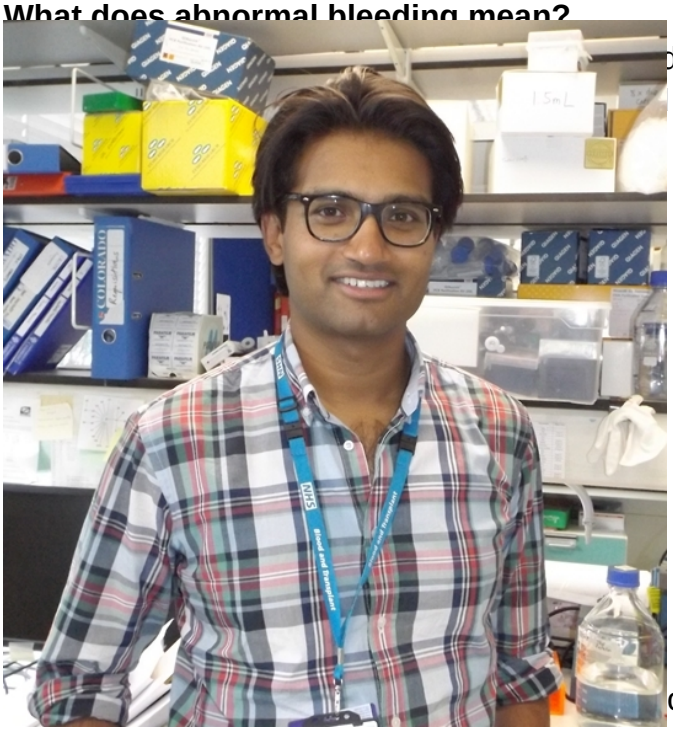
‘Looking at one person’s DNA to find the cause of their condition, is like looking for a single spelling mistake in 200 large telephone directories’

What is your research about?

Our team is under the leadership of Professor Willem H Ouwehand who works on the genetics of bleeding and platelet disorders. We try to understand why some people have abnormal bleeding. We both work on the clinical side seeing patients, acting as a bridge between patients and their consultants and the researchers.

What does abnormal bleeding mean?



d more easily than normal. This could be more than is expected after operations. Abnormal bleeding can happen at any stage of your life and for no reason. On a day-to-day basis these people can have

spontaneous nose bleeds or if they bump into something they can get a really big bruise.

How do people come to see you?
People are referred into the study through their haematologist (a doctor specialising in blood problems). Usually their routine tests have not shown any abnormalities, giving no clue as to why they are having these problems. The haematologist will ask the patient if they would like to consider being part of the study. If the patient agrees, we will receive a referral letter asking us to approach them. The next stage is to send out an invitation letter and the study information sheet so the patient can decide if they would like to find out more. If we receive a positive response, we will make contact and discuss the study with the patient further before arranging to see them.

What is the benefit of coming to see you?
We try to find out why people have abnormal bleeding. Using the patient's symptoms, blood test results and genetic data, we do our best to understand what is going on. We always tell the patient it can take a very long time to find the cause, if one can be found at all – there are no guarantees.

What happens when you see a patient at their appointment?
When we introduce the study, after the patient has told us they would like more information, we also ask if they have any family members that have similar problems or close blood relatives that may like to be involved. By recruiting family members we can compare physical signs and symptoms and genetic results to see if there is a pattern that may help point to what is happening. We try and get everyone in one place at the same time and then conduct the visit. We are able to offer home visits to make this possible as getting to Addenbrooke's is sometimes challenging.

When we see patients and their families, we talk them through all aspects of the study and try to answer any questions they may have. We want to make sure everyone is happy and understand what is going on before asking for their consent to participate. It is made very clear participation is voluntary and just because their haematologist has suggested they may like to take part it does not mean they have to. We also want to be sure they understand that the care they receive by their haematologist will not be affected in any way if they don't want to take part.

If they agree to take part, we collect a small blood sample. We then ask questions about their general health and their bleeding/bruising patterns. We supplement these answers with blood test results and additional information from their haematologist. To discover if there is a family history of problems we ask about other family members and create a family tree. This can tell us if the problem is inherited and potentially from which side of the family the genetic risk factors come from.

