Health Care and Society

Haemophilia

By Kaitlyn Egan

Over the past few years I have witnessed, through a close friend, the condition of haemophilia. Being a mild to moderate haemophilia sufferer he is still able to lead a pretty normal lifestyle and only requires treatment when necessary. However he is advised against playing any contact sports and must taken extra caution in social events as a head injury could be fatal. I have witnessed how joint bleeds can leave him with little movement in the joint and in some discomfort and understand that this can even lead to arthritis in the future. Through the A level biology curriculum I have also had the opportunity to understand the condition in much more depth, learning about the way in which it is inherited, through punnett squares, and the reasons behind why it is much more common in men, which I have found very interesting

Haemophilia is a potentially lethal congenital condition which occurs when an individual is unable to produce enough of one of the 13 blood clotting proteins. Blood clots slowly, or sometimes not at all, causing slow, prolonged bleeding. Normally, when the skin is cut, substances in the blood (clotting factors) combine with cells called platelets to make the blood sticky. This makes the bleeding eventually stop. People with haemophilia don't have as many clotting factors as there should be in the blood therefore they bleed for longer. There are two main types of haemophilia, haemophilia A and haemophilia B. The difference between them both is the factor that is missing or at low level. Haemophilia A is most common and is a low level of factor VIII (8) whereas haemophilia B is a low level of factor IX (9). Another type of haemophilia is acquired haemophilia which develops due to an illness, pregnancy or even from medications. This type is very rare and it usually resolves itself.

Causes and Inheriting

Haemophilia is caused by an inherited genetic mutation, which mainly affects males. This is because the gene causing hemophilia is located on the X chromosome. Females contain two X chromosomes which are identical whereas males have an X chromosome and a Y chromosome, which is much shorter therefore are not homologous. In these regions, females have 2 copies of each gene as they have two X chromosomes, and males only one copy, as they only have one X chromosome. If a female is heterozygous for one of those genes, the dominant allele will be expressed, as normal. Whichever allele the male carries is expressed, because even if he has the recessive allele, there is no second allele to be dominant over it.

Personally I found learning about the way in which haemophilia is inherited and using punnett squares to prove why the condition is much more common in males than females, one of the most interesting aspects of A level biology.

The allele coding for the normal version has the symbol X^H and the allele coding for the mutant version has the symbol X^h

There are 3 possible genotypes for females
$X^H X^H$ - Blood clots normally
$X^H X^h$ - A carrier female, she is heterozygous and carries a dominant allele so her phenotype is normal. She also carries a mutant allele.
$X^h X^h$ - a female with haemophilia

There are two possible genotypes for males
$X^H Y$ - Blood clots normally
$X^h Y$ - a male with haemophilia

Inheritance of haemophilia

If only the mother has the mutated gene:

	X^H	X^h
X^H	$X^H X^H$	$X^H X^h$
Y	$X^H Y$	$X^h Y$

There is 1/4 chance of having an unaffected female, 1/4 of having a female carrier (will pass gene onto children but won't often experience any symptoms), 1/4 chance of having an unaffected male and 1/4 chance of having a male who suffers from haemophilia.

If only the father has the mutated gene:

	X^H	X^H
X^h	$X^H X^h$	$X^H X^h$
Y	$X^H Y$	$X^H Y$

There is 1/2 chance of having a female carrier and 1/2 chance of having an unaffected male. There is 0 chance of having a male who suffers from haemophilia as he inherits his X chromosome from the mother.

If both parents have the mutated gene:

	X^H	X^h
X^h	$X^H X^h$	$X^h X^h$
Y	$X^H Y$	$X^h Y$

There is 1/4 chance of having a female carrier, 1/4 chance of having a female who suffers from haemophilia, 1/4 chance of having an unaffected male and 1/4 chance of having a male who suffers from haemophilia. This is the only way of having a female who suffers from haemophilia and is the reason why it is rare.

However it is estimated that in around 30% of cases there is no family history of haemophilia meaning that it is caused by a new mutation. For example during conception of the child who suffers from haemophilia, the egg from the mother or the sperm from the father underwent a mutation. In both cases, the mother is not a carrier and her other children will not not affected.

