant work up which began in 2004 was concluded in June 2013.

It had not been an easy journey.

Very soon after the donor listing confirmation letter, the first call came. Then the second and now the third call.

Would this be the one?

CHAPTER 19

11th December 2013 (part 3)

There was no rush!

Strange how the media portrayal of transplant stories is of a quick action drama, with blue lights flashing, does not seem to be so in the real world.

I finished the NICE meeting. My wife and my daughter went to watch our grandson's school play as previously arranged. My daughter had been to the hospital for the usual pre- transplant check for antibody compatibility etc.

Until the "go ahead decision" it was not thought odd that a prophylactic eculizumab infusion had not been done as per protocol for an aHUS patient transplant.

In the early evening she returned only to be told she could go home to wait and return in the early hours of the following morning. There was going be a transplant.

Our family went to the hospital as requested at 2am and got settled into a room on the transplant ward. Still no eculizumab infusion and we began to mention it to the staff who seemed unconcerned. Then we got the news that she was to be next in theatre and a porter would arrive soon to take her down to theatre.

We were alarmed after all the time spent getting access to the drug, she needed no one seemed to care that she was not to be given it. I spoke to the Sister in charge of the ward and told her that according to protocol my daughter was to receive eculizumab before surgery. With the usual affront to being challenged I was told that they knew what they were doing, they did it all the time. I pointed out that was not the case as this was the first UK cadaver donated kidney transplant supported by eculizumab ever, so this was different.

It made no difference they would not listen. In less than 24 hours I had been relegated from an expert witness being listened to at a NICE meeting about aHUS and eculizumab, to being a numpty over anxious parent who did not know what he was talking about. Yet I was the one who knew what the official clinical protocol was. I was on a committee that had established it.

This demonstrates that no matter how detailed and correct a clinical protocol can be decided upon by experts and eminent medical practitioners, it could all be for nothing in practice, let down by the weakest link in the delivery chain. That Sister, that night, was the weakest link. She did not know she was, she was used to the common routine not the rare and innovative. No one had told her. Now she would not listen.

We were as we were in the first transplant in 1999. *"Plus ca change plus c'est la meme chose"*

Except there was a new interim aHUS Expert Centre in Newcastle. aHUSUK had designed a patient card with contact details. We got the telephone number from it and asked to be helped. Within a few minutes we had a call back, it was Prof Tim Goodship he was on duty I had only seen him less than 12 hours earlier at the NICE meeting.

We told him what was happening, and he said he would contact the hospital.

Meanwhile the porter arrived, and my wife confronted the health care staff refusing to let our daughter to go to theatre until Prof Goodship had spoken to the hospital.

Time passed and then we heard that her operation had been rescheduled and that the pharmacy had now been asked to supply the drug. After nearly 13 years of waiting it is hard to believe that we would ever put anything in the way of a transplant but that was what we had been forced to do.

The drug came eventually, and infusion begun. It had not finished infusing when another porter came to take her to theatre, so off she went with the saline drip following her trolley.

Now the situation changed as it became what all families facing a transplant feel. Would the operation go well? Would the grafted kidney work? The risk in recovery while immunosuppressed and the regime of medicines to take daily (transplant patients in the media never seem to have to face that most dramatic of changes).

That is all aHUSUK had ever wanted for aHUS dialysis patients. Just to get them on a level playing field with other transplant patients. We knew that life with a transplant came with baggage, but it was nothing like the burden of dialysis. Even the two-week eculizumab infusion for life was more endurable than sticking needles in arms five or six times a week to link up to a dialysis machine. It was to be freedom as the Trustee for aHUS Patient Voice, who was now in theatre, had said

But at that time for the reluctant advocate it was just about sitting and waiting for the operation to be over. When all had been said and done that had led to that moment, that other realisation enters transplant patients' thoughts. Someone somewhere had lost their life today and their family were having the worst day of their lives.

They would be remembering those 24 hours for a much different reason today.

11th December 2013 - a bitter sweet day.

Chapter 20

Advocacy Lessons Learned So Far

By Christmas 2013 it was over two years since aHUSUK, and my part in it as a reluctant advocate, had begun

What had been learned so far from my experience of patient advocacy for aHUS?

- No one wants to be a volunteer but sometimes circumstances thrust it upon you
- If you must advocate, have an important reason, particularly a personal one to do it
- Find like-minded people for the cause as their support is essential, whether in your own country or abroad
- Learn about your subject, not just your own circumstances but also the journey of others
- Learn skills you do not have, it is sometimes very easy to do so when you must use them
- Understand the processes you must follow, become expert in them and try to keep one stage ahead
- It is not just about emotion, you are in competition with others just as badly off
- Decision makers need evidence, evidence in your favour is king, gather it
- For evidence against what you want, raise reasonable doubt about it if all else fails
- Have simple plans to follow
- Be prepared to change them if something new happens
- Develop your voice and be confident in using it
- Do not be afraid to challenge wisely and take calculated risks
- Develop a core message about what you want and repeat it
- The internet is powerful but use the social media sparingly and keep to the point

- Be patient, try to work smarter and not harder, you have more time than you think
- In their moment, ordinary people can achieve extraordinary feats together
- However sometimes people will let you down, their perception may differ
- Keep a sense of humour there will be dark times when you think you are losing
- And if the “wearing a tutu” is an option offered -TAKE IT! None of the above will then apply

Chapter 21

What will their fate be?

The NICE evaluation meeting had taken place in December. aHUS families in England entered January 2014 with the uncertainty of their fate and what NICE would decide and tell us later that month.

Unsurprising as we learned by then, we soon found out we would not find out in January as NICE announced the following to participants:

"Dear Consultees and Commentators

Highly Specialised Technology Evaluation

Eculizumab for the treatment of atypical haemolytic Uraemic syndrome (aHUS) [ID703]

Following the Highly Specialised Technology Evaluation Committee meeting on Wednesday 11 December 2013;

• If an Evaluation Consultation Document (ECD) is produced, this will be sent to consultees and commentators in the week commencing 17 February 2014

• If a Final Evaluation Determination (FED) is produced, this will be sent to consultees and commentators in the week commencing 10 March 2014"

The two documents needed some explanation.

The Evaluation Committee make its provisional recommendations in the Evaluation Committee Document, ECD. An ECD will be produced only if the recommendations from the Evaluation Committee are restrictive. A restrictive recommendation will be one that is more limited than the instructions for use that accompany the technology. Consultees and commentators have four weeks to comment on the

ECD. The ECD is also made available on our website so health professionals and members of the public can comment on it.

The Evaluation Committee considers the comments on the ECD if produced, then makes its final recommendations in the Final Evaluation Determination document FED on how the technology should be used in the NHS in England. Consultees can appeal against the final recommendations in the FED.

So, if an ECD is issued it would not be the end of the matter. If it was to be a FED it would be the end, one way or another, subject to appeal.

We subsequently heard that any ECD would be released in the week commencing 24 February.

That made us think.

As part of our involvement in NICE, aHUSUK had to sign a confidentiality agreement and it prevented us from revealing anything in the public domain about what we had been told for seven days after we had been told.

The earliest we could say anything to aHUS families about the result of an ECD would be 3 March, three days after Rare Disease Day 2014.

The Rare Disease community was wary about NICE's involvement in these decisions. Would a "not re commended" decision not be palatable in the Rare Disease community at a time of heightened awareness?

A negative result would not go down well on Rare Disease Day. Better for Government for it to come after March 10th for a Final Evaluation Decision would mean nothing would be heard by Rare Disease Day.

The wait continued, it looked like our fate was certainly not to end soon.

CHAPTER 22

Awareness break though?

A large part of patient advocate's job is about raising awareness of their illness. This is particularly true of rare diseases which few people get, and few people know about. After all most aHUS patients had never heard of aHUS until they got it themselves. Many would not even be aware of Rare Diseases.

aHUSUK had done so much to raise the profile of aHUS and had notable results in the political arena as well as the media, TV, Radio, Newspapers and Magazines.

Within in a few days of her transplant in December my daughter had been filmed in our house for a news item about organ donation and the need for families to have a conversation about what they wanted to happen just in case it should happen to them.

Even so it was an enormous surprise when a story line about aHUS featured a long running British Saturday night "soap opera" called "Casualty". Based on a fictional hospital in Holby City (somewhere in Southern England, although the series is filmed in Welsh Studios) each episode has two or three intertwined stories about medical conditions told in a dramatic way.

On 18 January 2014 aHUS was one of the medical conditions to be featured. It was about an aHUS patient Emily, or "Em" as her family called her. This synopsis of the aHUS story line was posted on the aHUSUK website the next day.

aHUS "CAR CRASH" CLIFFHANGER

In Saturday's episode of BBC's Casualty, a 21-year-old girl (who we find out had experienced what we know to be the "car crash" of aHUS),

became a victim of a "Casualty Car Crash". The story of Emily, who had been a dialysis patient for 18 months, had begun that day, her 21st birthday, with a hospital appointment at which it was decided that she would receive a new kidney from her sister, Nina.

A limousine then takes Emily, who is very non-compliant with dialysis treatment, and her sister to her birthday party. During the journey, because of an errant popping of a champagne cork the limousine ends up in the predicament hanging off a bridge.

It was while the Doctors were preparing for her rescue and her recovery that it became apparent that Em had a rare genetic disease called atypical Haemolytic Uraemic Syndrome and she was "one in million".

Both sisters are rescued.

They end up side by side in a Casualty Ward in A&E (ER), where concern about Nina's kidney function deepens because one of her kidneys may have been damaged in the crash.

Just as you might be becoming increasingly concerned about an aHUS patient receiving a transplant without a complement inhibitor; the girls' mother reveals that a drug had been approved to enable a transplant to happen.

But then she said after "18 months of hell, tests and diagnosing and waiting for the drug supported transplant may not go ahead…….!"

We never heard what happened to Em and her sister, but it was good to know the drug had been approved. Although at that date aHUSUK was not aware that it had!

Chapter 23

Rare Disease Day 2014 Across Borders

aHUSUK support for Rare Disease issues had grown each year. By 2014 it had reached a pinnacle for such a small organisation.

We were present for the unveiling of Alexion's "raise your hands " artwork in London. aHUS patients and carers had participated in it.

We attended all the Home Nations' Rare Disease Day events in their parliaments. I attended the one in Northern Ireland although sadly it was not to be held in Stormont, the home of the Northern Ireland Assembly.

Held in Queen's University Belfast, and with the theme "Joining together for Better Care", on Rare Disease Day 28th February 2014, the conference was attended by several hundred rare disease patients and patient organisations from both the North and South of Ireland.

Early in the proceedings the Health Ministers from both administrations gave talks about their respective Rare Disease Implementation Plans.

Edwin Poots, MLA, expressed determination to make things happen but was pragmatic and that it would be a matter of "incrementing progression" over time.

Alex White, TD, outlined some of the Rare Disease infrastructure being put in place, like the National Office for Rare Disease in Dublin. By the time it was opened in June 2015 he had been replaced as Health Minister by Leo Varadkar (future Taoiseach), and eculizumab had been approved for aHUS the preceding February.

aHUSUK was by Rare Disease Day 2014 aware of a small number of aHUS patients in Northern Ireland as well as several aHUS families in England with familial links with areas in the South West of Ireland.

Before I left my hotel for the conference, I was interviewed live over the telephone by Radio Wales about Rare Disease Day. This led to me talking about my family in a part of Swansea, a city in South Wales. The penetrance of aHUS in my family meant that they dominated the Welsh aHUS patient cohort. aHUS in my family had come from England.

Both Irish Health Ministers saw cross border collaboration as very much needed to make a difference for those with rare diseases.

I could identify with that on Rare Disease Day 2014.

Chapter 24

No one said it would be easy

aHUSUK had received the Evaluation Consultation Document the week before Rare Disease Day and it participated in Rare Disease Day events knowing what it knew, but not able to say anything in public. Patients remained unaware of NICE's decision,

"NICE were minded not to recommend eculizumab for aHUS."

The prime reason was Alexion's inability to explain why the price for eculizumab was as it was.

aHUSUK could not imagine that a company like Alexion had no clue about why its price was as it was, but trustees were at a loss to understand why it was unwilling to explain itself. Despite assurances that it would do all it could on price for use of eculizumab for aHUS, Alexion had failed. Transparency is important in-patient centricity.

The clinical and patient case had been made. Alexion did little different to what it had done at AGNSS. It had not made an offer for a patient access scheme nor was it able to explain its price. An accountant could easily explain it. It is what we said to NICE at the outset.

aHUSUK was as baffled by this outcome as it was convinced that as a patient organisation, it could not have done more to make its case. NICE had told us, as did AGNSS before it, the patient case was made.

aHUSUK was dissatisfied with the way aHUS patients had been treated by our health authorities over the past two years. aHUS patients would be devastated at hearing what NICE is now telling them.

aHUSUK was back to where it started and was having to keep that a secret for a week. It built up our frustration and annoyance. aHUSUK was unhappy with both Alexion and NICE.

I was invited to talk through the decision with the NICE patient engagement team in early March. I said before I left for the meeting that if NICE wanted to say “no” patients would be facing a Final Evaluation Document at this point so maybe it was a case of "needing to read between the lines”.

At the meeting I think I was as forthright and angry as I felt aHUS patients would be about this latest hold up. The explanation I got from NICE was to "read between the lines". I left assuring them we would do all we could do to lobby Alexion to concede what aHUSUK had implored them to do on price. I also said that we would challenge the figures being used by NICE to question the affordability of aHUS patient treatment.

Reading between the lines, NICE would wish to say "yes" but needed more reasons to justify doing so. Those reasons relied mostly on Alexion.

NICE said there would be another meeting in April after the formal responses to the ECD had been received from all.

So, this was now set to go on and into the Summer.

aHUSUK view on it at the time was:

“*Drawn out over almost two years, three separate evaluations have been carried out of a drug that everybody admits is clinically wonderful and life transforming. Has any other group of patients ever been put through such an ordeal and had its hopes raised, then dashed, then raised again now dashed again? And all the patients have done is to be unfortunate enough to have a rare genetic condition.*

Fortunately, we had CPAG’s Interim Policy because, without it, what had happened to aHUS patients would have been unbearable. Although it is yet to be confirmed by NHS England, whatever NICE’s final recommendation is to be the drug will not be withdrawn from those already benefiting from it to save their lives and preserve their kidney function.

The sticking point has existed for 21 months now and aHUSUK had, on several occasions in that time, exhorted both the NHS and Alexion to get around the table to talk, clarify and collaborate on a sustainable solution because simply that is all that is needed. But our exhortations so far had been in vain.

It looks now as though NICE sending aHUS patients back to square one was inevitable, even if unforgivable; but we can only hope that at last, a suitable and sustainable solution can be found. So, it is now up to those, whose job it is to do so, to use the next few weeks to simply get it done."

Enduring all this makes a mockery of those who would claim later that eculizumab for aHUS Patients was got by going through a "loophole" denied to them. Some bloody loophole!

It is not easy being an advocate. It is not irrational to not want to be one. It was not as simple as just occasionally putting some sentimental quotes on Facebook. It was now like being in a business environment, between multi-billion-pound organisations, but for no pay.

No one said it would be easy.

Chapter 25

A new global direction presents itself

By now readers will no doubt have grasped the expansion of work that naturally occurs when running a charity to help people get the best of health. Sometimes this work has a global impact.

Apart from creating awareness about rare diseases, a greater understanding was emerging of the range of issues that rare diseases patients face, from diagnosis to research and registries for their disease.

In April 2014 I attended a second meeting of the Rare Disease Group for aHUS, a part of the Rare Renal initiative of the Renal Association funded by major Kidney Patient Organisations like Kidney Research UK. Although I used the meeting to brief other rare kidney organisations about what had been learned from our experience of NICE, something else caught my eye.

This meeting coincided with the annual UK Kidney Week conference which that year was held in Glasgow, Scotland. Attendees were given a Conference Pack, and, for the first time I realised what was involved in such conferences. In addition to lectures there were what were known as “poster presentations”, in which hundreds of individuals in an exhibition room put up posters to explain what had been found in some research that they had done.

The pack included a memory stick containing files of the Kidney Week programme and I did a search for anything which related to “aHUS” or “eculizumab”. Among several search results I noticed a presentation by Dr Sally Johnson on behalf of something called the “The Academy of Complement Inhibition” about a Global aHUS Registry. The research was about the characteristics of just over 200 aHUS patients who had been enrolled in the Registry by then.

As Rare Disease Patients frequently face having no patient Registry for their Disease, here was one I knew nothing about for aHUS. So surprised and pleased to find it I wrote about it on the aHUSUK website having researched more information about it. Probably the first and only patient organisation to do so at that time.