Some of the blood sample will be sent for DNA analysis. We also store some for use in

future research projects. For certain patients or families we are able to run new tests that are not yet available in the NHS to help us find out what's going on.

How long have you worked here?

Suthesh - I started here in April 2015. Before this I was training in Amsterdam to be a consultant haematologist. I completed my PhD in the genetics of heart attacks. As part of this I was involved in a lot of family studies, this was the bit I enjoyed the most. This job combines the best of both worlds, clinical work with patients and their families, which allows me to continue my training and my desire to carry out high quality research to help future generations. The Department of Haematology at the University of Cambridge has an extremely good reputation and it is an exciting place to work.

Amy - I started here in May 2014. I have previously spent 9 years in intensive care specialising in brain injuries, worked on several brain tumour research studies and then within the Cambridge Clinical Research Facility. Blood and bleeding problems is a new and exciting challenge for me. The research we are carrying out is at the forefront of helping to diagnose conditions that may otherwise have no answers.

What does your role involve?

Suthesh –We see eligible patients and go through all their information if they consent to take part in our study. I spend time both here in Cambridge and in London seeing people with bleeding disorders. I help with the data analysis bridging the gap between our researchers in the University of Cambridge and what it will mean for our patients. There is also a lot of reading and trying to make sense of the genetic results.

Amy – In Cambridge, along with Suthesh, I am the main point of contact for patients and their haematologists. I specifically handle recruitment and all communications with patients. Once we have results I feed these back to the referring haematologist.

Both - We are part of a big team, we each have our own role to put the pieces of the jigsaw together to find answers for our recruited patients and future generations.

Why were you interested in this area of research?

Suthesh – In haematology we see many people with unexplained abnormal bleeding. I want to be able to identify if there is an ultimate reason as to why people have this condition. Many parts of the human body are interlinked and knowledge of one part may help us to understand diseases affecting other parts of the body. For example, if we can find a gene that causes bleeding and develop a treatment to counteract this, we could then in effect reverse this treatment to help someone who has had a heart attack, which is caused when somebody's blood clots too easily.

Amy – Professor Ouwehand's group looks at many different aspects of blood and so requires not only patients but also healthy volunteers to act as controls. As the nurse I am afforded the opportunity to work with many different volunteers and colleagues on a number

of different studies. My role and the tasks I perform are very varied and knowing that I am part of a team helping to improve health care for future generations is extremely rewarding.

Why are your roles important to this kind of research?
We are the eyes of the study. We see how this disease affects the people living with it. Without us, the team focusing on the science cannot relate their work back to the patients we are all trying to help. We are the clinical care members of the team, we interact with the patients and their families because we are trained in how to communicate with patients so they can understand everything using everyday language. We also work in reverse, translating the patient information back to the researchers in a scientific way. It is like learning a foreign language and we are the ones who can translate it back and forth. We also act as the central contact point not just for the patients but for the haematologists too. We have found that acting as the central hub is invaluable for all who are involved.

What do you hope to achieve with your research?
Bleeding problems can be life threatening. There are still so many things about them that are unknown and we hope genetics will help unravel that. We see a whole spectrum of people and this research can potentially save lives. Ultimately we hope to find new genes to explain what is going on but for our recruited patients. We really want to find the answer to their problem and find the best way to treat them. As clinical practitioners we are focused on looking after our patients.

Do you think eventually there will be new drugs to treat this problem?
Our research is not drug focused but eventually there could be. We concentrate on the biology behind what causes these problems by seeking to understand better how our blood system works and how genes affect this system. If we know more about what is going on and the causes then we may be able to prevent it. Researchers are already looking at gene therapy and even now there are new drugs being developed to treat patients with severe bleeding disorders.

How long will this research take so patients can feel the benefits?
Looking at one person’s DNA to find the cause of their condition is like looking for a single spelling mistake in a pile of 200 telephone directories each with 500 pages and we do not have any idea where that mistake may be. Once we think we have found it we then go back and check. This is where relatives come in, their DNA can provide more information to help us find the mistake. While we do not know exactly what we are looking for, thanks to technology, we do have the tools to look for it.

For individuals a benefit will only come when we find something in the genes - the quickest it could be is six months but it could take several years. In some cases we may not be able to pin point the ‘spelling mistake’ at all. To go on to create a better treatment, it could easily be 10 – 15 years of drug development.

