(Footage of patients and doctors)

What is MEN2A?

Narrator: MEN2 is a rare inherited condition which can cause tumours to grow in the thyroid, parathyroids and the adrenal glands. MEN2 can be divided into three subtypes; MEN2A, MEN2B and Familial Medullary Thyroid Cancer or FMTC for short, in which only the thyroid gland is affected.

(Footage of Gwen in field)

Narrator: Gwen Catley has MEN2A and lives near Doncaster in Yorkshire. She had her first symptoms in 2006.

Gwen: My dad had a Pheo in the late 80s. Two years before I was diagnosed with the Pheo, I started with severe abdominal cramps which they thought was polycystic ovarian syndrome or the last one, they thought it was endometriosis. I had a laparoscopy a year before I was diagnosed with the Pheo and they basically old me, I was a bit of a wimp, nothing was wrong with me, go home.

(Anatomical cross section)

Narrator: Phaeochromocytoma or Pheo for short are adrenal tumours and occur in around 50% of MEN2A patients. These are the first tumours to present in about a quarter of cases.

(Footage of Jo walking with her dog)

Narrator: Jo Grey is an MEN2A patient and lives with her family near Tunbridge Wells in Kent.

Jo: Originally, I began to be ill after the birth of my daughter, this is 1996 now. I had very sudden headaches and they were absolutely unbearable. They died off after a few weeks so by the time I saw a migraine specialist, it had all but finished and we put it down to pregnancy hormones. Until I had my son in 1999 and the migraine attacks as I called them then, started again when I was 7 months pregnant. My son arrived a month early after 12 separate attacks during the night and I think I must have been in bed for several weeks after the birth with very sudden migraine attacks. I was feeling very, very ill.

Gwen: I lost lots of weight and I could eat lots which was fantastic, I could eat as much as anyone else so I started going to the GP to say, “Look something’s not right here.” I started my period at the time as well and I was on for 2 months solid even though I was on the pill. So, they carried on doing tests, one doctor even accused me of being an alcoholic because my liver test was showing that there was something not quite right but it was alcoholic signs. In the end, it was an appointment with a doctor that knew the family history. Three weeks later I was diagnosed with a Pheo.

(Footage of Jo's home)

Jo: I felt quite depressed and I couldn't manage the children very well. At various points, my blood pressure was taken and it was extremely high but nobody seemed to twig that it was abnormal for some reason. I'm not sure why, slipped through the net there. When my son was about 9 months old, the attacks began to include vomiting and I just could not look after the children myself. My neighbour stepped in and helped out an awful lot. During the whole time, I was repeatedly going back to my GP and told that I was probably post nattily depressed and that this was causing the vomiting, the depression, the not feeling very well generally. Ultimately, I was almost incoherent and was sent to a psychiatric hospital. There, they actually tested my urine, I did 24 hour urine tests there and apparently had enough adrenaline for a herd of elephants and they obviously thought then that there was something not quite right with this woman. She's depressed because she's not very well. They sent me for a scan and they found a large tumour in my adrenal gland, in my abdomen which quite likely, my son had been bouncing on while I was pregnant and causing me to feel ill at the time. So that really was the breakthrough.

(Footage of Jo in her garden)

Jo: From feeling ill to being diagnosed to being treated to feeling how I am now, has taken 6 to 8 years. So it was a long, long time pre-diagnosis bashing my head against a wall with my then GP, who is no longer my GP.

(Footage of The Oxford Centre for Diabetes, Endocrinology and Metabolism)

Narrator: So what are the symptoms and affects of adrenal tumours? Professor Raj Thacker explains.

Raj: The phaeochromocytoma is sinister. This gives rise to high blood pressure and can be associated with attacks or flushing, palpitations which is fast beating of the heart, headaches and sweating. So when you get that sort of thing happening, we need to look much more carefully. Again, it can be asymptomatic and present for the first time as a stroke.