"*This registry sometimes referred to as an Alexion Registry has an official title of* ***An Observational, Non-Interventional, Multi-Center, Multi-National Study of Patients With atypical Hemolytic-Uremic Syndrome (aHUS Registry)*** *and is officially a clinical trial listed by ClinicalTrials.gov. It was established in 2012 and will continue to recruit until 2023 and the outcome will be published in 2025. By that time, it is expected there will be 2000 patients registered. Although sponsored by Alexion the data is being stored by Ohio State University*. Full information can be read about it on ClinicalTrials.gov website. The registry is being overseen by a Scientific Advisory Board of International aHUS clinical experts.*

* this was a misinterpretation of the site information where data was being collected as the website entry had not included all the enrolment sites, only the Ohio site.

And that was that as far as I was concerned. I knew the Registry would be operating until 2025 and so I expected no more than to see updates of what it discovers.

Then in June I got an e mail. It was from someone who was managing the Registry. The Scientific Advisory Board of the Registry had discussed and agreed at its May meeting that it should have patient input to what it was doing. Orphanet and EURORDIS/ Rare Connect had referred the Registry official to aHUSUK.

After the e mails and a telephone conversation, followed by a face to face meeting, I agreed with the Registry officials that it should be the aHUS alliance (of which they had no knowledge) not just aHUSUK which could provide a patient representative; but I could not make

that decision. It would have to be agreed by alliance affiliates at their next meeting, planned for November.

At its first meeting in Barcelona the alliance had identified working with international aHUS Research Networks as one of its aspirations. It now had the opportunity to do that. It could provide expert advice for healthcare and research for the benefit of aHUS patients globally.

Chapter 26

Here comes the Sun

aHUSUK formally responded to the ECD decision by 25 March 2014 as requested by NICE. Trustees challenged its decision; but agreed to do what they could to find evidence on affordability and asserted that NICE and Alexion find sustainable solutions on price.

There was no NICE meeting in April as planned. instead consultees were asked to comment on the accuracy of a piece of research that had been carried out for the NICE committee by some financial consultants. The 60-page report was of a study that had compared 26 (out of 168) highly specialised technologies (drugs appliances and surgery) including eculizumab for PNH (but not aHUS) in the NHS' Specialised Service portfolio.

It adopted a range of 10 or more quantitative performance indicators about severity of illness, impact on health, costs, value for money, innovation cost (R&D), and impact on specialised service delivery and budget to provide a holistic quantitative view of the relative merits of these technologies.

It was realistic about the data barriers that this attempt at comparison faced for all the technologies included in the study. So, for each indicator it assessed the data reliability (scale of 0 to 3) that could be put on it for each of the technologies.

It was a remarkable bit of research on rare disease technology evaluation that, as far as is known, has never got into the public domain.

The analysis presented to us was very difficult to understand, really difficult.

But what could be observed was that, except for the annual price per patient (based on adult doses at licensed dose levels) of eculizumab,

aHUS compared favourably with other illnesses such as PNH and Cystic Fibrosis, for which treatment had already been approved. Given its clinical effectiveness and exceptional Quality Adjusted Life Years scores, the comparative value of eculizumab for aHUS was looking good to the trustees, and aHUSUK said as much.

It was an example of opportunity cost in which an individual might not be able to run faster than a lion chasing him/her, but he /she could run faster than others the lion was chasing.

Rare Disease Day had come, and Rare Disease Day had gone. aHUSUK had not sensed that there was much interest or concern by the wider Rare Disease community in the plight of aHUS patients and the NICE decision. It would be normal for others to think what was happening to aHUS patient would not happen to them; and they would do a better job of it anyway. Fair enough.

For all the "better togetherness" of rare diseases in the drive to get equity for patients with such diseases, there was an emerging sense that as far as health care access to cash strapped providers is concerned there was an element of competition too. Let the devil take the hindmost.

All I knew was that aHUSUK had not said it was unfair that PNH patients got Eculizumab and we didn’t. I had also signed a petition supporting Cystic Fibrosis and Duchenne’s Muscular Dystrophy patients getting access to a drug they needed.

It was also making me think though, could "single mindedness" result from being a patient advocate, or was it a quality for doing it in the first place?

Back to NICE, aHUSUK knew that instead of a meeting on the 24th April, it had to meet an extended response period by 6 May to give our views on the Report. Soon after that we were informed that NICE were planning for a Final Evaluation Decision in September and for

that to happen the next meeting of the Committee would be on 23rd July in Manchester.

I had booked my summer holiday; my flight out was on 23rd July!

Here comes the sun, maybe?

Chapter 27

Broader picture of aHUS and greater outreach

As 2014 progressed, it was noticeable how much aHUSUK had become aware of other countries and their aHUS challenges and focuses.

From its formation in 2011 I had been posting news about the UK on the Foundation for Children with atypical HUS website. It had a wide international readership including many from the UK. It was interactive too; a sort of Facebook before Facebook took over.

The first thread about aHUS in the UK disappeared because the UK member resigned from the site. That thread had quickly attracted a lot of views and had been aHUSUK's only way to get news into the public domain until the aHUSUK website was launched. Or until a French member of the Foundation site had let me know about Rare Connect,

I began to contribute to both with increasing frequency on all manner of topics, including whether aHUS organisations around the world might benefit from working together.

Oddly during this time the Foundation, which had focused on children, began to see aHUS as an adult disease too (strange how people's encounter with aHUS drives their perception of aHUS, early advocates became so because of their children's experience) and a thread was established and ,like the "aHUS in the UK" thread, it quickly became popular and its views increased until they exceeded what had been the most popular thread about eculizumab.

That website is now dark. A decision taken by a new generation of aHUS advocates. In many ways the content of that website provided a history of early aHUS patient advocacy, not just of the USA, but around the world.

The call I made on that site for an organisation of aHUS patient organisations led ultimately to the meetings that created the aHUS alliance.

It is worth recalling what was said seven years ago on the RareConnect platform when the alliance was formally launched.

"***The Alliance is an organisation for aHUS Patient Organisations and is open to any national organisation which has been set up to represent younger and older aHUS patients, either specifically or as part of a wider related patient cohort.***

Although the representatives of patient organisations who gathered in Barcelona on 16 February initially thought an alliance was needed within the newly emerging FEDERG organisation; it became evident that to limit its scope to European Union member countries was an unnecessary constraint when aHUS affected such small numbers of people throughout the world.

So, although the Alliance will have a legal identity of its own as a Spanish Government approved organisation (note: it did not happen) it will operate globally with national organisations joining in and collaborating as they wish. Solutions will be sought to resolve communication hurdles so that Alliance meetings can be as fully inclusive as is practical.

The RareConnect Community's website (NORD and EURORDIS) will be the main platform for communicating aHUS Alliance news and activities.

Whilst it is important to talk, collaborating on action will be the key principle underpinning the Alliance's purpose. National organisations remain fundamental to the way aHUS patients are supported; but, encouraged by an Alliance, that support can be enhanced through the development and understanding of national organisation representatives.

The Alliance will also provide a platform for greater collective links with clinicians, researchers, and other professionals who along with patients themselves are resolved to overcome the challenges that aHUS presents.

On this Rare Disease Day 2013, aHUS Alliance is formally announced and begins its journey."

Because of these connections by 2014, the aHUSUK website had articles about the campaign for access to eculizumab in Australia and Belgium. aHUSUK had, at the Australian patient organisation request, contributed to the public consultation there.

But 2014 was the year of the first major collaboration by aHUS patient organisations. Supported by Rareconnect, which had become the aHUS alliance's chosen platform to promote its work, a group of advocates from Spain, USA and UK designed a global survey about aHUS.

Using the 6 key Rare Diseases issues (Diagnosis, Treatment, Research & Registries, Information and Expert Centre access) as its structure, 28 questions were "crafted". It is not easy drafting a questionnaire to get consistency of answers from all respondents. It was translated into 6 languages. The survey, or Poll as it became known, was launched on Rare Disease Day 2014.

Over 200 aHUS folk from 17 countries, with at least 1 from each continent, responded. The results were compiled and a picture of aHUS people by aHUS people for aHUS people emerged for the first time. The characteristics of aHUS patients, as well as their varied experience of diagnosis treatment and research was there to see. There was an insight into how those, who were affected by aHUS sought and found reliable information about aHUS.

Some data highlights was turned into a simple aHUS infographic by Rare Connect. A webinar was held with Professor Tim Goodship in which he commented on the results and gave some personal views on

current and future research. A compendium of graphs was produced, and I wrote an analysis report with key observations of what the graphs were showing.

Sadly, all these were lost to view when Rare Connect rejigged its website a year or so ago and links were destroyed in the process.

Looking back at the infographic now it is noticeable that there is no acknowledgement to the big part the aHUS alliance played. Nor is the quotation they used attributed to me. Perhaps that led to thoughts about the alliance having its own website.

Nevertheless, it showed how it was possible for all those affected by aHUS to come together to collaborate on projects and help each other. Not all though. Many thousands of aHUS patients had, and still have, no idea of what was happening for their diseases on their behalf. Furthermore, some of those who knew would choose not to become involved.

But a broader picture about our very Rare Disease was beginning to be revealed and that in turn was gaining more outreach and not just on Rare Disease Day, however important that day remains.

Chapter 28

£2billion a week and counting

By 2014 it was not unusual for aHUSUK to get emails from news journalists from newspapers, radio and TV. It was a big surprise however to get an e mail from a TV production company asking aHUSUK to consider featuring aHUS in a documentary about the NHS.

Trustees met with a producer to find out more before they could say whether aHUSUK should contribute.

The Producer told us the documentary was being made for one of the UK's main TV channels, Channel 4, and expected it to be broadcast in the autumn of 2014. The documentary's theme was about the choices facing the NHS in using its £100 billion per year budget (£2billion per week) It would be a three-part mini-series. aHUS would feature in one of the programmes as representing rare diseases alongside two other more common uses of NHS resources. (These turned out to be those suffering from drug and/or alcohol abuse, and those who needed better quality prosthetic limbs). The angle for aHUS would be the need for the most expensive drug in the world.

The Producer said it would be done in a novel way in t

hat there would be live social media interaction for viewers to give their opinions on what they were seeing and what their preferences were for spending by NHS. There may even be a viewers' vote, like a reality TV show. Although a bit apprehensive about the interactive facet, the trustees thought that it would raise awareness of rare diseases generally as well as making more people think about aHUS. (it might even result in someone getting an aHUS diagnosis in the future when they may have not)

aHUSUK also knew that it had a panel of "media savvy" aHUS patients/ families with good stories to tell.

With all approvals in place filming begun and by July several patients had been interviewed, one had even had her kidney transplant filmed. Even NICE would allow the documentary makers into its July meeting which I would be attending (although no sound recording of the proceedings was permitted).

Although I tried not to be included," I have a face for radio and a voice for newspapers" I told the Chair of the NICE Committee when he ribbed me about being filmed, increasingly the programme makers did begin to focus on my family. It was also clear the filming would continue until the NICE decision was made and its broadcast had been delayed until the New Year.

For that decision to be positive, the 23rd July meeting was now critical.

Chapter 29

Finding Baby Bodmer – learning about aHUS

All aHUS Patients and their families have had their own aHUS experience. When it hit them, most knew nothing of the disease itself, but they soon learned about what it did and felt like.

Bit by bit they would begin to understand why it might have hit them. But only “Bit by Bit” over the years; a decade or more ago there were very few sources of information about aHUS. Often their clinicians knew little too.

I was the same.

Although my families encounter with aHUS went back decades, I knew little about aHUS when in 2011 I attended the first UK aHUS patient conference hosted by Prof. Tim Goodship in Newcastle upon Tyne. Some of what I learned there stuck.

I also watched video recordings of the conference presentations several times to try to understand more. There was a lot of medical jargon to get past, and even when that was got past, the more that was learned the more questions came to mind.

When I was reading all the evidence provided for the evaluation of eculizumab by AGNSS, I was in a privileged position, unique in fact. I learned so much about many facets of aHUS, but also learned “how to understand” some very complex issues. I likened the process to the way 3D images appear from one of those computer-generated confusing patterns.

The more I read the more that certain things jumped out of the page at me. Somethings did not, so I would put those to one side and often they would crop again in another context and their meaning and significance would become apparent

Also, because I was struggling to understand topics, I could empathise with others who were also struggling. Certain topics like “What is a Rare Disease? ““What is the difference between the incidence and the prevalence of aHUS?”, “Why does aHUS not happen to all in families? ““Why does aHUS have barriers to diagnosis? ““What precisely is it about Complement that makes it a problem for aHUS patients? I tried to find why they matter to those with aHUS.

As someone who has an interest in history, I began to explore the history of the disease, about key discoveries and notable researchers. I noticed that most articles about aHUS, ten or more years ago, mentioned someone called Von Gasser. I delved into the work of Conrad von Gasser and found that he, in his hospital in Zurich had coined the term “Haemolytic Uraemic Syndromes” to give a name to the disease he had identified in several children in his hospital.

Prof. Conrad von Gasser in centre of photograph with Prof. Bernard S Kaplan to his immediate left

In time I learned more about him from aHUS researchers who knew Conrad. Prof Tim Goodship told me about a book written by Prof Bernard S Kaplan entitled “The Birth of HUS “. Eventually, I contacted Bernard and he gave me an electronic copy of his book. Reading that book about Von Gasser I even discovered the name of the first patient to be given “Haemolytic Uraemic Syndrome” as the cause of their death. He had crossed out the baby's original diagnosis, and wrote the three words in his own handwriting, and which have described our illness ever since. When Von Gasser finally published his findings, he

said the term covered syndromes, that use of the plural was significant as we now know.


Kinderspital Zürich

A baby whose surname was **Bodmer**. “Baby Bodmer”, as I called him/her, was the first named HUS patient and was a patient at Zurich Children’s Hospital, 65 years ago this year.

From Prof. Kaplan I also learned about Von Gasser’s “Swiss Cow Bell” and he sent me a photograph of it. The bell is now in his safe keeping.

Some years later I had an opportunity to visit the Children's Hospital in Zurich (Kinderspital Zurich), where Von Gasser had practiced, to visit a Dr Schaulke, the then lead paediatrician / nephrologist (Von Gasser died in 1982). When I was in the waiting room of the nephrology ward, a cowbell was rung to mark the end of the morning ward round. It was just part of the routine for them, but such a surprise to me, it raised goose bumps.

From 2014 onward I began to write articles on the aHUSUK website about all the topics I had researched and tried to explain them to

readers, as I had explained them to myself. I was very cognisant of how I had found them difficult to grasp and understand.

Advocates do need to know much more than their own experience. It makes them more able to advocate about the disease in a rounded way for others and not just about themselves.

So as a lay person, in a unique and privileged position, I was getting to know more and more about aHUS. The key thing I got to know about aHUS is that there is far too much to be able to know all. That does not stop anyone asking questions about what matters and seeking more answers to them. In time it would be surprising what can be learned.

On Rare Disease Day 2019 the alliance formally launched the "Global aHUS Patients' Research Agenda". A list of research questions about aHUS by aHUS patients. Together we can get more answers.

You are not alone We can find a way

Chapter 30

Nice decision NICE

The July 2014 meeting of NICE left us worried.

The meeting had been held on 23rd July as planned. I attended with my fellow aHUSUK Trustee expecting to just view proceedings, but we were seated in front of the Committee.

Most of the early part of the meeting was taken up by the Chair reprising what the evidence had been and explaining how the committee had arrived at its previous decision not to recommend eculizumab for aHUS.

The Chair did acknowledge that the Committee had received several letters from patients /families who had benefited from eculizumab to address the comment by a committee member about not having enough testimony from eculizumab patients at an earlier meeting.

aHUSUK had also submitted some estimates of the likely cost of treating aHUS patients for the next five years with revised figures for numbers and average dose cost. These were acknowledged too. It was our aim to create uncertainty about any unaffordability.

Little was expected from us, the focus was on Alexion and its evidence about price, or value as its representatives preferred to talk about. Nothing apparently had changed. There had been no patient access offer from Alexion.

Several committee members asked the Alexion representative in a variety of ways to explain the price of eculizumab and how it broke down into production, R&D, profit etc but Alexion were not willing, or unable to do so. “That was accountancy” explained its health economics advisor. I exchanged glances with the NICE officials we had met nearly 18 months previously.

I had to leave the meeting early because I had a flight to catch, I was going on my summer holidays. As I left the room, I was interviewed by the Channel 4 film team. They had been filming the proceedings. I was quite downbeat about it. Alexion's performance had been disconcerting.

aHUSUK had been told that a final evaluation document would be released in September. It turned out to be in October and a further meeting would be needed. Prior to the meeting aHUSUK received a copy of the decision.

"Eculizumab, within its marketing authorisation, is recommended for funding for treating atypical haemolytic uraemic syndrome, only if all the following arrangements are in place:

- ***coordination of eculizumab use through an expert centre***
- ***monitoring systems to record the number of people with a diagnosis of atypical haemolytic uraemic syndrome and the number who have eculizumab, and the dose and duration of treatment***
- ***a national protocol for starting and stopping eculizumab for clinical reasons***
- ***a research programme with robust methods to evaluate when stopping treatment or dose adjustment might occur.***

The long-term budget impact of eculizumab for treating atypical haemolytic uraemic syndrome is uncertain but will be considerable. NHS England and the company (Alexion Pharma UK) should consider what opportunities might exist to reduce the cost of eculizumab to the NHS"

The decision was qualified. Trustees did not care. Trustees agreed with them.

