'Just an unfortunate coincidence': children's understanding of haemophilia genetics and inheritance

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'Just an unfortunate coincidence': children's understanding of haemophilia genetics and inheritance

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Abstract

This paper presents the results of a study talking to children and young people affected with severe haemophilia A and/or B about their knowledge and understanding of genetics and inheritance. These data were gathered in a qualitative study using semi-structured interviews with thirty boys aged four to sixteen discussing the impact of haemophilia on their lives. Responses were tape recorded, transcribed and analysed, using thematic analysis; one of the themes identified was genetic knowledge which is presented in this paper. Genetic knowledge was formed within the context of normal day-to-day lives within families affected by haemophilia, with parents and haemophilia centre staff being sources of information about individual inheritance patterns as well as providers of information about the future genetic impact of having haemophilia.

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Introduction

Haemophilia A and B are X linked inherited disorders of coagulation, which are carried by females and affect males. Healthcare workers readily draw family trees of affected individuals and easily identify 'obligate' and 'at risk' females within the family. The focus of genetic counselling and support is weighed heavily in favour of these women [1] with little thought being given to the current and future genetic consequences of the affected male proband.

There is limited research describing communication of genetic information within haemophilia families [2] or about how parents share genetic information within families [3,4,]. Spitzer [5] wrote, in 1992, that children (aged 6-13 years) with haemophilia, knew 'very little about their disease and especially about the way a person contracted it'. Since then genes and genetics have become more widely discussed and debated, and at this haemophilia comprehensive care centre forms part of routine clinical review of all children, by the haemophilia team [6,7].

Children and young people with haemophilia in the twenty-first century, are the first to grow up in the genetic age with the human genome project, genetic testing, genetic modification of food, recombinant factor VIII/IX technology and gene therapy are talked about in everyday parlance [8]. Genetics and inheritance are taught in English schools as part of the National Curriculum for Science [9]. This is divided into four age appropriate 'key stages' with each 'key stage' being further divided into areas of scientific interest. Human genetics, reproduction and inheritance are taught in key

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stages 2-4 as part of the ‘life process and living things’ theme. The content of this teaching is shown in Table 1.

What has yet to be described in any detail is where young people with haemophilia learn about their own genetic make-up and its consequences. This paper presents findings about genetic knowledge and understanding as part of a larger qualitative study exploring the lived experience of boys with severe haemophilia.

Methods

This was a single site, qualitative study of 30 boys aged 4-16 years with severe haemophilia A (n= 27) or B (n= 3) undertaken in 2009 (see Table 2). Prior to commencement of the study ethical approval was granted by the South East Research Ethics Committee. The boys were invited to participate in a larger study evaluating the lived experience of haemophilia, where individual or group interviews were undertaken to better understand haemophilia, its treatment and its limitations, from the child's perspective.

The interviews were semi-structured and tape recorded, thus allowing the researcher to give full attention to what was being said. The tape recordings were listened to on several occasions, were transcribed by a professional transcriber and then analysed and coded by hand. Narrative content was identified and coded into recurring ‘themes’ which were identified as important aspects of modern day life with haemophilia. These themes were: family and siblings, school, sport, career, haemophilia – bleeds and treatment, good and bad aspects of living with haemophilia and genetics and inheritance. All of the themes, with the exception of genetics and inheritance, fit into a core category around the daily life experience of having

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haemophilia and will be presented in later publications. The narratives relating to genetics and/or inheritance are presented here.

Results

Twenty four boys of the 30, who were interviewed, offered a range of responses in terms of complexity and detail about genetic knowledge and/or understanding of inheritance of haemophilia. Those who did not offer a response were aged seven or younger.

Boys with haemophilia grow up in families affected by haemophilia and develop a gradual understanding of the implications of haemophilia for them and their family members. The youngest boys in this study are at an age where they are beginning to understand 'symptoms, treatments and physical differences from peers'[10], and their parents are starting to reveal genetic information, such as 'you were born with it' as they perceive their child to be developmentally ready for it [3,4]. It is therefore not surprising that the smallest boys in this study have a lack of 'real' knowledge about haemophilia genetics and inheritance as these are complex issues [11,12] probably beyond their developmental ability [5].