We are really only at the beginning of looking at genes to help diagnose diseases. The technology to help with this has improved at a vast rate and with continued advancements this should become quicker still. As everyone's genes are different they will still need to be looked at individually and one treatment may not necessarily benefit someone else even if they outwardly appear to have the same problem.

How do volunteers help you with your research?
For this particular study we want people who have known problems but also their unaffected family members. These family members act as our guide to what we are looking for. We are not necessarily presuming they are healthy, we are looking for close relatives who simply do not have the same symptoms as the patient. We can then cross check the DNA to see what is the same and what is different. Genetically speaking blood relatives are similar in make up so it is easier to spot any changes.

We have genetic information from healthy volunteers who have taken part in other research programmes like the 100,000 Genome project. We can see genetically what unaffected samples should look like and cross reference those to people with a bleeding condition. Donating blood through NHS Blood and transplant can really help the patients we see. People who bleed abnormally will often need blood products if they need to have an operation or are badly hurt, it is not just about research, it is about saving lives.

People who already donate blood, can you use it as part of your research?
Yes but people have to consent for us to look at it. As part of the normal blood donating process donors and their donations are tested to ensure they are healthy and their blood can be used safely in patients. Blood donors are therefore the ultimate in healthy controls. People who do consent to let us use the data collected means we do not have to spend time going out to recruit volunteers or asking people for blood sample because the data is already there. Most people that are willing to donate blood are happy for us to use their data in this way. We do not see individual results and cannot identify individual donors from this information, it is simply lots of data that gives an overall picture of what is normal. Ask about research at your next donation– there is always something going on that you may be able to help with.

Why should people take part in research?
It helps us gain more knowledge about both health and disease to improve the future of heath care. We would not know as much as we do today without research and we also know there is an awful lot more to learn. For the most part it does not take much time to participate in research but benefits the population immensely.

Some people are nervous about taking part in medical research, what actually happens with your research and how can you re-assure people?
As a doctor and nurse active in research, we are bound by confidentiality rules just the same

as our colleagues who provide NHS care. All the data we produce is anonymised. While we know who patients and their families are, to everyone else in the team who is looking at and interpreting the data, people recruited are just a barcode number. This is the case for nearly all medical research studies.

We would encourage anyone who may be interested in helping with research to start by simply asking the question. Helping is voluntary and the studies you choose to be involved with is up to you, it is always your choice. Ask questions to determine what the study is about, what is expected of you if you say yes, gather as much information as you can and ask as many questions as you need to make up your mind. You are the one in control of whether you want to take part or not. Even if you only do one study, it'is still helping.

Not all medical research is drug trials, they are just the ones grabbing the headlines. Medical research is so varied using things such as online surveys and thinking tests, to the more classical type such as donating a blood sample or having an MRI scan. There is so much more than drug trials out there and you can contribute in so many ways. No one is going to pressurise you to take part.

If people want to get involved in research, who should they contact?

Within Cambridge there are number of different ways to get involved. Please visit the

BioResource website for rare diseases for more information. Our healthy volunteer partner, the Cambridge BioResource is another great place to sign up.

If you are a patient, your GP or consultant will be able to advise you if there is any research available for your condition. Alternatively there is the NHS website that also has great information about what is happening.

Finally as mentioned before, blood donating is another excellent way to help. If you're already giving a sample you can consent to research at the same time without having to do anything extra.

What do you do in your spare time?
Suthesh – Outside work I enjoy lots of sports. Before I moved to London from Amsterdam I used to enjoy rowing in a men's eight. Now I divide my time between running, biking and swimming. I hope to enter a triathlon one day.

One of my major achievements on this front was climbing the Alpe D'Huez on my bike to raise money for cancer research. I am expecting a baby boy in April and very much look forward to being a dad.

What would be a wish come true?
Suthesh – Professionally, I would like to be part of a team that discovers a brand new gene to explain why some people have abnormal bleeding. Personally I want to do my first triathlon soon.

Amy – Professionally, I would like to be able to say that I have helped patients who might otherwise not have had answers to their problems. Personally, I would love to retire to the Caribbean as soon as possible.