It was October 2014 and, subject to someone appealing against the decision and against aHUS patients, every aHUS patient in England and subsequently Wales and Northern Ireland,) could access

eculizumab free at the point of treatment delivery when they needed it for as long as they needed it. Scotland would be different to England and would not approve eculizumab for Scottish patients, nor PNH patients, but that is another story!

We jumped for Joy.

The final NICE meeting in November was positive and short.

There were two memorable moments. Firstly, the actual base figure for those receiving eculizumab emerged. It was less than the base figure on which aHUSUK had estimated the five-year cost of treating aHUS. aHUSUK had given NICE costings based on a range of base patient numbers from low to high. Our mid-point patient figure had used to show how NICE's budget estimate had been vastly overstated by well over £100m.

The Chair of the Committee looked at me I was busily recalculating the budget effect. I said if the revealed base patient numbers figure was correct, it would take another £30million off our estimated five-year budget. Had we known at the time another £40millon could have been knocked off the budget as nearly two thirds of the aHUS dialysis patients, who we expected to have eculizumab supported transplants, have not yet been transplanted. No one knows why.

aHUSUK had also raised another affordability argument. aHUSUK had found out in a news item in the Summer about the way in which Pharma agree drug prices with UK's Department of Health. Agreed and operated by the Association British Pharmaceutical Industries, it set out the framework for price listing and discounting processes.

The new five-year agreement had been radical. It had set a “no growth” in the NHS drug budget for drugs for two years funded by rebates taken from the sales of all Companies listed in the agreement, of which Alexion was one. In subsequent years some growth of budget was allowed, but new higher rebates would be expected.

aHUSUK had said that this was in effect a reduction in price and would apply to eculizumab sales for PNH too.

At the meeting NICE were confused and questioned Alexion's representative about it, who seemed perplexed. Reasonably so as they had failed to raise this in the first place. As confusion reigned around, I said it was aHUSUK who raised it and made the point that it would further reduce the cost of treatment as far as the NHS was concerned. Though no one knew where that money had gone.

NICE argued it was not relevant to their decision as they were comparing eculizumab with other drugs and their prices too would be reduced. I was not too bothered about that as we had already seen evidence that aHUS could run faster than PNH and Cystic Fibrosis from the "Opportunity Cost" Lion!

NICE had told us the day it would release the decision in the public domain. The Channel 4 film crew came to our house to record our reaction and I got to read out the recommendation. My only speaking appearance in the whole documentary. I did not care as we had got it.

Over three years had passed since aHUSUK and my volunteering began, and now we had finally got it for all aHUS patients when they needed it for as long as they needed it.

It would take a bit more time for it to be turned into NHS England commissioning policy, NHS would be given three months to do that. Before that there was time given for any appeals against the decision, or aHUS patients as we saw it), to be made and reviewed.

There were none and on 28 January 2015 (yes, another Christmas had passed!) NICE made its final announcement on its guidance for eculizumab to treat aHUS.

The Channel 4 documentary was broadcast in February.

In the first week of April 2015 NHS England revised its temporary policy for treatment to become its final policy going forward.

Since then around 100 patients have received eculizumab when they became ill and went to their NHS for help.

No lobbying MPs, no media interviews, no gathering and presenting evidence to decision makers for them.

Their NHS, once a diagnosis for aHUS was made, just gave them a treatment.

Is that not all they could want?

Isn’t that world class?

Chapter 31

Iowa and Paris in a week

As previously mentioned, aHUSUK's outreach was extending due in the main to the links it was forming with other aHUS patient organisations. But in one week it went up a notch.

First, as guests of the then "Foundation for children with atypical HUS", I attended its conference weekend in Iowa City. This included the biennial University of Iowa aHUS patient conference on Saturday 25th October 2014, as well as several other presentations and social events over the weekend.

Almost in real time I wrote about it on the aHUSUK website and what I said can be seen at Appendix.

It was an early example of my reporting on conferences for those who could not be there and as a record of what are unique and historic events, often revealing how the paradigms of aHUS knowledge and patient advocacy were changing.

But what was clearly noticeable and insightful again was that aHUS patient's concerns differ little wherever they live, as I wrote:

"The early arrivals include grandparents of a young boy who became ill with aHUS in India just a few weeks ago and is recovering well having received eculizumab. The conversations around the room are typical of what happens when those who have encountered aHUS, whether early or later in life, meet up wherever they are in the world."

With hindsight, my concluding comment" The ***Foundation have set the bar high for putting on an educational event for the aHUS community.*****"** reveals that with the NICE evaluation of eculizumab behind us that it might be time to have second UK aHUS Patients Conference.

Phyllis Talbot Linda Burke with me in Iowa

Outside of the conference I also established the Foundation's affiliation to the aHUS alliance with its leaders at the time the "Talbots", the "Biermanns", and of course the alliance's biggest supporter, Linda Burke.

I believe all of them have a distinguished place as the early pioneers of aHUS Patient advocacy.

On a personal note, although I had been a frequent traveller to the USA before my daughter's illness this had been my first visit back in 18 years. Eculizumab had given back freedoms that had been lost because of aHUS.

No sooner had I recovered from jet lag that I was off again to Paris. The aHUS alliance had been planning its second meeting of affiliates at the George Pompidou Hospital in Paris. This time more countries were participating, including some by teleconference from Canada Italy India and USA.

A collage of photographs taken during the meeting

Apart from each nation's updates, which were recorded, two important decisions were made.

Firstly, affiliates agreed to hold an aHUS Awareness Day, and also , after presentations by Doctors Gema Ariceta of Spain and Veronique Fremeaux-Bacchi of France it was agreed that the alliance would accept an invitation ,which I had received earlier in the year, to partner in the Global aHUS Registry.

The meeting ended with the news that the next meeting of the alliance was now being planned for London in June 2015.

Having all signed the "certificate of attendance "and agreed to fight for aHUS patient group rights" a picture was taken of the group jumping for joy at the very recent news from NICE about its positive recommendation for eculizumab to treat English aHUS patients.

With the what had been a very busy year, 2014, ended, 2015 would bring different challenges.

Chapter 32

A journey for life

From its beginning aHUSUK had not been a research fundraising organisation. We had always told people who wanted to raise funds to donate them to Kidney Research UK or the Foundation for Children with atypical HUS to help more research.

After a Rare Renal meeting with other rare renal patient organisations a year or so earlier, the Trustees had resolved that, when time permitted, aHUSUK would organise its own fundraising project.

So it was that at the first aHUSUK Annual General Meeting following the NICE guideline for aHUS and eculizumab being published, a fundraising effort began.

With the project title **Journey for Life**, its concept was that aHUSUK members would walk, run cycle whatever, from a one point in the UK to another in an actual or virtual relay. The search was on for two places called Illand to Welland to provide starting an end points for the journey

An Illand was found in the most south westerly county in the UK, Cornwall. There was a Welland in London near Greenwich, but the plan changed so that the journey would end at the Centre for Life in Newcastle upon Tyne., in the north easterly corner of England.

As it was a relay, a baton was provided (a plastic test tube- symbolic of research).

The special guest attending aHUSUK's AGM was Sandra Currie, the Chief Executive Officer of Kidney Research UK, and she was invited to hand the baton , which contained a letter for Prof. Tim Goodship , the then Chair of Kidney Research UK , to member Kimberly, who was to be the first fundraiser on the journey.

The following week on 28th February, Rare Disease Day 2015, Kimberly, who did not live far from Illand, a very small village, walked over the weekend from there with friends and family to her hospital in Exeter, Devon. They not only raised several thousands of pounds for research but also created a lot of awareness about aHUS through publicity about their walk.

Kimberly and Dr Corelli Bingham passing the test tube baton at the end of the walk

And so, it went on through Devon, with aHUS patients there who were all related through a common ancestor from several centuries ago. There are far more aHUS patients in Devon than there should be.

Although not living in Devon myself I was one of those relatives. So, I chose to walk the 13-mile route from the village of Burrington via South Molton to North Molton (having driven over 200 miles to get there!). All places which my aHUS ancestors had lived and farmed. Very little had changed in this very rural part of UK, so I walked along lanes where my ancestors had lived and walked themselves.

The oak tree in the centre of Burrington village

Starting off from the Burrington Oak, a tree believed to be over 300 years old, which was a mere sampling when my ancestors walked by it, I was joined by my daughters and we raised nearly a thousand pounds for research.

And onward the journey went. Although there would be some discontinuity in the route as aHUS patients joined in the journey north and eastward, some imagination was deployed in choosing what would follow at each subsequent fundraising stage.

A family cycled from their hospital in Bristol to the English side of the long suspension bridge crossing the very wide estuary of the River Severn. A Welsh Patient then took the baton and walked across the bridge into Wales.

The next stage was an 87-mile-long distance walk over a weekend along a prehistoric footpath "The Ridgeway" through South Central England. For aHUSUK member Mathew and friends it was a stag weekend before his wedding. No doubt creating a lot of thirst to be quenched as well as raising thousands for research.

The stage through London was even more bizarre. Member Sylwia made it a virtual walk by walking up through the foothills of the Himalayas to the iconic base camp 2 beneath the peak of Mount Everest. She took the test tube baton with her for a photograph. She pointed the baton towards the top of Everest but with the camera angle it turned out to be pointing towards another mountain peak next to Everest. That other peak has been renamed Mount aHUS!

Some members raised funds with static events like BBQs, coffee mornings and tea parties. Trustee Christine in Scotland cycled hundreds of miles in North East Scotland. Another volunteer walked through the Yorkshire Dales. The virtual miles by someone who ran the Great North Half Marathon, brought the journey to the Angel of North a famous sculpture by Anthony Gormley.

The final stages of the Journey for Life was from the Angel down to the River Tyne and the walkers were joined by dozens more when they arrived at the river. The walk then continued back and forth five bridge * crossings over the river, including the famous Tyne Bridge. a scaled down version of the Sydney Harbour Bridge, which had been made in Newcastle upon Tyne. (The Newcastle upon Tyne Walk is still a fundraiser but for Kidney Disease in general)

So "*Ganning alang the Scotswood Road"* in the local *Geordie* dialect i.e. going along the Scotswood Road, the fundraisers entered the Centre for Life and the baton was finally handed over to Prof Goodship. Refreshments were well earned and deserved and nearly £30,000 overall had been raised for research since the baton had left Illand on Rare Disease Day. (in time that would increase to £60000 as more donations came in).

Later Prof. Goodship told me that “Five Bridges” had been the title of a song by a Newcastle rock band in the 1970s- their name **NICE** ! How appropriate for aHUS in 2015.

It was the 20th September 2015, exactly 60 years to the day that the term "HUS" appeared in public for the first time, coined as it was by Conrad von Gasser. Since 1955 it has been quite a journey for life for all aHUS patients too.

aHUSUK and its members had once again done something extraordinary.

Chapter 33

A second UK aHUS Patient conference

The journey of the Reluctant Advocate moves along in 2015.

Just after the Paris meeting of the alliance I was contacted by Prof. Tim Goodship. He thought, like I did, that a second UK aHUS Patient and Family conference was overdue.

This time such a conference would be an aHUSUK /Rare Disease Group for aHUS collaboration.

Instead of my preferred anonymity as in the first conference in Newcastle I would have a more active role.

aHUSUK would manage the arrangements and Tim the RDG would find the speakers.

Having been to the University of Iowa Conference I felt that we had a lot to live up to.

I made two decisions quite quickly. Firstly, the education part of the conference would be structured around the “aHUS Venn Diagram.”

So, talks would focus on genetic pre-disposition and modifying risk factors as well as triggers with a special emphasis on pregnancy and transplant. Further talks would be about withdrawal from treatment

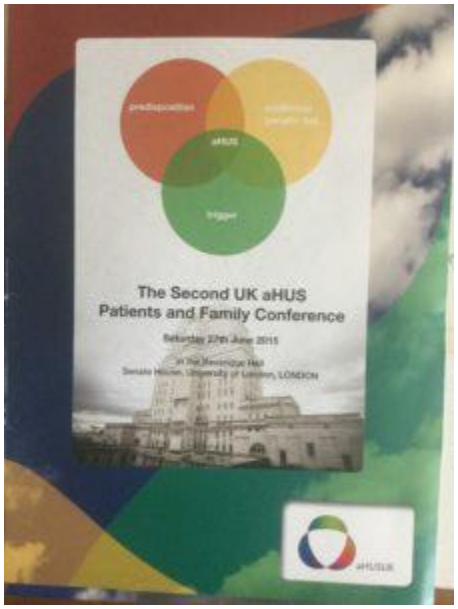
research, patient registries and research fundraising which would add to the topicality and planned research fundraising programme that aHUSUK had in mind for 2015. (see Journey for Life)

Secondly, because I hoped that the alliance affiliates meeting could follow the patient conference on the next day, I felt that international aHUS delegates could get the chance to speak to UK patients.

A date of the weekend 27/28 June 2015 was selected, long almost midsummer days, so if it was to rain in England it would at least be warm rain.

I looked at a few venues in London, a venue which would be most suitable to UK travellers and the international delegates gathering for their meeting. It would give the best travel options.

I settled on The Senate House of The University of London. An impressive 1930s structure with much history. It had inspired George Orwell to use it to describe the location of "The Ministry of Truth" in the novel 1984 and has been used in many films and TV programmes like Batman and The Bodyguard (The explosion scene was set where Alliance delegates had stood). Yet another impressive venue to have visited as an advocate.



Date set, agenda designed, venue booked, speakers agreed, conference announced, publicity sorted, catering booked, conference materials printed and collated, roles assigned for reception etc. We were ready if a little exhausted. The first UK conference had been organised by a professional conference organising company; we could not afford to pay for such a service. It was a case of DIY.

On an exceptionally sunny and warm and (almost) mid summers day in London, the conference began. Over 100 delegates attended. It was co-chaired by my daughter and Prof. David Kavanagh.

It was recorded and those talks are still viewable on YouTube.

Enough visiting delegates to the alliance meeting came to the UK meeting to talk about aHUS in their countries There was a place on the agenda for them and their brief talks were among the highlights of the day. They told UK patients what aHUS was like in Germany (Nacho) Australia (Keri) India (Kamal) The Netherlands (Joyce) Russia (Marina) and the USA (Linda).

A video of this session can be viewed on YouTube this short video titled "A World of aHUS" encapsulated how by 2015 international aHUS patient organisations had become interconnected. It gives insights to both the common and different challenges that each country faces.

All in all, the objectives of this “project” were achieved. It went by so quickly and the audience were kept interested and informed throughout. The video record is still available and remains a legacy of the day.

aHUSUK and alliance delegates then had a social evening by the banks of the River Thames to prepare them for work the next day.

Chapter 34

For aHUS Good will come together

The third aHUS alliance affiliates meeting was held on 28 June 2015, the day after the second UK aHUS patients and families conference, which most of the international delegates had attended. Joined by others it had been a late night with exceptionally sunny and hot weather, the delegates enjoyed the sights of the city from the London Eye, and a meal of English cuisine (there is always a downside) at the Sherlock Holmes restaurant. Quintessentially English but, as always in the brief time we have together, the conversation was about aHUS.

So, chaired by my daughter Emma, the meeting began the next morning in another room in the University of London's Senate House. It was the largest attendance for an alliance meeting to date and all countries were represented in person apart from aHUS Canada whose representatives had a personal event to attend.

After the usual updates of aHUS activity in each affiliate country, talks were given by Prof Tim Goodship about the aHUS Expert Centre in Newcastle and UK aHUS treatment. A representative from another Pharmaceutical company making a complement inhibitor was to follow.

Three other highlights were:

Kamal Shah alliance affiliate from India had studied the progress made by countries in the alliance in accessing eculizumab since the first alliance meeting in Barcelona. From his analysis, Kamal showed what were the key steps to progress and the extent to which they had been reached in each country. A fascinating study and of value to any aHUS patient group aiming to get treatment in its country.

I took the opportunity to report back on the alliance inaugural representation at the Global aHUS Registry's Scientific Advisory Board. To get an answer to the question asked of me " What do aHUS patients regard as priorities for aHUS Research?" The ideas for research topics were captured, analysed and I reported them back to the aHUS registry. Little did I know where that would ultimately lead to!

I also led a discussion about how the alliance's stated **aspirations** from the Barcelona meeting could be turned into a *mission statement* and simple *vision* for the alliance.

I had condensed the 30 or so aspirations into seven over-archiving strategic objectives, and from those the following, even more overarching, mission statement was drafted.

The aHUS alliance, through the collaboration of its affiliates

will promote global awareness of aHUS,

will work with international aHUS researchers and,

by supporting newly emerging national aHUS patient groups,

will bring relief and support to those affected by aHUS to save, and improve the quality of, more lives.

Taking that one stage further and seeing that it would be its collaborative efforts which could help to make the lives of aHUS

patients and their families better, a simple vision for the alliance sprung out

Good will Come Together

Although not all alliance affiliates were convinced that this was the best stated alliance mission and vision, enough supported it as something to use until something better could be proposed. That is the way it has remained.