A rudimentary understanding of haemophilia genetics is demonstrated by some of the youngest boys through statements such as '*I just came out that way*' (Jack aged 4*) '*girls can't get haemophilia can they?*' (Nick aged 9) and '*she didn't get it because she is a girl*' (Murray aged 5). The data from boys is presented in two sub themes:

- Genetics, their haemophilia gene and its mutation and

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- Inheritance - how they inherited haemophilia including implications for them and their family in the future.

These themes are discussed in more detail below:

Genetics

Four of the older boys described the gene mutation/genetic component of their haemophilia in a medical/scientific way indicating that they understood the importance of genes and chromosomes in causing both haemophilia and bleeding:

‘It’s a blood disorder when you don’t clot fullyor nothing at all [I got it] because one of my chromosomes are bent [he has IVS 22 inversion] Matt aged 13

‘It’s in part of our genes – our mums got part missing, but she’s got two and that’s why girls can’t get haemophilia ... but boys only have one so when part of our gene is missing which means our blood doesn’t clot’ Henry 9

‘My mums a carrierit means its in your DNA or whatever, but you haven’t actually got it. It just means that if you have a child they are more likely to have it’. Will aged 10

‘It’s in the the X chromosome, only males have XY and YY or something [questioning] that’s a girl so no haemophilia’ Mark aged 16

The knowledge demonstrated by these boys, exceeds the background genetic knowledge that is expected for boys of this age [9]. Haemophilia specific genetic knowledge has thus been gained either from their families, their haemophilia care providers or from both. Most parents see themselves as having ‘prime responsibility’ in discussing genetics with their children yet struggle with ‘what and how to tell’ at different stages of children’s lives [13]. Women (mothers) are often seen as ‘genetic housekeepers’ and ‘kinkeepers’ (those who hold the family (or kin) together) [14] for family members, often negotiating genetic testing and coordinating counselling for

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family members, it is imperative that these women have the correct information and support to correctly inform family members [1].

Inheritance

Approximately half to two thirds of boys with haemophilia come from 'affected families' i.e. those where there has been haemophilia in previous generations. Spontaneous genetic mutations, either in the mother or the child are responsible for causing haemophilia in the remainder of those affected. This prevalence is reflected in this study where 10 of the 30 boys were the first affected member in their family. Despite being the first, or only, affected individual in their family the boys demonstrated an awareness of the impact of haemophilia on other family members: their mothers, siblings and their own future children.

Edward, aged 9, the only affected member of his family with haemophilia described its inheritance as '*just a rare unfortunate coincidence*', something that his parents confirm they have told him repeatedly, and that his children might not be affected as '*it might not run in the family*'. Edward has an older unaffected brother, his mother has chosen not to be carrier tested and there are no other 'at risk' females in the family. If Edward only has sons then he is correct in thinking that haemophilia will not run in the family, however all of his daughters will be carriers and their children might be affected. This notion is better narrated by boys with previously affected family members:

'Well it runs in the family so my granddad had it and he had a girl, my mum, and so she's a carrier and she carried it to me' Oliver aged 14

'I was born with itbecause my mums a carrier but she doesn't have it my mum's uncle and cousin and a brother do' James aged 13

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Two boys came from families where genetic knowledge of ancestors was limited or unknown. David aged 13, whose mother is adopted, said:

'It's from my mum and then I don't know how it passed on [to her]. I don't know from my mum's mum or my mum's dad she carries it but she doesn't have to deal with it as bad as boys [affected carrier]'

Sixteen year old George, who knew that his maternal grandfather was not his biological relative, described his inheritance of haemophilia from a known affected individual as:

'My mums' birth father had it so that made her a carrier and I got it'

These four boys were able to describe complex genetic inheritance patterns both from knowledge of their own families and from learning about genetics and inheritance at school and at the haemophilia centre where frequent discussion about this occurs. Miller [15] describes treatment centre education and counselling protocols and states how affected boys and men are often 'forgotten' in this, assuming that they know the obligatory carrier status of their daughters. Several of the boys in this study showed a good understanding of the impact of haemophilia on their own children and their children's children:

'It means when men go on to have kids the boys will be OK and the girls will be carriers it's a never ending circle really' Mark aged 16

'The girls will have the gene and her children, if she had a boy or a girl there is a 50/50 chance that either of them would have it' David aged 13

'Well the boys will be fine but the girls will carry it and the girl's boys will be half haemophilia' Matt aged 13

'Our [sic] boys will be perfect ... but myif I get a girl she will be a carrier ... she then has a boy and he has haemophilia' Jonathan aged 10

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It's in part of our genes – our mums got part missing, but she's got two and why girls can't get haemophilia ... but boys only have one so when part of our gene is missing which means our blood doesn't clot.' Henry aged 9 on behalf of himself and Isaac aged 6.

Sixteen-year old George (who had an affected Grandfather whom he never knew) describes how being an affected grandfather himself would benefit his grandchildren:

'It would be a big advantage because they would know all the stuff I did when I was young – so it can only be good'

This 'untapped expertise' [16] of the expert patient whose life story is more knowledgeable about the impact of the illness than the expertise of the haemophilia health care professionals, shows how people can be 'successfully ill' [17]. This is enhanced in inherited congenital disease where there is no 'before and after' to compare life with and without the illness, and where older affected individuals can have a significant impact on younger people:

'I've got a friend who is about 42-ish and he's got haemophilia and we chat, I think I look to him for a friend because he is older and he has lived with it longer than me, then we have a discussion about it, and I find it nice because things that kept on going for him he has been through as well, and I might go through exactly the same so that means quite a lot. He is someone I can actually relate to on a level where they know where I am coming from I suppose'. Mark aged 16

The sense of belonging to an extended family or a unique 'haemophilia community'[14] through shared genetics (or genetic mutations) makes living with haemophilia an unexceptional everyday reality [18] bound within individual, family, and cultural values. Modern day, openly communicated day-to-day lived experience enables boys to communicate freely about genetic inheritance and haemophilia management within their families. This leads to an understanding of the potential carriership of their sisters, and a relationship that 'becomes stronger as siblings grow

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up’ [14]. Having this knowledge enables the next generation to confront their fate [15], laying down a foundation for their future communication within his family [4].

‘She is fine, she is normal, she has been tested’ James 13

‘She had like a test to see if she was a carrier, like my mum, and she wasn’t a carrierthat’s good because is she has some boys when she is older that means that it won’t have haemophilia’ Tom 12

‘They [his mum and dad] had this special treatment – they had like IVF and then some special treatment which had never been done before and it worked out she’s not a carrier she can’t ever get it again it wont just randomly pop into the boy again ‘ Oliver 14

Genetic testing of female siblings in families with X linked inherited disorders is an area of debate, but many children state that they are glad to have been tested and been able to grow up with knowledge about carriership [1,4,14,15,19]. However in a paper about Duchenne Muscular Dystrophy (DMD) carrier testing and status was not routinely known by ‘at risk’ girls as parents felt a need to protect them from the knowledge that they were carriers [20]. The girls in this study felt that they should know everything about the genetics of DMD even if that knowledge was upsetting at the time, as this gave a better ‘family view’ of inherited disease.

Unaffected siblings are recognised as not being part of the immediate ‘haemophilia family’ but of being affected by it, and therefore being part of, the global haemophilia community:

[It’s good he] ‘didn’t have it, because he does not have haemophilia cause he is only littleI don’t want my little brother to have haemophilia so I am better off having it myself’. Nick aged 9

‘I think my brother, my older brother who hasn’t got haemophilia it affected, I think in a way he feels guilty that we have haemophilia and he doesn’t and he goes out of his way to help us out. In fact I know he does because we are only a year apart me and my older brother, me and him have a good relationship so I know for a fact that if certain things he’ll do for me which are just little

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things that mean a lot..... we have had discussions about it, and obviously it's not his fault [that he doesn't have it] and he says he finds it hard sometimes I know that he's always stuck close to me cos of that'. Mark 16

Family membership and relatedness is a construct of genes and genetics that cause disease as well as those that do not – for example those that cause haemophilia and those which lead to blue eyes or curly hair and a family resemblance. Genetically unaffected siblings may still be affected by having a sibling with, or who is a carrier of, haemophilia. These siblings experience haemophilia on a day-to-day basis and understand how it affects family life and relationships both today as well as in the past and future.