Symptoms

The symptoms of haemophilia depend on how severe the condition is. This can be split into 3 main categories these being mild, moderate and severe. The main symptom of all 3 is prolonged bleeding which can be seen from sudden nosebleeds, joint and muscle bleeds and bleeding gums. The severity of the condition is dependent upon the clotting factor activity in a person's blood.
Mild haemophiliacs have between 5 and 50% clotting activity, moderate have between 1 and 5% and severe have less than 1%. A person without haemophilia has a clotting activity between 50 to 150%.

People with mild haemophilia may not experience symptoms for years. However symptoms may become apparent after dental procedures and surgery causing prolonged bleeding. People with moderate haemophilia experience similar symptoms to mild but will bleed for longer after surgery or from a wound. They also experience joint bleeds if they fall which is an internal bleed around joints, which starts with a tingly feeling and slight pain. If this process reoccurs in the same joint it can lead to stiffness and even arthritis. Severe haemophiliacs experience severe and frequent joint bleeding which without treatment can lead to join deformity, soft tissue bleeding and more serious internal bleeding. This bleeding is more frequent (once or twice a week) and occurs spontaneously without any reason.

Diagnosis

Worldwide around 400,000 suffer from haemophilia with around 75% of these receiving inadequate treatment or even have no access to treatment, this is due mainly to where they live. Haemophilia A occurs in 1 in every 5000 male births and is four times as common as haemophilia B. In 2012 in the UK alone, 5467 people were registered to have haemophilia A with 54.71% of these being treated and 1156 people were registered to have haemophilia B with 54.58% of these being treated.

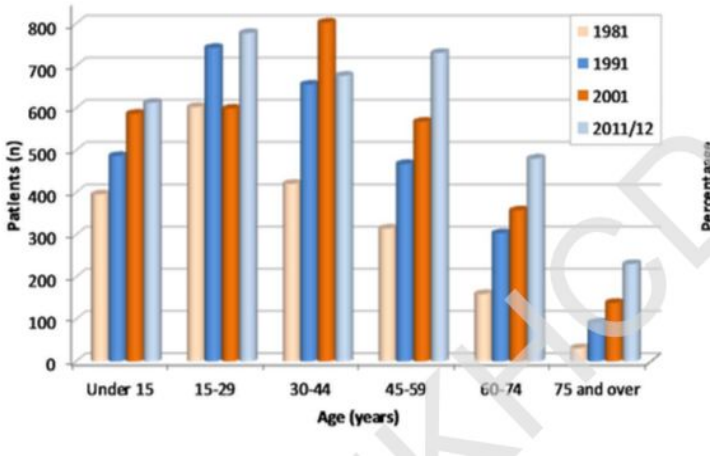
Haemophilia is usually detected and diagnosed at a very young age. Based on data the average age of diagnosis is around 36 months for mild haemophilia, 8 months with moderate and 1 month for severe. Data also shows that in two thirds of cases there is haemophilia in the family history. If a couple with haemophilia in the family history plan on having children, they can have genetic testing and counselling to help reduce the risk of passing on the condition to their children. Tests during pregnancy can also determine if the baby has haemophilia. These include chorionic villi sampling, at around 11-14 weeks, where a sample of the placenta is removed and tested for the haemophilia gene or amniocentesis, at around 15-20 weeks, where a sample of amniotic fluid is tested. Haemophilia can be diagnosed through a blood test which shows the amount of clotting factors and most babies can be tested soon after birth.

The majority of diagnosis occurs when children are less than 1 month old. Data from the Centres of Disease Control and Prevention (CDC) shows that only a small amount (2.8%) of diagnosis occurs after the child in 2. This reflects the fact haemophilia test have advanced in recent years and how it can be diagnosed quite easily with the use of blood tests. This is important because treatment for haemophilia patients is vital.

New registrations of haemophilia from 2011 to 2012

Coagulation Defect	Age (years)	Number of Patients (factor level iu/dl)			
		≤1	>1 & <5	≥5	Total
Haemophilia A	0 : 9	32	8	35	75
	10 : 19	3	1	12	16
	20 : 29	7	4	9	20
	30 : 39	2	0	7	9
	40 : 49	2	0	7	9
	50 : 59	0	1	5	6
	60 : 69	0	0	10	10
	70 : +	0	0	9	9
	Total	**46**	**14**	**94**	**154**
Haemophilia B	0 : 9	11	3	6	20
	10 : 19	0	0	3	3
	20 : 29	0	1	2	3
	30 : 39	0	0	2	2
	40 : 49	0	0	1	1
	50 : 59	0	0	1	1
	60 : 69	0	0	3	3
	70 : +	0	0	2	2
	Total	**11**	**4**	**20**	**35**