Led by Francisco Montfort and Linda Burke, the alliance considered whether it should have its own website as a platform for its work, rather than just use Rare Connect, which had been its chosen platform at the start. Francisco showed the meeting an interim alliance website he had created himself, but it lacked capacity for development. The alliance having agreed to have its own website, a task group was set up to work on a website design acceptable to the alliance affiliates,

Also led by Linda and Francisco, the meeting discussed and agreed plans for the first aHUS Awareness Day on 24th September 2015. The theme was to be a message for the social media by individual patients around the world (using an "air mail letter format" to emphasis it was international). This was the first unifying event of the alliance, but national aHUS organisations were encouraged to hold their own awareness events too.

The alliance meeting ended on time and was a great success. It demonstrated how, despite distance and language barriers, a group could collaborate on projects with a common mission towards a common vision. All in all, it was very promising.

It was gratifying to the aHUSUK that it had hosted a very successful gathering of alliance affiliates.

Prior to the alliance conference aHUSUK had received an e mail from a Canadian TV documentary maker. It was asking about aHUS advocacy organisations in different countries and what they did. I offered them the opportunity to come to the alliance meeting to see for themselves, as there was nothing to hide to my mind. They declined my offer.

Several months passed and the documentary appeared on Canadian TV. It did a hatchet job on patient organisations which had been funded by Alexion, and in the process demonised aHUS patient advocates “as not wanting to bite the hands that feed them”. It did damage to aHUS patients’ organisations around the world, painting them as” advertising groups for Alexion " instead of the unpaid volunteers who just wanted a treatment for their families and others. I would have welcomed the chance to show the TV company the reality of patient advocacy, but I guess that would not have been good TV.

My wife and I had spent hours doing unpaid menial work preparing conference packs and badges behind the scenes for that conference weekend, and it felt like the media now portrayed that as something to be ashamed of. That kind of thing could make someone reluctant to advocate, even though it was for people who through no fault of their own have had their lives taken away , diminished or burdened in a brutal way but that’s not a good story for these investigative journalists who were treating a specific group of patient advocates unjustly using all the power the media held.

Patient groups, and increasingly individual patients working independent of national patient organisations, do need to be fully aware of the need for ethical relationships with Pharma. Rules covering such interfaces exist in all countries. In the UK they are set out in a Code of Practice by the Association of British Pharmaceutical Industries (ABPI) and are independently “policed”.

A year or so later the alliance was approached by a reporter from Bloomberg about a matter along similar lines in the USA. A scandal was brewing there, involving non aHUS patient charities which would result in a $13 million fine for Alexion ultimately.

The alliance put all this to one side and just got on with the agreed programme of projects to achieve our vision

“Good will come together”.

Chapter 35

The first aHUS Awareness Day

The alliance had agreed to have the First aHUS Awareness Day on 24th September 2015.

The theme was "communication" and the idea was for aHUS patients to send out on the Day an "air mail letter" in the social media with an aHUS message.

aHUSUK supported the project and posted news items letting people know about it and explaining how to make an air mail picture.

The message I sent out on the First aHUS Awareness Day

The Awareness Day alliance leader, Linda, also suggested a ten-day programme of promotional news items to draw peoples' attention to the day.

I chose to reprise some aHUSUK material, premier several videos from the aHUS Patient and Family Conference. But as a centrepiece on 20 September 2015 I featured an article about Conrad von Gasser which had been written especially for aHUS Awareness Day by Prof. Bernard S Kaplan.

The programme was:

10 days to go:

Video premier of Dr Kevin Marchbank's talk at the conference together with a blog written by him about the " knowns and known unknowns of complement and aHUS".

9 day to go:

A reprise of the aHUS Patients Experience Report aHUSUK evidence to AGNSS, CPAG and NICE. written to give insights into what having and living with aHUS is like for those who do not know. A rare outing in the public domain for this ground-breaking piece of qualitative research by aHUS patients about having and living with aHUS.

8 days to go:

I gave a brief overview of the access to eculizumab status in 15 countries around the world.

7 days to go:

An article by Prof Tim Goodship to accompany the video premier of his talk at the Conference about how genetics explains why some family member onset and others have not in a family in Devon UK

6 days to go:

A very special day it was the 20th September the day on which Prof. Conrad von Gasser's article using the term ***haemolytic Uraemic Syndrome*** (in Swiss) appeared in public for the first time. To celebrate it, Prof Bernard S Kaplan wrote a special tribute to Conrad for the first aHUS Awareness Day

The 20th was also the day that aHUSUK members were completing their research fundraising walk " Journey for Life " across the 5 bridges over the river in Newcastle upon Tyne. As a postscript to that, Prof

Goodship told me about a song he recalled from his student days, "Five Bridges" performed by a group from Newcastle called...."NICE"!!!

5 days to go

"**Think aHU**S " my message for aHUS Awareness Day. In June I met transplant surgeon Mark Stegal from the Mayo Clinic Rochester USA. He had been speaker at the "HUS and other disorders" conference in Innsbruck, Austria. He had been introduced as a "rockstar" of transplant surgery. He talked about a case study of a patient of his where the transplant went wrong. The graft was OK, but a TMA was evident. The patient had aHUS, it was found he had CFH mutation. Mark said that could have been known as the cause of the original kidney failure, but it wasn't thought about. He said, " if you are not thinking aHUS you are not going to diagnose it" Getting people to "Think aHUS " is what aHUS awareness day is about.

4 days to go

I reprised material about aHUSUK raising "political awareness" of aHUS.

3 days to go

A premier of the video of Prof (then Dr) David Kavanagh's talk at the Conference about the triggers of aHUS.

2 days to go.

Well not the day itself in UK, it already was in Tuvalu, near the international date line. aHUS Awareness Day lasts for 48 hours. I had put 3 "countdown to aHUS awareness day" clocks for the furthest east , GMT, and the Midway, the furthest west now the aHUSUK Reminded about that, (I recently checked the website and I had not switched the clocks off so at the time of writing it has been over 1619 days since the first aHUS Awareness Day began!!!.)

1 day to go.

aHUS awareness day itself so I marked it by premiering the video of the International delegates of the aHUS alliance talking at the Conference. It can still be seen by clicking here. What the speakers say still resonates within, and from, the aHUS alliance.

I also wrote an epilogue as the day closed in the far west Pacific Ocean about what I thought the day had been about. This is shown below together with some comments it received:

" So, the First International aHUS Awareness Day is over what was it about?

Posted on September 25, 2015 by aHUSUK • 4 Comments

As the sun sets on the Pacific Ocean somewhere near Midway Island. the First International aHUS Awareness Day comes to a close.

All across the globe aHUS people have done something to make a noise, whether it was appearing in the media, holding awareness stalls in hospitals, posting stories on the internet or making a personal statement about their situation.

Everyone is different but underneath it all, there is something, maybe a genetic pre-disposition, or a similar shocking encounter with the disease, that unites us.

Some did not participate because the outreach was not enough, others chose to play no part lucky enough to have access to treatment and for them that is enough.

One notable single achievement of aHUS Day was hearing from an aHUS patient from Pakistan who had heard about the day and wanted to make a statement.

It was interesting to read the personal statements that came by "air mail letters".

aHUS is with everyone for life, but maybe their treatment will not be. Having aHUS does not define a person, nobody can see the life-threatening events going on at micro biological level, To the world an aHUS person is just a person.

Except when complement is not inhibited and organs are destroyed, because then the world may not see the complement disorder, but what the destruction of major organs can do to someone's outward appearance, including consequential damage to other organs and severe scarring from chronic dialysis.

aHUS patients with eculizumab can dodge that bullet. Having eculizumab is like taking a supplement to boost something in the body that is lacking, by adding a micro biological entity to make complement work for, not against the person. With that boost the person is no different to anyone else.

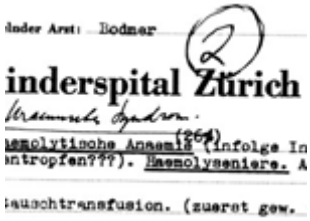
aHUS patients do not live to infuse complement inhibitors but infuse a complement inhibitor to live, a free and regular life.

For some what happens to others with aHUS can be shut out, for others it may mean they want to share information so that those others encountering the frightening onset of aHUS can have someone to talk to or lookup on the internet, for others it may mean raising funds so that more answers for aHUS can be found, or that their aHUS health service delivers excellence.

Who knows what it will mean for that aHUS patient in Pakistan now that they are engaged with others?

As for the aHUS website, the blogs in the 10 day lead in to International aHUS Awareness Day has left a legacy of information for those with aHUS including five videos of the June conference talks, some information of what happens elsewhere in the word in 2015, some items about aHUSUK's achievements and a specially written article about the History of HUS.

Baby Bodmer remains defined by aHUS as the handwritten amendment to the baby's cause of death shows.



The lack of a complement inhibitor meant that Baby Bodmer and family were denied a 60th birthday party in the past twelve months.

It makes you think! But that is what International aHUS Awareness Day was all about.

→

4 Responses to "So the First International aHUS Awareness Day is over what was it about?"

1. *YT Liu says:*

   September 25, 2015 at 9:44 am

   As a parent of young child with aHUS in Australia, I would like to say an immense thank you for all the information that has been posted here in the lead up to the International aHUS Awareness Day. I have learnt so much and especially liked the video links to the recent conference, it has really got me more passionate about spreading the word of aHUS and also being a more confident advocate for my child's health. Thank you!

   Reply

   - *aHUSUK says:*

September 26, 2015 at 5:24 am

Thank YT I am glad it was of help to you. Yeh keep spreading the word and make people think about aHUS even, tell your Clinicians about the videos as they can learn too. If they need help the speakers in the UK would no doubt be happy to hear from them.

Reply

2.  *Cheryl says:*

September 25, 2015 at 1:08 pm

Excellent, thank you.

Reply

-  *aHUSUK says:*

  September 26, 2015 at 5:19 am

  Thank you very much Cheryl and let's hope that on your lad's 60th birthday he looks back at what you and Bill have said and done for aHUS.

Chapter 36

An alliance collaboration- its website begins

International collaboration was beginning to pick up considerably after the 2015 London meeting of affiliates.

At its first meeting in Barcelona the aHUS alliance agreed that its communications would be made on the Rare Connect platform provided by EURORDIS.

And that is what the alliance did.

At its meeting in Paris the alliance decided to move into the social media, Facebook and Twitter, to raise its profile further. In the time between that meeting and its next meeting in London one affiliate created a website which comprised a few pages with some photographs taken at the Paris meeting.

In London it was decided to explore the possibility of creating the alliance's own website. It was too late for it to help with the first aHUS Awareness Day but a task group, including myself, was set up to work on a design and a plan for funding and implementation of an alliance website.

A domain was bought, the original URL was not allowed to be used, and an interim website structure was set up to be available for hosting the 2016 Global Poll on Rare Disease Day 2016.

Meanwhile behind the scenes the development work continued. Alliance affiliates were involved throughout and asked for ideas for content (a Skype group had been set up to allow discussion and decisions).

Finally, the alliance website **www.ahusallianceaction.org** was ready to go public at the end of May in time to announce the results of the Global aHUS Poll.

That was it, the alliance had its own place to connect, inform and collaborate.

It just needed the aHUS community to know about it and that would take time. Certainly, at that time an “aHUS” search term would not bring the website to the first page of Google search engine results.

That would take a long time, but then it had been a joyous moment when the alliance website appeared on page 50 of Google search engine results!

Bit by bit the alliance website moved up the search results. As more and more content was written which seemed to attract more and interest.

As with the aHUSUK website I found plenty of material to write about but this time I was not alone as others joined in to give anyone interested a better mix of interesting aHUS subject matter.

For me it was just another collaboration. After all the alliance only exists when there is collaboration.

Chapter 37

aHUSUK 2011-2016 RIP

aHUSUK had been created to support existing aHUS patients, and those in the future, to get the treatment they needed when they needed it (for as long as it was needed).

By mid-2016 the organisation was becoming very tired, the remaining trustees were, as those who had dropped out along the way, exhausted by doing something that was only expected to last for a few months.

Advocating for aHUS, however, came at a time of momentous change for those with Rare Diseases and we were in the middle of this maelstrom because the drug we needed , eculizumab , came with a notorious price tag and it seemed to break existing evaluation and approval processes throughout the UK necessitating reforms of policy causing delays which aHUS patients ,unfairly, had to endure.

The Trustees therefore asked members if the charity should be wound up. Most people had an enormous respect for aHUSUK and felt it would be a great loss if it was to end. But there was no appetite to rise again as those early Trustees had done at Wimpole Street. (The irony being that the last Annual General Meeting in May 2016 was being held in the very same building that aHUSUK had been created in 2011). The members gave the Trustees instructions on what to do with assets and outstanding commitments.

The aHUSUK website came out in protest to the decision and crashed, preventing a report of the AGM being posted, so RareConnect was used as a backup.

aHUSUK was akin to *Nanny McPhee* when it was needed it was not wanted by many, but although many now wanted it, it was not needed.

aHUSUK had done its bit

A few months later the last aHUSUK news item on its website reported its demise.

"Today Monday 3 October 2016 is the day that aHUSUK ceases to be.

For just over five years it has worked for aHUS patients and families doing what it said it would do when a group of aHUS patient families came together in Wimpole Street, London on 10 September 2011.

It became a registered charity.

It provided a patient voice as the AGNSS, CPAG and NICE evaluations of eculizumab were done.

It provided a network for patient support and advice

It established relationships with renal, rare disease, specialised NHS service, complement and aHUS organisations at home and abroad

It provided news and information about aHUS in over 400 wide-ranging blogs on its website

It introduced a patient card now held by over 1500 people around the UK, just in case they need it.

Its website has been a record for history of what happened to aHUS in the UK in 2011 to 2016.

Its website is ranked in the top 18 million websites out of over 600 million globally.

It run petitions which tens of thousands of people supported.

It has raised over £50,000 for research

Its trustees worked with members to punch far above their weight, replicating much of what larger and highly financially supported health charities do

Whilst it cannot be said that it involved every person affected by aHUS all of the time, it was supported by enough of them for some of the time

It is now time for another organisation to engage all of the aHUS community for enough of the time to do even more for the disease which embraces and unites us all.

Goodbye from, and to, aHUSUK as it joins the ages."

As the Reluctant Advocate story draws to an end, I would like to acknowledge the "Few" who made such a difference. The aHUSUK honorary Trustees who served with honour, and the members who notably helped with aHUSUK's media and fundraising campaigns.

Honourable Trustees
Ian Mackersie
Emma Woodward
Debbie Thelwell
Vera Mackersie
Elena Lilley
Christine Western
Lisa Barker
Margaret Squires
David Squires
Shaun McCowie
Kelly Bazzichi

And finally, an acknowledgement to Prof Tim Goodship whose work I have known about for over 20 years. His research team's findings about a small difference in a small part of Complement made a big difference for all aHUS patients. But for me it was personal. The small difference he found is something that has been passed down through my family's ancestors for centuries. It was the reason that I needed to overcome any reluctance to advocate. It was Prof Goodship who made the call to action that led to aHUSUK.

On first meeting him in Newcastle nearly 10 years ago, he explained all about a "solution" that we had already heard of and had been waiting over 5 years for. He told us that "we may have to campaign to get it, write to our MP, because it might not be easy to access, it was expensive". We told him "we would be up for that; our MP may well become Chancellor of the Exchequer after the next general election" (and he did do and was very supportive of my daughter's cause). Little did we think then what else it might entail.

I know now

.

Chapter 38

The Epilogue

I set out in the series of blogs on the aHUS alliance's website to not only tell the tale of a Reluctant Advocate, but also put on record a "History of aHUSUK".

It is now history. When those of us, who were the in the middle of a fast moving, yet frustrating, series of events, had a chance to chat about it all, we said there should be a book about this. Then quickly dismissed the thought, believing no one would be interested, nor even believe it.

Well a "book" has been written and will be kept in the aHUS alliance "library" in the website's "info centre". Maybe in years to come someone might possibly be sufficiently interested in the history of aHUS patient advocacy in the UK back in the old days and find it insightful. Just as I was interested in Von Gasser and the "Birth of HUS" over 60 years since those much more significant events happened.

For most aHUS patients being part of a formal advocacy organisation is unlikely to happen, and what they would do if called upon will never be tested. Neither will they know how they could have coped with it all.

Many of us have faced other serious illnesses and relied on others to do what needs to be done without knowing just what that might have entailed. Nor giving much thought to why those others did so.

For my part I did what I could. There were many thousands of people in Pharma, Clinical Research and Healthcare sectors who had played their collective part leading up to the moment in time when a decision was made to recommend eculizumab for aHUS patients in England. All I could do as part of a patient group was to advocate with all the skills and knowledge I have acquired over the years.

The Reluctant Advocate is my testimony to what part I played among extraordinary people in extraordinary times doing extraordinary things and really achieving extraordinary results. Personally, I had not done anything like it before nor I had I ever wanted to do anything like it.