Discussion

This is the first paper that the authors can identify, which presents the genetic understanding and knowledge of children and young people who have haemophilia. Studies of young people and adults with haemophilia have shown that 69% of patients aged 13-25yrs [21] and 96% of patients aged over 25 [22] were aware of heredity i.e. a healthy son and carrier daughter. When asked to rank genetic knowledge about haemophilia 80% of respondents, patients (aged > 18) and parents, ranked knowledge as high or medium high [23]. These data are from studies about disease and treatment and not specifically about genetic knowledge and understanding.

Within this study the role of the families in supporting and educating boys about haemophilia is apparent. Growing up with a brother with haemophilia leads to strong sibling relationships [14], experiential knowledge [16], and communication of family values about the condition which may support carriers and boys with haemophilia in future reproductive choices. The boys in this study understand the implications of

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genetic disease on their own, their siblings and their future children’s health. This knowledge develops in an age appropriate way: where the youngest of the children knew only that girls do not get haemophilia (*‘she didn’t get it because she is a girl’* Murray aged 5), in contrast to older boys such as Henry aged 9 who showed a greater understanding of inheritance:

‘It’s in part of our genes – our mums got part missing, but she’s got two and why girls can’t get haemophilia ... but boys only have one so when part of our gene is missing which means our blood doesn’t clot.’

The boys in this study will have all had science education at school using the National Curriculum for England (science) teaching programme [9]. This knowledge will be enhanced through parental discussion of genetic knowledge with children. This occurs in a developmental way from basic information for preschoolers, family relationships and genetics for school age children and understanding of the implications of genetic disease on their own reproduction for adolescents [10]. The boys in this study demonstrated genetic and inheritance knowledge that exceeds that expected for their educational age (see Table 1) this demonstrates knowledge acquisition from parents, families and haemophilia care providers.

The oldest boys in this study were able to perform ‘verbal drawing of family trees’ [24] fully describing the genetic implications and inheritance patterns of haemophilia for them, their ancestors and their descendants including Georges biological (and unknown) grandfather:

‘My mum’s birth father had it so that made her a carrier and I got it’

Simon (aged 15, who is the first in his family to be affected) understands impact of haemophilia on future children within his family:

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'It will be good for my sisters' kids, my girls and my grandsons... 'cos they will have me to help them through it .. so better for them than for me who had no one who knew'

For some this will be following formal education about genetics and inheritance in science at school [9] however in day-to-day life communication about haemophilia within the family is in the domain of the everyday (as treatment is given etc) and judgement about it as a condition, where individuals can lead fulfilling and worthwhile lives. [2,18].

The narratives told by these children are not only about themselves but are also 'partly stories about others in their family' [16] providing self identity which relates them to 'others': these are family members identified as relatives as well as those belonging to the haemophilia community as described by Mark when talking about his 42 year old friend with haemophilia.

Conclusion

Genetic knowledge, testing and technology have been major scientific breakthroughs in haemophilia care in the twentieth century, and will continue to improve as further developments occur in genomics and genetic therapeutic options. Comprehensive strategies are needed to ensure that those affected, either directly or indirectly by haemophilia, fully understand their own genetic risk. This paper is a first insight into genetic knowledge of young people affected by haemophilia and should be used as a evidence for future education and support of both affected boys and their (potential or actual) carrier sisters who may pass on the haemophilia gene to future generations.

This paper demonstrates that the children and young people in this study have a good awareness of haemophilia genetics and inheritance. Some of this information comes

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from within the family whilst the remainder comes from haemophilia care providers whose responsibility it is to inform and correct misinformation. The study is limited in that it only includes children from a single site where knowledge of inheritance and genetics are seen as an important part of haemophilia care and are repeatedly addressed at review clinics. Haemophilia health care workers should provide tailored, age appropriate information to those with haemophilia as well as to those who do, or may, carry it addressing age appropriate issues such as reproductive choices, as they occur.