Barney: For patients with MEN2 who have adrenal disease, this is nearly always phaeochromocytoma, a tumour of one or both adrenal glands that can produce adrenaline. (Footage of operating theatre) To avoid complications, the patient needs to be very well prepared before surgery with protection against adrenaline surges during surgery.

John: Preparation will start many weeks before the operation itself and that will involve coming to clinic and seeing an endocrinologist who will establish exactly what type of Phaeochromocytoma it is, what hormones it's secreting and how they should be worked up for surgery. The anaesthetist will get involved at quite an early stage to decide whether there are any additional investigations that are going to be required and assessing the patient's fitness for anaesthesia and surgery. The patient will be started on medication usually to control the symptoms of the Phaeochromocytoma

and that will usually be Alpha Blockade and sometimes Beta Blockers as well. When patients with Phaeochromocytoma come for their surgery and anaesthesia, it is very important that they are managed by a team who are used to dealing with these types of conditions. That's because when the tumour is handled during the operation, there can be quite profound changes in heartbeat, blood pressure and performance of the heart so it's important that the team knows what to do, they are familiar with the situation and have all the expertise, experience and drugs at hand to deal with any eventuality. The management afterwards is quite important because often there can be quite profound changes in their blood pressure and sometimes that's a hangover effect of the medication they've been put on for the surgery. They may require their blood pressure to be increased by using special drugs and drips on the high dependency unit so it's important that a specialist multi-disciplinary team is looking after them at that point so they can be properly assessed and managed.

(Jo at her computer)

Jo: I was in hospital for several weeks prior to the operation being medicated to control my blood pressure. That was a wonderful relief to have the medication take away the palpitations, the headaches and everything. It left me very tired and very dizzy when I stood up and I had to take everything very slowly, but once that had been done; I went down for surgery, they made a large incision across my abdomen and removed a very large tumour from there.

(Footage of an operating room)

Mark: Most adrenalectomies now are done with keyhole surgery, laparoscopic surgery as we would call it. Most patients will have a small incision where the glad is actually removed, perhaps no more than 3cm across and then a number of incisions, perhaps 5-10mm at most in order to insert instruments to remove the gland.

Gwen: My surgeon was hoping to be able to go through my back, do keyhole surgery through the back. I informed him that that would not be happening as I'd just had a new tattoo and it wasn't quite finished and he wasn't ruining it yet! He wasn't too impressed but once he saw the tattoo he was quite happy and he said "Ok, that's not a problem as long as I can have a picture of it." So I said "Fine, you can have a picture of it and I don't mind." and he went through the front. It went well and I was home about three days later.

(Jo reading on her sofa)

Jo: I spent under 24 hours in the intensive care unit where they monitored blood pressure and absolutely everything and I was kept sedated during that time anyway and I was out within 14 days in total. After which, I just felt fantastic and life started to get back to normal until I was told I should have a DNA test and also a test on my thyroid/ then my mother and son were diagnosed as well.

(Anatomical cross section)

Narrator: As the name suggests, Medullary Thyroid Cancer forms in the thyroid gland. Almost all patients with MEN2 will develop Medullary Thyroid Cancer so what is the current recommended surgery?

Barney: Treatment of patients with MEN2 will nearly always require intervention for Medullary Thyroid Cancer either in patients to stop them developing Medullary Thyroid Cancer or treating Medullary Thyroid Cancer that has already started and this requires removal of the thyroid gland and in many cases the lymph nodes around the thyroid.

Gwen: From my last scan, they had thought that there was nothing wrong with the thyroid glands, they were looking completely normal but with the MEN2A diagnosis, they just wanted to check that there was nothing there so we went for an ultrasound scan on my neck where they did find three nodules but they weren't that bothered about them, they just said "Let's do a biopsy and we'll wait and see."