Maybe it was a case of fulfilling a destiny of my aHUS ancestors, maybe it was more selfish than that. I am predisposed.

Or just simply a deep-seated optimism back in 1997, when, in a room on a Nephrology ward in a decrepit northern English hospital with plenty of evidence to the contrary in front of my eyes, I believed that somehow good would come.

But I did volunteer, and I did advocate.

Would I want to do it all again? I still do not want to. Over the five years I felt extreme anger, disappointment, confusion and frustration but also moments of joy, clarity, added purposefulness in my retirement and yet laughter with tears in my eyes such were some of the absurdities we faced, and achievement attained.

Would I do it all again if needed? If I had to. If equity of treatment for my family was at risk certainly, but I would do somethings differently.

It all remains a part of my life still and I have continued to fulfil the last wishes of aHUSUK members.

Under a new guise of Answers for aHUS I have been committed to seeing that the research funds raised are used for something that will be a legacy to the “few” that raised them. That baton has been passed to cTMA UK for the future.

I am still a member of the trial management team for the SETS study of the safe withdrawal of eculizumab , a NICE condition to its approval and which underpinned that part of aHUSUK’s vision for eculizumab

that it should not only available when needed but also only “for as long as is needed”

I still keep the UK a part of an international aHUS alliance, which it helped found.

I still enjoy meeting and working with eminent aHUS Researchers from around the world and speaking for aHUS patients in their Registries.

I still scan the UK healthcare world for potential risks to UK aHUS patients’ continued care (at green alert since the NICE decision but currently raised to yellow).

But by the end of this sentence, I will have completed one long standing commitment, to write the Reluctant Advocate’s story as a part of aHUSUK.

Appendix A

THE LIFE EXPERIENCE OF aHUS PATIENTS, THEIR FAMILIES AND CAREGIVERS IN ENGLAND AND WALES

1. Introduction

This report describes life with aHUS and how the disease affects patients, partners and family members. It focusses on current diagnosis and treatment, rather than providing a historical perspective on how disease management has changed over time. The report is based originally on the findings from 16 interviews with people with direct experience of the condition, patients, parents, partners and other family members and supplemented by later findings from interviews by aHUSUK. Direct quotes from interviewees are *in italic* and attributed to the category of interviewee: patient (all adults), parent, or partner/family member.

Many impacts of the condition and its treatment are similar for patients and their families, whether the patient is affected as a child or later in life. Sections 2 and 3 describe these general impacts. Section 2 reports on people's experience of obtaining a diagnosis and accessing services and information. Section 3 describes the impact of the condition and its treatment.

Sections 4 and 5 describe the specific impacts on children and adults respectively. Many of the consequences of the disease depend on the age at which people are affected. Section 6 reports on the experiences of patients who have received Eculizumab.

2. Diagnosis, access to treatment and information

2.1 Patient/ carer experiences of obtaining a diagnosis

The initial symptoms of aHUS in both children and adults are mild and similar to other minor ailments. They include headaches, sickness, diarrhoea, oedema and tiredness, symptoms also common to kidney failure. Babies become pale and distressed and stop feeding urinary problems are sometimes indicated by '*pink nappies*. The condition is therefore not immediately recognised by GPs and other more benign explanations are given, despite in some cases there being evidence of kidney disease in the family. Patients often report repeat visits to the doctors while symptoms persist, until the point at which their kidney failure becomes life threatening requiring hospitalisation. This happens within a very short timeframe (a few hours, days or weeks).

I went to the doctors about five times over Christmas and New Year and they didn't know what was wrong with me. They thought maybe glandular fever, then they said I might have got a dose of gastric flu…and eventually I got sent for some blood tests and then one morning I was really, really poorly…we phoned the doctor and he checked my blood results and at that point he was round in

about 10 minutes and he told me that I'd got a problem with my kidneys and I needed to go to hospital. (Patient**)**

Initially she was diagnosed with baby anaemia…until six weeks later when I noticed her nappies were very little and she was really bloated and I said 'This is not possible, she's not eating, how come she's putting on weight?'…I thought there must be something wrong with her kidneys… she was shiny and it looked like fluid on her legs, her legs were really big…I took her to the hospital and they took a blood sample. Then we went home, and they called at nine at night to say it's HUS and she must be admitted urgently. **(**Parent**)**

It was a case of not knowing really even though it was in my family. ***(***Patient**)**

One of the major concerns is that aHUS is not diagnosed quickly enough because it's so rare. Failure to do so mean those patients can all too quickly end up with life-threatening kidney failure:
I had done everything in my power – taking my son to the doctors repeatedly, taking along a sample of urine that looked like Coca-Cola. And the doctor didn't pick up on it at all. I'd much rather they sent hundreds of kids for a blood test to catch one or two – because that time is so precious. In 48 hours, my son was in kidney failure. But if we had picked it up straight away *…* ***(***Parent**)**

I remember one Doctor said to me " We think you've got kidney failure but you are too young to have it so I think we are going to rule that one out" So I pointed out that my mum had kidney failure at 26 so it was not too young. I was transferred to HDU and put on dialysis and plasma exchange straight away. **(**Patient**)**

Patients are immediately sent to their local hospital. Once kidney failure is detected, affected children are sent by emergency ambulance to one of the children's hospitals in the country with renal specialists. Adults are sent to the nearest renal unit. Immediate treatment is focused on restoring kidney function and treating the anaemia (See Section 3.1) although doctors are often unable to identify the underlying cause. Patients are usually tested for a range of other conditions. When these come back negative, the typical form of HUS is often suspected despite the unusual presentation, and tests carried out for a preceding gastrointestinal *E. coli.* infection.

They tested me to see if I was pregnant and I wasn't, and they tested for HIV and I didn't have HIV…they didn't really know what was going on. They said…something like, we want it to be E-coli because we'll know what to do and it came back that they didn't know what it was, and that was the worst-case scenario*.* ***(***Patient**)**

Parents who had lost a child with aHUS were told that their child had died from the typical form HUS. They were told it was rare and very unlikely to happen again and encouraged to have more children. It was only when subsequent children also became ill that the atypical form was diagnosed. One mother was pregnant with her third child when her second child was, like the first, affected by aHUS and an accurate diagnosis obtained. The doctors offered a termination at this point, but she refused as she was already five months pregnant. Her third child was unaffected.

Adult patients who have been given an initial diagnosis of HUS are informed that the condition is unlikely to reoccur and that their kidney function may come back. It is only when test results come back negative for *E. coli*, or the disease reoccurs or kidney function is not restored, that aHUS is diagnosed. It typically takes several months to receive a final diagnosis. One patient was diagnosed in three weeks because by chance their senior house officer had recently worked with a registrar with an interest in aHUS. Another had waited ten years between their initial illness and final confirmation of aHUS because they became ill some time before the aHUS gene was discovered. In recent years, once aHUS is suspected, genetic tests have been carried out to confirm the diagnosis and identify the individual's mutation. However, the gene mutation has not been identified in all affected families, so this is not possible for everyone diagnosed with the condition (See Section 3.6). Many interviewees reported that this experience of incorrect and delayed diagnosis had '*rocked their faith in the medical profession*' and they no longer felt the same confidence in their doctors.

2.2 Patient/ carer experiences of accessing treatment and information

Patients are usually assigned to a kidney specialist for their treatment, because often the immediate and most pressing concern is the loss of kidney function. Patients therefore receive the care they need at the initial stages. They also receive clear information about their kidney failure and sometimes an explanation of HUS. However, kidney specialists may not have sufficient understanding of aHUS to recognise, treat and explain other aspects of the condition. This becomes a greater concern over the longer term.

They just told me I had HUS and that was it, there was nothing else said about it. It was just "You got HUS". I did not even know it was aHUS, I didn't know anything about all that.
(Patient**)**

The doctors as good as they are, are not aHUS specialists. My consultant is a nephrologist and aHUS is a blood condition. Having a specialist service would stop an awful lot of anxiety because for example my son has had tummy aches for a few weeks now. They've found out that people can have small eruptions of the condition. They think these rumblings are going on in the body, which could all gather up to be an acute attack. That's what's been concerning me – are there things bubbling away in his colon? I wish I could pick up the phone and ask the doctors whether there's something that needs to be done – but I don't have the confidence that my local team know enough about the condition. **(**Parent**)**

It beats me that when my partner goes to all these outpatient appointments at the hospital and she has regular visits by home dialysis nurses as well there is no talk about aHUS, no mention of it. **(**Partner/Carer**)**

Similarly, people may be incorrectly diagnosed with other conditions which may in fact be aHUS. For example, one parent of a child with aHUS had themselves been diagnosed and treated for many years for a rare form of life-threatening asthma. Only after discovering that they themselves carried the aHUS gene, did they consider that their asthma attacks could be due to aHUS affecting their lungs. They are concerned that their chest physician will not know about the condition or its treatment and are therefore seeking referral to a specialist.
Some patients have been lucky as they happen to live close to a hospital where doctors with specialist knowledge of aHUS have been available.

Others feel frustrated that their experience of diagnosis and treatment has been poor simply because of where they live. The lack of knowledge of aHUS amongst a majority of the medical profession means that patients/ families have not always received a full picture of their condition. Many interviewees reported that they only fully understood aHUS following the conference in 2011, despite having had the condition for many years.

There's an awful lot I've learnt going to the conference… We weren't even informed that adults could get this – we were under the impression it was only children. We were absolutely gobsmacked to see that…. For us that was massive – yet again. Nobody told us that it's life-threatening every time they have a reoccurrence. We also thought it was just in the kidneys. (*Parent***)**

Many of the interviewees had initially found information for themselves using the internet. American websites were the only source of patient information until last year. Since then, the work of aHUS UK has helped to increase people's understanding of the condition. Many said they now feel they know more about aHUS than their doctors. They feel better able to recognise the symptoms. They are more proactive in monitoring and are better prepared for repeat attacks.

As they have gained in confidence, they feel able to ask for services that might not otherwise have been offered.

I don't think my doctors understand this condition – because when I took him in last – they checked him over – but they didn't ask for a blood test. Really, I should have pushed it and said, 'the only way you can tell if there is low level complement activity is by checking his blood'. I've since been on the patient website and I've printed off all the information, as it's about empowering yourself and saying to these doctors 'This is what you should be looking for.'. **(**Parent**)**

Families with experience of aHUS are also better informed to ensure a more rapid diagnosis for other affected family members:

When some of my nieces and nephews got the test and knew they got the gene – when their children got ill, we sent them all the papers we had on it. They talked to their doctor and said, 'Could it be aHUS?' The doctors looked at them as if that was impossible, they didn't know what aHUS was*. (*Partner/ Family member**)**

2.3 Patient/ carer experiences of accessing genetic testing

Most families in England have accessed genetic tests without any problems. However, one family reported delays in getting tested and getting the results for one of their sons living in Scotland, a similar problem was reported in Wales. One family in England experienced delays as well as receiving incomplete results because their samples were sent to a research laboratory in Paris, rather than a UK diagnostic facility. Some of the delay was caused by a local trust refusing to pay for the test.

It took nine months to find out who would pay for it – because our local hospital trust refused – they didn't think it was serious enough. The courier service to Paris was expensive and that's what they were quibbling paying. So, my husband and I were going to have to go to a panel to say why it was so serious. That was all traumatic as well…in the end the specialist hospital paid…Our team want to have a specialist centre – which I totally agree with after the nightmare we've had, with everything taking so long and not doing the full test*...* **(**Parent**)**

I have not been tested. I want to have the testing done. None of my family has been tested. My father had kidney failure (recently deceased) and my Doctor thinks it was passed down from my father's side. **(**Patient**)**

2.4 Patient/ carer experiences of living with a rare condition
Many of the interviewees commented on the difficulty of the rareness of aHUS. They reported feeling lonely, isolated and '*a bit different*'. Until last year, they had not been able to access any peer support, having not been able to find anyone else in a similar position. The patient conference in 2011 was a positive experience for many. Hearing other people's stories had been informative, inspiring and reassuring. This provided the motivation and inspiration for setting up a patient support group.

I just thought I was the odd one out, as it were, I never really questioned it. **(**Patient**)**
You see people going for transplant and it works....and you are thinking you cannot have that*...* **(**Patient**)**

3. Patient/ carer experiences of aHUS and its treatment

3.1 Patient/ carer experiences of an aHUS attack

The acute phase of aHUS is life-threatening. Two of the families who contributed to this submission had lost children with aHUS. One family had lost two babies in the 1970s. Another had lost four children in the 1980s and '90s, three as babies and one child aged six.

My son had had four relapses – and during the fifth one he had really bad neurological involvement and we lost him just before he was seven. It's very difficult to control once you have neurological involvement – it just seems to be completely overwhelming and then the brain can't control the heartbeat or the respiration and then there's nothing that can be done then. **(**Parent**)**

During the active phase, many patients with aHUS require intensive care for weeks or months. Three of the patients who contributed to this submission (two adults and one child) had experienced heart failure and were resuscitated. This was either a consequence of the loss of kidney function or followed an allergic reaction to the treatment. Some adult patients do not have any memory of this time. Others can remember very painful experiences. Where aHUS has been triggered by pregnancy patients may experience the loss of a child or the anguish of separation from their new-born infant. This is obviously a traumatic time for partners, parents and family members. A number were told that their loved one was very unlikely to survive. They reported that they had coped by remaining positive, especially in front of the person with aHUS.

The whole family came running. We wouldn't have that thing where you sob by the side of them – we wouldn't let people be negative. They had to be very positive and you had to tell [the patient] what was happening…We had to keep upbeat and stay positive even when the doctors were saying 'Don't be ridiculous'. That wasn't us by nature, but that was the way we played it, because we had to find a way to cope with it. **(**Partner/ Family member**)**

It was very traumatic because it was so full-on – my son felt so ill – we were having to rub his back, rub his stomach – distraction tactics – really full-on as well as trying not to show your emotions in front of him - so he didn't realise how ill he was – that was really difficult. When you're in hospital with children, you don't know sometimes what time of day it is – it's a very intense kind of time – very surreal. **(**Parent**)**

It was pregnancy that brought mine on you know and I lost the baby*…*
(Patient**)**

… ***because I had a caesarean, had some infection in there as well, so at that point they were more concerned about that... then I went into intensive care …*** **(**Patient**)**

Before their illness, the patients showed no signs of ill-health. There are no warning symptoms or signs, so the initial attack is unexpected – *'a bolt from the blue'*. Families are greatly shocked by this experience and their lives completely changed as a result. Many reported that this was a time they consciously tried to put behind them.
You're just trucking along normally – nothing bad had ever happened to us. Then it just hits you like a car crash – you go into shock. The severity of how ill [X] was in the beginning was just beyond stress. It was very, very hard. That was the bit we had to put into a box for a long time and forget about and try and not dwell on. **(**Partner/ Family member**)**

We felt out of control, the control of our lives seemed to have been taken away by it. **(**Patient)

Many also reported that this trauma had contributed to heightened levels of anxiety ever since, a general feeling that '*something bad is going to happen'*. This is true for adult patients, parents and carers. At the same time, some felt that the experience had given them a different perspective on life. It had encouraged them to make the most of each day and appreciate what they have. Many said they coped with aHUS by staying focused on the positive.

3.2 Patient/ carer experience of hospital care

Once the initial acute phase is over, patients can remain severely ill for some time. Typically, they remain in hospital for a further 2-20 weeks, depending on how seriously they are affected. Patients who have not suffered renal failure continue to receive plasma exchange to suppress the disease activity. Patients with renal failure start dialysis. The impact of these two treatments is discussed in Sections 3.3 and 3.4.

For parents and family members, a long stay in hospital often means '*putting their life on hold*' to provide their loved one with vital care and support. Children often need their parents to be with them full-time. Parents may therefore need to take extended leave from work and as well as ensuring that any other children are cared for. The lives of parents, grandparents, other family members and siblings are therefore severely disrupted.

My son found it very hard in the hospital. He doesn't cope with pain very well and he was in a lot of pain. He found the machines really hard work – he couldn't stand the lights and the bleeps – so both my husband and I had to be there in shifts – because my son needed to have us there. **(**Parent**)**

You have no life. You just live at the hospital. My husband and I took it in turns to go back and look after our son at home. All you do is come to your house, have a shower, pick up your son from school, cook for him, sleep, or work, drop him off and go to the hospital again*...* **(**Parent**)**

3.3 Patient/ carer experience of plasma exchange

Plasma exchange (PEX) is typically carried out daily in the initial stages requiring patients to remain in hospital. As patients improve, the number of exchanges is reduced, with constant monitoring to track disease activity. When the number of PEXs is reduced to 2 or 3 a week, patients can usually go home, returning to hospital for their treatments. Although the treatment only lasts 2-3 hours, these visits usually take much longer with the travel time, waiting times, blood tests and recovery time. Parents/ carers need to attend these sessions with their children, which

is disruptive to daily life and the wider family. Parents reported that their children appeared to cope well with the PEX treatment.
Some patients can be gradually weaned off PEX and go into remission. Others may be more severely affected and find they are unable to reduce the number of treatments to below 2 or 3 times a week without a reoccurrence. The treatment needs to continue all the time the disease is active. For example, one child with aHUS had received PEX three times a week for over three years, with repeated reoccurrences, before being given Eculizumab in 2011 (see Section 6.1).
PEX is carried out via an implanted catheter or ‘line’ in a vein. Patients require an operation to place the line and this is difficult to do in babies and young children. Lines need to be protected from infection, which prevent patients from having a bath or swimming. Large, very sticky, waterproof dressings are used, but infections are not uncommon. These can be 8

serious and life-threatening, especially for young children. Infected lines may need to be taken out and replaced. During this time, while infections are being treated, the patient is no longer receiving treatment and the aHUS can reoccur, requiring hospitalisation. There is a limit to how many times lines can be replaced.