Data from United Kingdom Haemophilia Centres Doctors Organisation (UKHCDO) further confirms this as it shows the age group with the largest number of new registrators is 0-9 years for both haemophilia A and B. This is also shown by the overall trend that as the age group increases in age the number of new registrators decreases except for a few anomalies. I decided to further investigate why the number of haemophiliac patients begins to increase in the older generation. From this further research I discovered that acquired haemophilia peaks at an age range of 68-80 causing people in that age range to develop haemophilia who have not experienced it from a young age of have a family history of it.



More data from the UKHCDO shows the change in haemophilia A patients registered in the UK between 1981 and 2012. The general overall increase in patients registered indicates to me that modern advances in treatment of haemophilia is allowing patients to live for longer. Another reason for this increase may be due to the rising population of the UK

which has increased from 56.33 million in 1981 to 63.7 million in 2012.

A further topic of the A level biology course in which I enjoyed learning about was how sickle cell anaemia, another blood disorder, is most common in Middle Eastern, African and Indian people, because those geographical regions are most prone to malaria. Due to this I chose to research whether haemophilia was more common in any particular community of people. However using data from the CDC I now understand that haemophilia can affect people from any racial or ethnic group.

Treatments

Up until recent years there were considerable number of deaths in haemophilia patients mainly due to the result of injuries and surgeries. However according to Medical News Today, treatment has vastly advanced resulting in most haemophilia patients being expected to live longer and experience normal lifestyles. Data from NCBI shows how in 1979 the average life expectancy of a severe haemophilia patient was around 25.5 years. However new research shows that this has now increased to 63 years proving that treatments have advanced greatly. In the past, one of the main treatments was patients receiving whole blood or plasma infusions to control bleeding. However this method of treatment was not fully effective as it would never allow the patient to reach levels of clotting factors required and levels could not be maintained.

Now with more advanced treatments haemophilia sufferers can be treated by 2 approaches, depending on the severity of the condition. Firstly severe cases are usually treated with preventative or prophylaxis treatments which is the regular injecting of blood clotting medicine e.g octocog alfa medicine for severe haemophilia A suffers. This is a substance that helps the blood to clot by replacing the missing factor VIII. For haemophilia B a similar medicine, nonacog alfa, is injected which replaces the missing factor IX and gives temporary control over bleeding.

The second type of treatment is known as on demand treatment which is normally used by mild to moderate patients. This treatment may only be needed as an immediate response to bleeding and therefore is not regular unlike preventative treatments. On demand treatment includes injections of octocog alfa and nonacog alfa when needed. However haemophilia A suffers may also receive injections of desmopressin. This synthetic hormones promotes the release of von Willebrand factor and then the subsequent increase in factor VIII which is why this method is not suitable for haemophilia B sufferer.

One of the main issues with the use of these medicines to treat haemophilia is the development of antibodies, which is another aspect of the A level biology course I

enjoyed studying in an immunology topic. Antibodies are protective proteins produced by an individual's immune systems in response to an antigen (foreign substance). Antibodies produced by B lymphocytes attack these antigens by binding to them. If this occurs in a person suffering from haemophilia, their body stops accepting the factor treatment product as a normal part of the blood. The immune system thinks the factor is an antigen and destroys it with an inhibitor, making the treatment ineffective. If this occurs daily treatment of immune tolerance induction (ITI) can help the body stop producing inhibitors.

Conclusion

I chose to write about haemophilia because I believe it fits in with the title of ‘healthcare and society’ with over 400,000 people worldwide suffering, but also because it is a topic which I have great interest for and have enjoyed studying about in my A levels. However I feel that the awareness of haemophilia is not as great as I had expected and with numbers increasing I believe it is important to spread increased awareness.

Even though there is no cure for haemophilia, due to recent and ongoing research and advanced treatments, data shows that there are far less premature deaths due to haemophilia and patients these days are expected to have the same life expectancy as a non sufferer and are able to lead a pretty normal lifestyle. Life expectancy data showing that a severe haemophilia patient is now expected to live 37.5 years longer than in 1979 proving that research is going in the right direction, with scientists believing the cure could soon be found from advances in gene therapy.

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