*Pseudonyms have been used throughout this paper to protect the identity of the interviewees

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For Peer Review

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Table 1

National Curriculum Key Stage	Expected age of achievement	National Curriculum teaching programme : Scientific knowledge about genetics/inheritance	Quotes which demonstrate advanced genetic knowledge in boys with haemophilia
2	11	<ul style="list-style-type: none">recognises the roles of drugs as medicineare knowledgeable about human life cycles	<ul style="list-style-type: none">children aged 5 (data not shown)<i>‘it might not run in the family’</i> (Edward aged 9)
3	14	<ul style="list-style-type: none">human reproduction with inherited variations within species	<ul style="list-style-type: none"><i>‘she didn’t get it – she’s a girl</i> (Murray aged 5)<i>‘it’s good he didn’t have haemophilia’</i> [about his little brother](Nick aged 9)
		<ul style="list-style-type: none">selective breeding can lead to new varieties	<ul style="list-style-type: none"><i>‘I just came out that way’</i> (Jack aged 4)<i>‘Just a rare unfortunate coincidence’</i> (Edward aged 9)<i>‘I was born with it ... because my mum’s a carrier’</i> (James aged 13)
4	16	<ul style="list-style-type: none">composition and function of blood,	<ul style="list-style-type: none"><i>‘part of the gene missing’</i> (Henry aged 9)<i>‘you don’t clot fully’</i> (Matt aged 13)
		<ul style="list-style-type: none">the mechanism of inheritance with recessive and dominant genes	<ul style="list-style-type: none"><i>‘mum’s got part missing ...but she’s got two</i> (Henry aged 9)<i>‘it’s from my mum ... she carrier it’</i> (David aged 13)
		<ul style="list-style-type: none">that some diseases are inherited	<ul style="list-style-type: none"><i>‘the girls will carry it and the girl’s boys will be haemophilia’</i> (Matt aged 13)<i>I was born with it ... because my mum’s a carrier’</i> (James aged 13)
		<ul style="list-style-type: none">genetic engineering is possible	<ul style="list-style-type: none"><i>‘they had this treatmentlike IVF So she’s not a carrier’</i> (Oliver aged 14)

Knowledge/Education about genetics/inheritance in National Curriculum in England and (in column 4) haemophilia genetic knowledge demonstrated by this cohort of boys

Table 2

Pseudonym	Age (Years and Months)	Diagnosis	Previous Family History
Jack	4 y 11m	Severe haemophilia A	Y (brother of Duncan)
Murray	5 y 3m	Severe haemophilia A	N
Isaac	6y	Severe haemophilia A	Y (brother of Henry)
Jimmy	7y 10m	Mild haemophilia A with high titre inhibitor (severe phenotype)	Y
Neil	8y 1m	Severe haemophilia A	Y
Duncan	8y 9m	Severe haemophilia A	N
Edward	9y 2m	Severe haemophilia A	N
Nick	9y 2m	Severe haemophilia A	Y
Robert	9y 8m	Severe haemophilia A with high titre inhibitor	N
Henry	9y 11m	Severe haemophilia A	N
Will	10y 2m	Severe haemophilia A	Y (brother of Paul)
Jonathan	10y 8m	Severe haemophilia A	Y (brother of David)
Tom	12y 3m	Severe haemophilia A	Y
Michael	12y 10m	Severe haemophilia A	N
James	13y	Severe haemophilia A	Y
Matt	13y	Severe haemophilia A	Y
David	13y 3m	Severe haemophilia A	Y
Peter	14y 5m	Severe haemophilia A	N
Oliver	14y 5m	Severe haemophilia A	Y
Paul	14 y 10m	Severe haemophilia A	Y
Ian	15y 3m	Severe haemophilia A	Y (brother of Neil)
Simon	15y 6 m	Severe haemophilia A	N
George	16y 4m	Severe haemophilia A	Y
Mark	16y 10m	Severe haemophilia A	Y

Boys who discussed knowledge of genetic information.

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