The body only has so many ports – places where they can put lines and we were warned that she would run out of ports eventually... That was a major concern – because you have to keep at least two ports available for a future transplant and she was running out of ports. **(**Parent**)**

Lines can also come out causing great distress to all involved.

I was taking my son to school in the morning as always, I was on the driveway, and the lady who was helping us at the time, she came running up and said the blood is coming from everywhere and basically my daughter's line had fallen out, because of the pressure there was blood everywhere…**(**Parent**)**

Adult patients reported that the treatment itself can be difficult to tolerate as there are many side-effects (see Section 6.1).

*...**After fourteen years it does take its toll, it is bound to take its toll on your body** ...* **(**Patient**)**

3.4 Patient/ carer experience of dialysis

Dialysis may be required temporarily if kidney function is lost during the acute stages of aHUS. If a patient's kidneys are permanently damaged during this phase, they will need dialysis for the rest of their lives. People with aHUS may not have the option for a transplant (see Section 3.5).

You have kidney failure and that's really what living with aHUS is for me, ***it's living with kidney failure. I don't live with aHUS, because I only got it twice, when it first happened and when it came back in the transplant - those are the only two episodes that I've ever experienced.*** **(**Patient**)**

In the short term, haemodialysis is carried out through a central line either in the neck or groin. This is uncomfortable and liable to infection. Peritoneal dialysis is often the first choice for long term dialysis as patients can return home quickly. However, it is difficult to manage, often not as effective as haemodialysis and is associated with serious side-effects. Two of the patients who contributed to this submission had developed encapsulating sclerosing peritonitis (infection and scarring in the abdomen that interferes with bowel function and prohibits further peritoneal dialysis). Many patients therefore switch to long-term haemodialysis.

I had opted to try a system of dialysis at home which involved an exchange of fluids through a catheter in my peritoneum. It frequently went wrong. I hated every minute and every aspect of it.

***It required a lot of equipment, training, and had to be done 4 times a day taking about half an hour. It did not make me feel better, I was permanently anaemic, exhausted and frequently ringing my husband who was trying to work, to take me to hospital to sort the catheter out. My days consisted of lying on the settee too weak to do anything, unable to eat due to 2 litres of fluid in my abdomen causing discomfort - quality of life nil*.** (Patient)

3.4.1 Preparation for long-term haemodialysis

For long term haemodialysis a site for vascular access needs to be prepared, which is the site where blood is removed from and returned to the body. The best way to do this is with a fistula, which requires surgery and involves connecting an artery directly to a vein, most often in the forearm. Sometimes veins are removed from the leg and grafted to the arm. The fistula causes more blood to flow into the vein. As a result, the vein grows larger and stronger, making repeated needle insertions easier. It can take weeks or months for a fistula to be ready for use. Fistulas need to be carefully maintained, placing some restrictions on the patient's life. Patients are advised not to carry anything heavy or to have blood taken from that arm. The fistula is unsightly which affects what people wear and makes them feel self-conscious (See Section 5.2). Fistulas need regular checking to ensure they do not become infected or blocked by a blood clot. Treatment is required if this happens. Some may need stretching with angioplasty which is painful. Keeping their fistula clear can be a source of constant anxiety and concern for patients on dialysis, especially when previous grafts or fistulas have failed.

At the end of the day I'm being kept alive through this access to dialyse, and if that access goes, then that's that. So, they [the doctors] are really fighting to keep this lifeline, but I don't know how much longer I'm going to be able to keep it… **(Patient)**

If patients choose to dialyse at home, parents, carers and adult patients need a month's training in managing the process, learning how to put the needles in, how to set up the machine and how to cope with any emergencies such as blood clots, infections, a blown vein (pushing the needle through the wall of a vein leading to painful blood loss into surrounding tissue) and air bubbles in the line which can be fatal.

3.4.2 Managing dialysis day-to-day

For aHUS patients with kidney failure, it's dialysis that has the biggest impact on their day-to-day life. They have no option but to dialyse 3-5 times a week, which severely restricts their freedom. Every day is scheduled around dialysis. Children's freedom is restricted in simple ways, for example not being able to stay over with friends.

The main thing about dialysis is the lack of freedom, and the things that people take for granted…Trying to plan things is a nightmare because I don't know how I'll be feeling. I don't know where I will be in 2 weeks' time because I could change things around or swap things over. You can't ever be spontaneous… **(**Patient**)**

There is some variation in how much individuals need to dialyse. There are different kinds of dialysis and choices about whether to dialyse at home or at hospital. Going to hospital is more restrictive as patients are

given a time slot (e.g. 5pm on a Monday, Wednesday and Friday) that they cannot change. Several patients are given the same time slot, and all have to wait their turn to be connected to a machine by a nurse, causing delays. Some people prefer this option as they are able to clearly separate dialysis from the rest of their lives.
Some patients/ parents choose to dialyse at home. This gives them some flexibility and control over their time. Although patients can never miss a session, they can be flexible over the timing of their sessions within a 24 – 48-hour window. This makes it considerably easier to manage day to day life. For example, one mother described how she timed her daily sessions so as to be able to drop off and pick up her daughter from nursery. However, managing the process takes a considerable amount of organisation and planning. 10

Having dialysis at home can feel invasive. Therefore, if they have the space, patients/ families tend to set up a dialysis room, to keep it separate from the rest of their home life. However, there is still a large volume of equipment required in addition to the dialysis machine, for example paper towels, new lines, artificial kidneys that are delivered regularly and need to be stored '*all round the house'*.

Dialysis is extremely time-consuming. One of the adult patients who has dialysis during the day, five times a week estimated it takes 35-40 hours a week. Some patients have chosen to dialyse overnight, which minimises the impact on daily life. For parents, managing their child's dialysis and working, leaves very little time for anything else.

I come in from work about 6 - 7 and the first thing I have to do is set up the machine, I finish that by 8… then you obviously have to connect her. So, this is it. This is my evening… For me it's a constant, constant rush. It's just a daily struggle to cope with everything. And it's the other things like deliveries, and you have to order the medicine, and cleaning, and check-ups. (Parent)

*...**It is like another job to me and I am going to do my job**.* (Patient**)**

I think of it as like spring cleaning, something you don't like to do but you have got to do it and that is the way I look at it. **(**Patient**)**

The process is also demanding, as it requires technical skill and careful management to avoid infection. The entire process from start to finish involves:

- Heating the machine to disinfect it
- Washing patients and carer's hands – for two minutes with harsh, antibacterial soap
- Setting up a syringe that drives an anti-clotting agent into the blood throughout the dialysis
- Priming the lines with saline to prevent air bubbles getting in
- Calculating how much fluid needs to be removed – based on the patient's current weight and past dry weight (immediately after the last session). This is programmed into the machine. As much as 3.5 litres can be removed at any one time, but removing this much fluid leaves patients drained and exhausted, which is why they restrict their fluid in between dialysis sessions
- A blood pressure check.
- Two large (1.6 mm) needles are then inserted into the fistula and the dialysis begins – 400 ml of blood goes into the machine – this blood loss can cause blood pressure to drop and make the patient feel ill.
- While on dialysis constant checks are made to ensure the machine is working properly, there are no leaks in the lines, the needles are positioned properly etc.

 Being on the machine is draining and there can be serious side-effects – painful muscle cramps, migraines and a fall in blood pressure – which can make the patient feel extremely ill.
 At the end of the dialysis, the blood in the machine is washed back into the body using saline. The needles are removed. The blood in the fistula is under the same pressure as an artery, so the site needs to be taped/ pressed on for 10 minutes to prevent blood loss.
 The machine is cleaned, and the room cleaned and sterilised.

The entire process takes 4-5 hours. It is not relaxing. Patients often need to sleep for a couple of hours afterwards to recover.
Whilst on the machine you feel progressively drained and your anxiety to come off increases… I also get very itchy all over my body…. It is hard enough that you are trapped on the machine, but you also feel uncomfortable whilst you wait. Clock watching is a common past time (Patient)

The common frustrations of modern life take on a greater significance for dialysis patients.
If there's a technical fault, you can't go on dialysis until a technician can fix the machine. Technicians don't work on Sundays or after 4.30pm. Another complication is when the water pressure drops or there is a power cut. When people were talking about the petrol strike, I was worrying about how I was going to get to my dialysis… **(**Patient**)**
Patients cannot dialyse alone. A parent or adult carer needs to be on hand at all times in case something goes wrong. The machines are fitted with an alarm. A number of parents/ carers reported that they feel quite anxious during dialysis, constantly listening out for the alarm. During overnight dialysis for their children, some parents report they have a much poorer night's sleep. One parent described how she had once slept through the alarm when her daughter's line had become clogged with a blood clot. She was able to take her daughter to hospital to have the problem resolved, but she lost her confidence. She now chooses to put her daughter on dialysis late in the evening through to one or two o'clock in the morning, even though she has to go to work the next day, because she knows she can stay awake during this time. Being a parent or carer for someone on dialysis can therefore feel like a huge responsibility. Many interviewees said it feels '*unrelenting*' as there is no option to stop or take a break, no matter how ill the patient or the carer may be feeling.
If I had severe diarrhoea, severe sickness and I was crawling on that floor I would still have to go to dialysis…Two weeks ago I had

a really severe chest infection and I had to be taken there in a wheelchair. I didn't feel like going but you have to… (Patient**)**

3.4.3 Impact on quality of life

Patients do not always feel well on dialysis. Children are often tired and sick because of the shifts in fluid. Adults report sleepless nights, cramps, headaches and migraines. This is because dialysis is a poor substitute for a functioning kidney. Other aspects of kidney function are compensated by other treatments e.g. injections of the hormone erythropoietin to regulate red blood cell production, but these treatments are also not as effective at maintaining the body's balance. Dialysis patients therefore experience see-saw side-effects of high or low blood pressure, overly high levels of haemoglobin or anaemia.

Dialysis patients and their families are able to go on holiday, but only with considerable planning and organisation. It is not a simple choice. Some patients are too fearful of the risks. Others reported that it took five years for them to build up the confidence to do it. Parents have taken their child's dialysis machine with them. Adult patients are able to book dialysis sessions at the local hospital at their holiday destination, abroad and in the UK, although availability may be limited. This restricts families' choice about where they go on holiday and for the person with aHUS, much of their holiday time is spent in hospital.

You just wouldn't believe what we had to take on holiday, how long we had to spend arranging everything…It is possible, and I wanted to go for holidays like everyone else…I think we started to arrange it more than half a year ago. The fluids had to be delivered, we had to take the machine…We had to arrange a hospital over there so that if anything was to happen, we could go there…And for me particularly it's not a holiday because we still have to do the dialysis. **(**Parent**)**

3.5 Patient/ carer experience of kidney transplants

Patients with aHUS are not always recommended to have a transplant because of the likelihood of the new kidney being damaged by the disease. Amongst the aHUS affected patients in the UK, 16% have had a successful transplant (personal communication – Professor Tim Goodship). Six of the adult patients who contributed to this submission had undergone this procedure. In two cases, the patients felt the doctors had not sufficiently explained that the aHUS might come back and had every hope of the transplant working. In the four other cases, the patients and families were aware that there was a reduced chance of success, but there seemed to be no other option. None were successful. Patients had their new kidneys removed within a matter of weeks. The physical and emotional impacts were severe for the patients as well as for parents or partners who had been donors. This was a topic interviewee felt unable to talk about.

Well they left me in the room with people whose [transplants] are working. Well they were being so happy; I think that is what got to me in the end. I never talk about anything to do with transplant, I never talk about it. **(**Patient**)**

*...**and I have seen people coming back and it would be working, and they are happy and then they tell you your kidney was failing, and you've gone through all that for nothing.*** (Patient**)**

3.6 Patient/ carer experience of living with a genetic condition

In some families, there is no history of aHUS, prior to a single family member becoming ill. Others are able to trace the disease back through 2 or 3 generations and have several family members affected at the same time. Therefore parents (and other family members) often only become aware of their own risks, once their child or sibling has been affected. Once discovered, this leads to increased anxiety about their own health as well as concerns for others. Many reported managing this anxiety by trying not dwell on their fears.

Knowing that I've got the gene, I've sort of put it to the back of my mind. My philosophy always has been that you live life. Recently I've been thinking what about the rest of the family that have got the gene, but there's nothing you can do. You can't think about it all the time. **(**Partner/ Family member**)**

My worry then is, if it's been passed down, about my nephews and nieces, I worry about them. **(**Patient**)**

Parents with an affected child often choose to have genetic tests themselves either to allay concerns about their health or because they have been tested as potential donors. Once identified, the affected parent then faces the challenges of informing the wider family, their own siblings and nieces and nephews. Some people want to know about their genetic risks to inform their life choices. Others say they would

prefer not to know their status to avoid the anxiety, particularly as not everyone with the aHUS gene mutation develops the condition and there are no measures to prevent the disease occurring. Decisions about who to tell and what to tell them, can place considerable strain on individuals and family relationships.

Parents also face difficult choices about whether to have all their children tested once one child is known to be affected. Some choose not to have their children tested so as to reserve their children's rights to find out for themselves. Others find they become so anxious whenever their children become ill, that they feel them simply '*need to know*'.

Some families do not have this choice, because although a family member has been diagnosed with aHUS, doctors have been unable to find their particular genetic mutation. This means they cannot look for it in others. These families therefore continue to live with the uncertainty as to who might be affected. This occurs in about 10% of cases.

People say to me, 'It won't be long before you have grandchildren' and I think 'Oh no'. All that worry again – it's just going to be horrendous. And other people in our family of the same generation as my children are now having children – which is a worry as we don't know where it's come from. For now, everybody just pushes it to the back of their minds. But it's something that never goes away*. (*Parent)

)

3.7 Patient / carer's overall experience of living with the condition

There are many sources of stress and anxiety with aHUS. After the initial trauma of a life-threatening episode, patients and their families live with the constant threat of a reoccurrence. Each reoccurrence is likely to lead to further kidney damage and eventually renal failure or could potentially be fatal. Some patients report that their emotional well-being is much affected by a fear of dying and knowing they have a reduced life expectancy.

There are currently no markers to indicate whether a reoccurrence will happen, when it might happen or how serious it might be. This means families have to live with a great deal of uncertainty. Patients with other reoccurring conditions with severe relapses, for example multiple sclerosis, find this uncertainty to be one of the most difficult aspects of the condition to live with

Living with the effects of MS. The MS Society. www.mssociety.org.uk

It's this constant worry, constant stress that you don't know what will happen. The unpredictability is just killing. **(**Parent**)**

My son's first episode was so traumatising – and then to find out that you might have to go through that again… It's that million-dollar question - will he be one of those lucky people who never get it again? It has been a lot for me and my husband to get our heads round – so how do you tell a child about that? I don't think he needs to carry that on his shoulders yet. If he asks about it, I'll tell him, but I'll be fairly blasé about it until I feel he's ready to take it on board. **(**Parent**)**

Parents with children with aHUS in remission, (as well as those who know their unaffected child carries the gene) report having to manage their anxiety every time their child becomes ill, because the start of aHUS looks like many other common childhood illnesses. However, all concerned, including family GPs, now feel more confident about recognising the signs of aHUS so that if there were a next time, their child would be treated more quickly.

We try not to over worry or otherwise every time she got a runny nose we'd take her down the doctors, so we try not to do that – if she's got a cold we keep an eye on how often she's going to toilet – it's always on the back of your mind. **(**Partner/ Family member**)**

Those patients who have reached end stage renal failure report that '*aHUS has done its worst*'. However, they and their families have to manage the daily stresses of life with dialysis (See Section 3.4).

Many parents, partners and carers of people with aHUS reported that living with the condition had taken a toll on their mental and physical health. These problems included high blood pressure, anxiety and panic attacks. Some were receiving medication to manage these problems. Others were receiving counselling. One parent thought counselling should be offered routinely for families with aHUS. This is not often the case.

...I do not go out anymore you know I am frightened something else is going to go wrong... **(**Patient**)**

All of the interviewees talked about how they had learnt to live with the demands of the condition and its treatment and to some extent had forgotten what it was like to live a 'normal life'. It's only when looking back or talking to other people that they wonder how they have managed.

The questions you would expect, like, why me, why now, they sort of disappeared, because you get used to this life and you think that it's been like this forever, and it's almost forgotten that it can be different. **(**Parent**)**

4. aHUS in babies and children

Children were not interviewed for this submission, because all of the children involved (except for one) were under the age five. The oldest child is not aware they have aHUS. Therefore, this section is based on the reports of parents and other adult family members.

4.1 Impact on the child's well-being

Most babies and young children appear to cope extremely well with their early experiences of their condition. (See Sections 3.1 - 3.3).

My daughter was obviously very young when she was diagnosed which I'm grateful for – as she hasn't known anything different. She's quite comfortable in hospital and looks forward to it – which sounds crazy – but the hospital staff are almost friends to her. **(**Parent**)**

One part of the treatment which is particularly difficult for children is the large numbers of blood tests required and the repeated access to veins for infusions.

They had to take him into theatre and give him an anaesthetic to get to a vein because he was still under two. But he was reacting very badly to the anaesthetic every time. Normally he's a placid child, but he would scream for an hour or two after the anaesthetic. **(**Partner/ Family member**)**

Some children need to be held down initially, but over time they become more used to the procedures involved. Other children develop hospital or needle phobias after the trauma of the initial aHUS episode.

It's had an impact on my son's mental health. Being in a hospital or at the doctors – he's very anxious – he can be under the table – sometimes he never even makes it into the room. We've learnt over time how to manage it and calm him. He hates needles – when he has blood taken, we've had to have 4 or 5 of us hold him down.

Last time he had gas and air and he thought it was great – so now we've got something that will reduce his anxiety. *(*Parent)

The ongoing impact of aHUS depends on which organs have been affected. Children with kidney failure face the similar challenges to adults in managing the restrictions of dialysis (See Section 3.3). Some children also experience brain damage during an initial aHUS attack with consequences for their daily life and ongoing care.

My son later had problems with his balance. It didn't manifest itself until about 15 months when he was having difficulty walking. Then he was having a lot of physiotherapy and we got quite involved in conductive education because he had ataxia. So, he had a lot of input from other services and he couldn't go to a normal school. (Parent***)***

(

4.2 Impact on daily life

Children with aHUS who have lost their kidney function often do not eat because they lose their appetite. They are therefore fed through a nasal gastric tube or directly into their stomach. The latter is better for children at school as the tube can be kept out of sight and the children themselves find it easier to cope with. One of the children included in this submission is supported at school by a teaching assistant who has been trained by the hospital to feed her twice a day and to monitor her fluid uptake. School staff are often very supportive and heavily involved in managing the condition.

4.3 Impact on schooling / education

Children with aHUS who continue to receive treatment inevitably miss time at school. Not only do they miss the days they are having treatment, but every time there is a problem, e.g. an infection, they may miss weeks of school while in hospital. Parents and teachers cannot always compensate for the loss of time.

Initially the first year it happened she wasn't basically present at school, now later on, at least once a month we have to go to clinic, then there's all the other extras on top of that…when I speak to the teachers, they say she's making good progress but she's always in a lower group, and I think she's a bright girl, but she missed a lot, and I cannot give her that time at home, to make her catch up, because we struggle with time so badly [with dialysis]. I think I would need to quit my job to take care of that problem. **(Parent)**

4.4 Impact on parents' well-being

In addition to the long-term stress and anxiety (see Section 2.7); some parents also develop a 'fear' of hospitals.

For the last four years I'm just like a robot, but still I do everything to stay out of hospital. I'll do anything because I had such bad experiences…In the hospital every single child has a very serious disease…So if you are around that all the time, you're just going down… (Parent**)**

4.5 Impact on parents' work and ability to earn a living

Parents whose child requires continuous care, e.g. regular plasma exchanges in hospital (See Section 3.3), may have no option but to stop work. Others report that they are fortunate in being able to fit their work flexibly around their child's treatment. Nursery or childcare may not be an option. Other family members are relied upon to provide more specialised childcare as they will have been trained in managing the condition. Grandparents, who are retired, often provide a lot of childcare. In addition, grandparents and other family members sometimes provide financial support.

4.6 Impact on siblings/ other family members

The brothers and sisters of children with aHUS are often affected by being left in the care of others, while their parents spend long periods in hospital with their sibling.

The other child doesn't see their Mum and Dad as often as they'd like. It's not good for children to be separated from their family. I don't think my granddaughter could understand why she was with grandma for what seemed like weeks on end. We took her up to see her brother when we could – but Mummy and Daddy were away a lot of the time. You try to make life pleasant for them but it's quite a strain on grandparents too. **(**Partner/ Family member)

Parents report that they find it difficult to give their other children sufficient attention.

My son's life was very limited because our life was, unless friends offered to take him somewhere, we couldn't...It was very difficult. Even a trip to the cinema, you're there, but you're not there, you're thinking what if I have to go back, what if something happens… and he became part of it, and he's like 'It's time to do blood pressure, let's go and hook her on the machine'... and at the same time I have to say to him 'Don't come into the room, because you've got a cold, you didn't wash your hands' *...* ***(***Parent**)**

Some siblings cope extremely well. Others had exhibited behavioural problems, most likely resulting from the stress and lack of attention.

When you are constantly involved with one child, it's obvious that you don't have much time for the other one and he's been affected by that…he's got these aggressive outbursts… it's kind of he wants attention basically, but everyone in the household is really emotionally exhausted. It's been four long years. No one has any more patience in this house. **(**Parent**)**

4.7 Impact on relationships

Having a child with aHUS places considerable strain on relationships. A number of parents are no longer together. However, some parents say the experience has made them closer, and that they work well as a team supporting their child.

5. Impact on adults

There are two peak ages where adults develop aHUS, in their early 20s and in their 60s. The impact of the condition on people's lives is very different at these two life stages. These are highlighted in this section.

5.1 The impact of the condition on life events

In their early twenties, young adults are just about to embark on their lives and make choices about relationships, careers, where they want to live, buying houses and whether to start a family. Developing aHUS at this age therefore has an impact on all these life decisions.

It's like one of those pivotal moments in your life. I don't think I'd be living in here; I don't think I'd be living in Britain if I hadn't got

***kidney failure…I was ready to leave home and do my thing and it just stopped me in my tracks really*. (**Patient**)**

After the initial attack, some people never become well enough to return to work. Some have managed to do so but have taken 2-5 years to recover their health to the extent that they could go back to work or resume their lives, for example to **return** to university to finish a degree. They relied on their parents for a lot of care at this time (See also Section 5.5). They report the sense of having lost a significant chunk of their lives to the disease.

***I had to go back living with my mother, and I couldn't afford my own place anymore*. (**Patient)

Women of child-bearing age with aHUS (or with a genetic risk of aHUS) are advised not to have children, because pregnancy is thought to be a trigger for the condition. Young women with kidney failure are also warned that it is not possible to carry a pregnancy to full-term on dialysis, and that their babies are likely to be still born or severely disabled. Young women with aHUS have therefore often made the difficult decision not to have children. Couples have also been turned **down for adoption because of one partner's kidney condition.**

...I lost the baby then, but I wouldn't try again, you know thinking "are they going to have it?" **(**Patient**)**

Developing aHUS at a later age clearly doesn't have these same impacts. However, patients report that their life-long plans for retirement have been stalled or prevented by aHUS.

5.2 Impact on adult patients' well-being

Following the initial acute phase, patients report experiencing depression, loss of confidence, self-esteem as well as problems with anxiety and nightmares.

I suffered panic attacks quite a lot which was brought on by the dialysis and when you're first on dialysis your heart starts to beat a bit faster anyway… and the reaction to that and the stress and the panic…**(**Patient)

Patients report that their emotional health improves to some extent over time, particularly with support from families and counselling. Parents and siblings have often provided the necessary motivation and encouragement to enable patients to make the effort to get stronger and resume their lives.

People on dialysis report that the treatment itself also affects their emotional well-being:

I've got memory loss and depression because the kidneys don't just filter. I get aggressive when I need dialysis because of the toxin build-up, and I get really upset when I can't get my needles in…I do cry, and I feel like I could smash the house up – I don't obviously. Once I've done it, I'm fine. **(**Patient**)**

...*it has affected her health, wellbeing, attitude, it is sad to see, I mean when she's on top form... but she is not on top form often enough. It is really getting to her now...* **(**Partner**)**

Some patients can also feel self-conscious about their scars, which can be large and considerable in number. After years of aHUS, patients have scars from their lines, fistulas, vein grafts, kidney removal/ transplants and catheters. Young women have experienced loss of self-esteem from the scarring, but report finding it easier to cope with as they grow older. They still tend to keep their scars covered. Some report feeling judged by other people.

People see my arm and see my fistula and think I'm a drug addict. People pull their kids away from me. That's not their fault because they don't know about it. **(**Patient)

5.3 Impact on daily life

Adult patients on dialysis are severely restricted in their diet and daily fluid intake. They are advised to limit their daily fluid consumption to 500-1000 ml per day, which also includes any fluid in food, e.g. gravy, yoghurt. They need to maintain a low-potassium diet because if their blood potassium levels become too high, they are at risk of a heart attack. Potassium-rich foods include all fruit and vegetables and chocolate. Any vegetables need to be boiled twice to remove the potassium. Patients also need to limit their phosphate intake as this can lead to calcification of the arteries. Dairy products are therefore restricted because of their phosphate levels. Salty foods are avoided as they make people thirsty. Some people avoid alcohol as it reduces their willpower to stick with their regime. People find this diet difficult to manage.

I want to eat the whole bar of chocolate, and I pretend I don't want to, but actually I can't, and it's just so restricting, ridiculously restricting. Every time I eat anything I always calculate the potassium content, the phosphate content so that I can think for the 48 hours that I'm not on the machine what could I get away with, how sneaky can I be, and how much can I get away with*.*** **(**Patient**)**

It's a big balancing act with everything. We have to keep a balance on my wife's diet – if she has too much of something, she can feel tired and dizzy – but there's no blood testing kit you can have at home, like there is for people with diabetes. If you take your bloods off to hospital you can have the reading in five minutes – but there's nothing like that for renal patients. So that's always a constant worry whether something is going to be too high or too low*.*** **(**Partner/ Family member**)**

I think getting up and going and doing whatever you like without having to think "Oh god I've got to get back for dialysis" that would be the best, the best way to live your life*...* **(**Patient**)**

These restrictions inevitably affect other family members when shopping for food and cooking family meals. Meals may have to be prepared separately for unaffected family members, so that they get the nutrition they need. However, family members can feel uncomfortable about eating and drinking in front of the person with aHUS as it seems '*unfair and marking them out as different'*.

Patients/ families find it difficult to eat out as there may only be one choice on a menu available to them. There may be nothing they can eat on special occasions which often centre on eating and drinking.

I went to a wedding and I didn't eat at the wedding and with all those situations, I hate the fact that I have to be so controlling, it's

not in my nature to be so, I'd like to be more laid back about things… **(**Patient**)**

5.4 Impact on patient's ability to work and earn a living

Some aHUS patients of working age are well enough to continue work and manage their dialysis. However, trying to manage a job and regular daytime dialysis leaves very little time for anything else and patients have found it unsustainable. They have reported becoming more ill as a result and have had to stop work temporarily or permanently to recover. Some people with aHUS have therefore chosen to dialyse overnight to give them more free time in the day. However, as one patient described, she still does not have the physical energy or emotional resources to cope with a full-time job. She therefore works part-time which is a source of some frustration, because she feels discriminated against in terms of her pay and access to promotion. 1

I worked all my life and when I had this kidney failure first of all I had to give up work. **(**Patient**)**

Other patients have reluctantly chosen to take early retirement as they have become too ill to continue working.

I was in my job for twelve years and I loved it. My bosses and colleagues were really supportive, even when I needed to take time off. But they kept saying to me 'When will you take ill-health retirement? You do need to'. I put it off and put it off, until my consultant said you really need to increase your dialysis. You won't live past 40 if you don't. Three days a week isn't enough for you. So now I dialyse at home five days a week and I'm loads better**.** **(**Patient**)**

Some families have found themselves in serious financial difficulties, having to rely on a single wage-earner and maybe forced to make unwelcome changes such as moving to a new house or selling their car. Some receive benefits. Home haemodialysis patients are entitled to disability living allowance. This can go some way to helping with the additional costs. Some of the main costs are parking and travel for regular hospital visits, estimated by one patient to be between 50-100 visits a year. People who have stopped work through ill-health are also entitled to employment support allowance. However, proving eligibility for this benefit, managing the continual changes in allowance levels, and the knock-on consequences for other entitlements is '*hard work'* and another source of stress. Some people find it difficult to be on benefits.

The aHUS it takes away your self-respect in a way, because I've always been brought up, you have to work for what you earn… I went to college, I did my nursery nursing, and then all of sudden to go on DLA, I hated it… **(**Patient**)**

Now it's a financial struggle to be honest –if I could work tomorrow I would*.* **(**Patient**)**

*...**it took me four years to get disability [allowance} because they would not give it to me**. (Patient**)***

5.4 Impact on quality of life

All the adult patients reported having adapted their lives to be able to manage the treatment for this condition in ways that have surprised them. For example, one young woman described how she would have never believed she was capable of putting her own needles in, but now does that five times a week. This is largely because people have no choice but to dialyse, and therefore have to manage its stresses and complications. They feel this is an unacceptable quality of life, but it is one they have to accept.

I see a lot of blood. I see a lot of blood clots. The other day on the machine, I forgot to put a clamp on, and the blood poured out of the

machine, so my blood was in a pool on the floor. It's 6 o'clock in the morning so I'm shouting to my mum to come and help me because she hates the alarm. Something had gone wrong with the machine and I was having to pump blood back into myself… and me and my mum were just laughing, she was like mopping up blood off the floor and I was like 'When did this stop being shocking to us…anyone else would be shocked*…'* **(**Patient**)**

I would not needle myself I was like "ooooh" and they had to chase me to needle me because I was petrified ...I was petrified! But now it's a job to me and now I have to do my job. (Patient**)**

5.5 Impact on social life / relationships

Adults with aHUS say the condition affects all their relationships. Young people embarking on new relationships, worry about when to tell new partners about their condition and how they will react. Many early relationships end for this reason, because other people feel unable to cope or manage their fear. This obviously impacts on the patient's self-esteem and emotional well-being.

When you meet new people or start going out with someone it's really hard. For the first date I pretended to go to the toilet. I don't go to the toilet, how weird is that? But I pretended to go to the toilet so I would look like a normal person… **(**Patient**)**

All family relationships are altered if young adults are forced to become dependent on their parents again. Family dynamics can change, as the affected person takes prime position in the family, even if they may not want to, and everyone around them feels they have no choice about it. Children may not receive the attention they need when their parent becomes ill.

My youngest son was a teenager when my health first started to deteriorate. Consequently, he was really rather neglected at a difficult time in his life. Neither of us was able to support him and normal family life was crumbling around him. His education suffered, he gave up A levels, changed direction several times, went from job to job. When he had started high school, he had had a bright future. **(**Patient)

Families supporting a person on dialysis can end up spending a lot more time together than they might otherwise do, and not really because they choose to. Partners, parents and siblings tend to share the responsibility of supporting the patient during dialysis, as the main carer may not always be well enough or may need a break. On the positive side, this experience tends to bring families closer together.

Most people with aHUS report that their friends are understanding and supportive and will organise social events so as to make it easier for them, for example, ensuring that '*nights out won't all revolve around eating and drinking'*. Some people feel their social lives are affected, because they aren't invited out as often, because friends assume, they won't be well enough or for example, that they won't be able to stay over for a weekend.

5.6. Impact on partners/ carers

As well as the high levels of stress and anxiety associated with this condition (see Section 2.7), partners and carers also have to manage the restrictions on their own lives. Their social life and other interests/ hobbies may be limited by dialysis and the unpredictability of the condition. Some partners/ carers have given up work or gone part-time to be able to provide care, which again has financial implications for the family.

Doing dialysis at home you're never in a routine – you never know what's going to happen or how well she'll feel after a session – then we can't do stuff as a family... Or we have to cancel things at the last minute. Then people stop inviting you and asking you to go out. It's had a knock-on effect with my mates asking me to go out to the pub…we try to do our best to juggle and keep all of us happy at the same time. **(**Partner/ Family member**)**

Partners/ carers may have to take on more responsibility in the management of day-to-day life than they might do otherwise, which affects their own well-being.

My husband can get a bit down because when I'm well I try to do things like gardening or decorating – and he'll say "rest, rest, rest" because you'll make yourself bad the next day, which I do. But when I'm well I want to make the most of it, I hate not doing something, I hate just sitting – it's not me. I think he takes on stuff sometimes that is too much, just so I won't do it… **(**Patient)

Partners can find themselves, more often in the role of carer, than as husband or wife. Dialysis can also restrict their physical relationship.

5.7 Impact on siblings/ other family members

Other siblings/ family members report that their lives have changed dramatically as a result of having a person with aHUS in the family. Their life choices, for example about where to live and their jobs, can be restricted by needing to be close to their family. This is ongoing and affects their own families too, for example their husband/ wife may not be able to take a job promotion if it means moving to a new house. To some extent this is a choice individual make for themselves, but at the same time, they can feel a responsibility to others, to provide support to the whole family and do their share of the caring e.g. in managing dialysis.

Some family members who take genetic tests and find they are unaffected, report feelings of guilt, particularly when this means they can make life choices that are not open to the person with aHUS.

The impact was massive on the family – it has affected us all and changed the course of all our lives. It still does. Every day. It's so engrained in us now – you're not always aware of what impact it's had. It's only when you talk to other people and they react. You can't think about it – it would just eat you up. **(**Partner/ Family member)

6. Patient /carer experience/ expectations of Eculizumab

6.1 The impact of the new drug on patients with aHUS

The impact of Eculizumab depends on how seriously people are affected by the condition and the stage of life at which they are affected. It can eliminate the need for time-consuming and invasive treatments. It can help patients retain whatever kidney function they have retained since having aHUS and in some cases can improve kidney function. For patients with kidney failure it offers the opportunity for a transplant and a better quality of life.

The different impacts of Eculizumab on the lives two children with aHUS and an adult patient are described in the following case studies.

Child A

Child A first became ill with aHUS at the age of 4 months. She spent 3 weeks in intensive care and remained in hospital for a further five months. She received plasma exchange during this time. She returned home but was unable to reduce the frequency of treatment without the disease reoccurring and therefore continued to go to hospital three times a week for treatment, for the next three years. She also had regular line infections and repeated relapses which required hospitalisation. Her mother stopped working to provide the necessary care. As with many young kidney patients, she stop about the possibility of a combined liver and kidney transplant. This was a very bleak time for the family.
The following year aged 4 she was given Eculizumab. She has been receiving the drug for nearly 12 months. During this time, she was admitted to hospital on one occasion for a planned operation to have her non-functioning kidneys removed. She no longer needs plasma exchange but continues overnight dialysis. She has had no further relapses. She has been placed on the transplant list for a new kidney. Her parents describe the impact:

She stopped eating at around age 2 and had a gastric tube fitted into her stomach. At the age of 3 she lost her kidney function due to the relapses and started dialysis. Her parents began discussions with the doctors.

She became a lot less lethargic – even her nursery said she was coping with everything a lot better – she was more active and interested in things – like a different child. The main impact for us is that she's been able to go to school with children of her own age. We were thinking she might not be able to go to school. She's a lot better socially because of school. She's very sociable and enjoys life very much… The drug has also opened up the possibility of a transplant and a return to normal life for all of us.

Child B

Child B started to become ill at around 6 months and was admitted to hospital with kidney failure at age 7 months. She was in hospital for two months and received plasma exchange. Her kidney function did not fully recover. She returned home where she continued with overnight peritoneal dialysis and hospital visits three times a week for plasma exchange. She was also receiving a blood transfusion every two weeks which was a cause for concern as it may have affected the success of any future transplants. She was on a strict diet and limited fluid intake. She was then given Eculizumab at age 1½ and stopped the plasma exchange. Within two weeks her kidney function was restored as her mother described:

We were still really strict on how much fluid she was taking and weighing every single nappy to see if everything was OK. She was drinking around 600mls then a day and she was weeing everything out. You couldn't believe it - how well it worked and how quickly.
Child B was then able to stop the overnight dialysis and had her lines removed. She has been receiving the drug for a little over a year. She goes to hospital every two weeks for an infusion. This is given through a canula, which is distressing for her. She has to be held down while the canula is fitted. She does not appear to experience any side-effects, other than headaches the first few times and a bit of dizziness during the infusion. She lies down during the treatment which lasts about an hour, remains under observation for an hour and then '*she's fine and walks away'*.
She has had a few common childhood illnesses during this time, colds and flu. She caught a stomach bug and returned to hospital because she was dehydrated and needed a drip. Everyone was concerned this would trigger a relapse, but she had no problems and her blood test results have all been fine.
Her mother describes the impact of the treatment:

She is thriving again. She started eating, whereas before she wasn't eating much... She's allowed to drink as much as she wants. Her kidneys, she's got almost 50% of kidney function now, which is incredible. She's always going to need to take medication, but it's nothing compared to what she had… We've taken her abroad whereas before I would have never dared to go anywhere with her. Our lives were really very difficult... Now we are having a normal life, as normal as possible. Then, we lived each day at a time. Now, we can make plans.

Adult A

Adult A was 63 when diagnosed with aHUS. She was given plasma exchange treatment in hospital every day initially. She describes her experience of this treatment as follows:

I just found it horrendous to be honest, because I found this treatment very intrusive…At first I was very sick while I was on it, then another day I had a full anaphylactic shock, and some days my blood pressure would just suddenly drop, and I'd have to be quickly taken off the machine…I came out in rashes, I had hives which spread down my whole body or other days it would be big red lumps, I didn't know how I was going to react each day… we were like rabbits in the headlights, we didn't know whether we were coming or going… And at the same time, I was filling up with fluid, I put on about 2 stone in weight, and it was fluid, so my legs were like tree trunks… I didn't have lot of energy, I couldn't wash properly, because the tubes were sticking out of my neck, there's always a risk of infection, so I couldn't go in the shower as normal, I couldn't wash my hair… my legs were so full of fluid I couldn't bend them to wash and dry my feet. Simple things like that were such a big chore…

After several weeks she returned home and continued to receive plasma exchange at the hospital every other day. She received 65 treatments over a course of six months. The side-effects were reduced but she did not feel completely well.

I was existing, once my plasma exchange was reduced, but I felt as though I was sitting on the side-lines watching all this going on. It was an odd feeling. I went through the motions, I gradually was able to do more, go out for little walks, go for lunch with friends, but it wasn't my life back again.

She was then entered onto the Eculizumab trial. She now receives an infusion for 35 mins every two weeks and has stopped the plasma exchange.

After a few weeks on Eculizumab the tubes were taken out and that was a big, big day for me, it was wonderful. The Eculizumab is so much easier than the plasma exchange was… I cannot find the words to stress the huge, huge difference it has made to me and my family; it's just given me my life back. Instantly I felt a difference, but you gradually over the months do feel stronger, and you think, ooh, I can do such and such and I haven't been able to do that for a while, and walking further, doing more, it has just been wonderful, absolutely wonderful. We've now been away for a week;

for weekends and we can do that sort of thing…I am doing loads more now. I've got my independence again.

6.2 Patient/ carers expectations of Eculizumab

Patients with renal failure

Patients with aHUS who have kidney failure are facing the prospect of remaining on dialysis for the rest of their lives. Eculizumab offers the potential for a kidney transplant, and therefore restoration of their health and a life free from the restrictions of the treatment.

All of a sudden there's a possibility of a drug which could mean I could have a transplant and what I see as having a normal life again. My husband could work, I could possibly work. We could go away and see my husband's family who live miles away. I'd love to be able to jump in a car and be spontaneous… I'm not saying a transplant is the be all and end all. It isn't easy. But dialysis is hard for me and for everyone else. (Patient**)**

It is difficult to plan for the future, because the future is dialysis ;but all of a sudden ,now there's a little bit of light at the end of the tunnel, and I think that's the future that is what we have got look for now. **(**Partner**)**

For partners/ family members/ carers, the possibility of a transplant would also be life-changing, giving them more time, less responsibilities and reducing their anxiety. Some find it hard to imagine and to some extent are fearful of the consequences. They have adapted their lives around the condition for many years and have been through hopeful times only for the disease to come back again. They believe it would take them some time to feel confident that the drug was really working.

If the drug came in, the change would be immeasurable really it would be massive. We'd have to get our confidence up – I can't imagine it now. The stress would be better – we'd all sleep better – but I don't think we could shake it all off – there would always be a bit of you thinking I wonder if it's going to go wrong… **(**Partner/ Family member)

Opening up the possibility for kidney transplants also means parents and family members will be faced with difficult decisions about whether to donate a kidney to the person with aHUS. Donating a kidney is not without its risks. It involves a major operation and women of child-bearing age are advised not to donate their kidney if they want to have children. However, because there is a waiting list for transplants, there is always a fear that the person with aHUS may become sicker or even die while waiting for a suitable donor. This can place enormous pressure on individuals and family relationships.

Patients with active disease

The disease is currently suppressed in these patients with continued plasma exchange, although this does not always prevent relapses. This treatment is time consuming, can make people ill and is associated with

risks of line infection. If people continue to relapse, they are still at risk of losing their kidney function over time.
Eculizumab offers the possibility of avoiding end stage kidney failure, dialysis and kidney transplants as well as any other organ damage. It offers patients the chance of retaining whatever residual function they have in their kidneys without the need for further treatment and may sometimes restore some kidney function.

Patients in remission or with known genetic risk of aHUS
For these patients and their partners or families, the concern is always that the disease could start or reoccur at any time leading to kidney or other organ damage. Families affected in this way live with a great deal of anxiety. Eculizumab takes away a lot of this fear.
If you imagine that your child could become ill anytime and that it could affect his kidneys, his brain, his lungs – anything and there's no cure for it – that's bloody scary to live with. To then find out there's now a drug that will stop it in its tracks – I can't tell you how that feels – it's elation really – it makes living with it bearable. It gives you hope when there wasn't any hope. **(**Parent**)**
For couples where one partner is affected by the gene, knowing Eculizumab was available would influence their life choices.
There's the possibility when I have children, they can do tests during the pregnancy to see of the child carries the aHUS fault – and if it did, that would be a decision we would have to make. If we knew the drug was available for that child – that would be a positive for us. (**Partner/ Family member)**

APPENDIX A SUMMARY: BURDEN OF CURRENT CONVENTIONAL TREATMENT

The following summary of the burdens of current conventional treatments was included in aHUSUK's patient submission to the Clinical Priorities Advisory Group and elicited from information supplied in the Life Experience Report and from an on-line survey completed in May 2013 by aHUSUK members. To fully appreciate the huge improvement in treatment that eculizumab brings it is necessary to understand the two existing treatments.

1. PLASMA EXCHANGE

"In recent years plasma exchange (PEX), that is the replacement of the body's entire blood plasma in one session, has been the standard pre-dialysis treatment for adults and children. It is not pleasant. Patients have told us about daily treatment sessions lasting several hours.

The side effects and risks as follows:

• Oedema causing shortness of breath and mobility problems,
• Hives, allergic reactions and anaphylactic shock,
• Hypotension,
• Nausea and fatigue,
• Inconvenience and risk of fixed lines becoming dislodged or causing infection.

Although there were occasional reports of patients going spontaneously into temporary remission, these are rare, and when PEX failed to maintain kidney function, as it often did over the longer term, dialysis was the only remaining option.

2. DIALYSIS

Dialysis is required when kidney function is lost. It is a replacement therapy and not a complete substitute for a functioning kidney. Patients are subjected to a strict diet and fluid restrictions of 500 ml a day. Dialysis can be done in hospital or at home. Many patients resigned to a lifetime of dialysis prefer the flexibility of being able to dialyse at home; but that requires space, equipment and training in its use. All patients found treatment a huge burden.

They reported the physical and mental effects as follows:

• Requirement for operations to create access points for treatment and surgery to maintain effective fistulas and avoid catastrophic bursts, but knowing that these access points are finite;
• Risk of tesio line in jugular vein becoming infected, splitting or becoming detached;
• Those dialysing with a fistula having to place two large and sharp needles into their own arm;
• CAPD dialysis requires a permanent catheter into the abdomen, which results in scarring and body image issues

• Having to cope with technical faults/power cut/water supply issues in the equipment in mid treatment on home dialysis (with the risk of losing 400ml of blood volume)
• Constant vigilance required to spot infection and possible air entry into lines
• On CAPD it is inconvenient and tying to exchange dialysis fluid every four hours every day
• Extremely low blood pressure causing patients to 'crash ‘and lose consciousness during treatment
• High blood pressure causing seizures and migraine headaches
• Cramps, nausea, faintness and/or headaches during and following a dialysis session 27

• Fatigue due to anaemia and requiring blood transfusions or self-injection of EPO
• Fear of fluid overload causing respiratory failure and drowning in your own body
• Fear of potassium levels so high they can cause a heart attack
• Greater risk of heart and blood vessel disease including strokes and fluid around the heart and severe damage to the heart valves requiring open heart by-pass surgery
• Steal syndrome associated with fistulas causing pain and requiring surgery
• Losing hair because of blood thinning drugs required for dialysis
• Episodes of extremely painful and life-threatening peritonitis
• CAPD treatment causing encapsulating Sclerosing peritonitis which requires major abdominal surgery and on-going treatment which can cause ovarian cysts
• Anxiety and depression resulting in need for counselling and medication
• Body image problems resulting from scarring and from unsightly fistulas and from weight gain and loss from treatment
• Parathyroid problems
• Pulmonary Hypertension
• Carpal tunnel syndrome
• Gall stones and gall bladder removal
• Renal bone disease causing joint pain and need for hip replacements
• Restless legs syndrome
• Dry and extremely itchy skin
• Impaired cognitive function
• Coping with aftermath of miscarriage and premature births during episode of aHUS.” 28

APPENDIX B
Methods used to develop the Patient Experience Report*
M1 What methods were selected and why
One-to-one interviews were used to gather the information for this patient submission. This method was chosen because aHUS UK members had stated they would prefer this approach to focus groups. This method also ensured that:
 in-depth, qualitative findings about people's experiences of aHUS were obtained
 interviewees felt comfortable talking about sensitive and distressing topics
 the work of aHUS Action was not duplicated through repeating a survey

Although preparation of this submission did not require formal ethical approval, the principles of good ethical practice were still applied, for example, by addressing issues of confidentiality and ensuring interviewees were fully informed about the project before agreeing to take part. Helpline support was made freely available to the interviewees so that they were able to obtain professional support if they became distressed as a result of taking part.
M2 How participants were selected and recruited
A purposive sample of interviewees was selected to ensure that the full range of experiences of aHUS was captured through the interviews, as well as the most common experiences of the condition. Parents, partners and other family members were also interviewed to understand how the condition affects their lives.
A brief review of the literature was conducted via an internet search, drawing mainly on reports of patient experiences from international patient organisation websites2. Advice was also sought from aHUS UK Trustees and Professor Tim Goodship on the most common experiences of aHUS. The sample was then chosen to include:
2 http://ahus.org.uk/
http://atypicalhus.50megs.com/
http://atypicalhus.ning.com/page/a-parents-perspective-ahus
www.rarediseasecommunities.org/en/community/atypical-hemolytic-uremic-syndrome-ahus
1. Patients with different ages of onset. aHUS can affect people at any age, but there appear to be peaks in the numbers of people affected at a young age (0-6), in their early twenties, and after the menopause in women. Patients were therefore selected within these peak age ranges.

2. Patients and other interviewees of both genders. More women were interviewed than men, which may partly reflect the greater incidence of aHUS in females, or different individuals' willingness to contribute to this submission.

3. People with experience of the different outcomes of the disease. In terms of the impact on kidney function, this included patients with no kidney damage through to patients with end stage renal failure. Others were included with experience of aHUS damage to other organs, or loss of family members with aHUS.
29

4. People with experience of the different types of treatment used to manage the condition, including plasma exchange, different kinds of dialysis and kidney transplant.

5. People who have experienced the impact of the hereditary nature of the condition and the effects on the wider family.

aHUS UK contacted their members and recruited a total of 16 people, who as a whole were able to contribute information about the most common experiences of aHUS across these different dimensions. Professor Tim Goodship was consulted and confirmed that this sample would be illustrative of the most common aHUS experiences.
At the time the interviews were carried out there were four patients (2 adults and 2 children) known to aHUS UK who had been given Eculizumab. One of the adults and parents the two children were available for interview and included in the sample. The characteristics of the interviewees are listed in Table 1, without any personal information so as to maintain anonymity.

Table 1: Characteristics of the interviewees	Interviewee	**Patient/family experience**
Age/ gender		
Baby girl, aged 9 months	Mother	In remission after treatment with Eculizumab.
Child	Mother	4 children who died as a result of aHUS, 3 as babies, 1 at age 7.
Child – (boy aged 2)	Grandmother	In remission after plasma exchange. Grandmother lost 2 of her own children to aHUS as babies.
Child (girl aged 5)	Father	Receiving dialysis at home, awaiting transplant, receiving Eculizumab.
Child (girl aged 7)	Mother	Receiving plasma exchange and on long-term dialysis

Young person (boy aged 13)	Mother	In remission.
Young female adult	Patient and sibling (2 interviews)	Has end stage renal failure and is receiving dialysis at home. Transplant failed. Working.
Young female adult	Patient and husband (3 interviews)	Has end stage renal failure and is receiving dialysis at home. Transplant failed. Retired due to ill-health.
Young female adult	Patient and husband/daughter (3 interviews)	Has end stage renal failure and is receiving dialysis in hospital. Transplant failed. Retired due to ill-health.
Adult late onset – female	Patient	In remission after treatment with Eculizumab.
Adult late onset - female	Patient	Has end stage renal failure and is receiving dialysis at home. Transplant failed.