Jo: I was more scared of having my thyroid removed than I was of having my stomach cut open. I think just the thought of having your throat cut, is a little bit alarming and you think of big blood vessels going up to your head, that sort of thing. In reality, particularly for me anyway, it was actually the easiest surgery that I had. I was in and out in a week and the scar healed quite quickly, quite nicely and I was up within a couple of hours of waking up from the anaesthetic, having lunch and discovering that actually, I could swallow and it wouldn't be painful. And that was easier. I had quite an experienced surgeon on the thyroid front.

(Footage of an operating room)

Narrator: So what is the surgical procedure?

Mark: So most thyroidectomies will be done by through a scar on the front of the neck approximately 4 or 5cm in line with a skin crease but if you're doing a lymph node dissection of the lateral compartments then you do need to extend the scar towards the ear or make a separate scar in order to remove those nodes safely.

(Footage of operating theatre)

Mark: For those older patients who present with Medullary Thyroid Cancer or who, when they are investigated by virtue of their family history, are found to have Medullary Thyroid Cancer; then the operation would be to remove the whole of the thyroid very carefully, to leave no residual thyroid tissue and we would remove all of the lymph nodes that are adjacent to the thyroid going from between the ceratoid arteries and down into the upper part of the chest. Those are the lymph nodes that the Medullary Thyroid Cancer would spread to first. They can spread to the lymph nodes on either side of the neck and that can require further surgery to clear those nodes as well.

Barney: There may be patients who have isolated spread of their Medullary Thyroid Cancer to for example, a bone and that metastases of the surrounding bone can be

removed but generally speaking, the surgery is confined to absolutely perfect removal of tumour if that's possible from the neck and chest and that way the lymph node spread can be minimised. Complications that may occur, result from injury to one of the voice box nerves but that should be rare or to inadequate parathyroid function after surgery which leads to a low calcium and this can be treated with vitamin and calcium supplements after the operation.

Raj: For the thyroid tumours, the Medullary Thyroid Carcinomas, it is best to have them taken out very, very early. If it's MEN2A, we will say as soon as is possible and certainly in early childhood.

Stephen: Again, if the children of patients with MEN2 who are known to be carriers, present a particular issue because the recommendation is that we perform a fairly early removal of the thyroid gland by surgeons at an early stage of their lives to try and protect them from development of Medullary Carcinoma of the thyroid.

Barney: Surgery for Medullary Thyroid Cancer in children should be performed in specialist centres and there are quite strict regulations about this so this is not an operation that should be performed in centres not used to performing surgery for Medullary Thyroid Cancer in adults.

(Diagram showing how MEN is passed through families)

Narrator: Each child of an MEN carrier has a 50% or 1 in 2 chance of inheriting MEN. Detecting MEN2 in early childhood provides an opportunity for early preventative or curative treatment.

Jo: In true 50/50 inheritance style that goes with MEN, I've got two children, one of whom does have MEN2A and the other one who doesn't. The one who does, the youngest, my son is the first boy in the family that we know of to have MEN and he's already had his thyroid removed. He had this done at age 3 and a half about a year after his diagnosis just to ensure that there would be no cancer there and that this would therefore be prevented completely. Being that age when he had his surgery was, in a lot of ways, a great idea because he really didn't know anything about it. He doesn't remember anything about it, even now. He also recovered extremely quickly, he was up and about within an hour eating jam sandwiches and finger painting.

(Footage of Jo's son)

Jo: He was very unaware of what was going on. It looked almost like a playschool, the ward where he was going to stay. When he came out, we were fetched to go down to the recovery room to see him and I was just absolutely amazed that he was fine and he was just waking up. We went up rather tearfully and sort of, you know, said "Are you alright?" and he said "Go away" so I knew that his voice was fine and he was going to be fine but it was an unusual way to greet your mother!

(Footage of Jo and her son)

Jo: He is aware that he has something called MEN2A and he would be able to tell you that he's had his butterfly taken out of his throat but any more than that, he's not really aware of at the moment. He's just coming up for 7 and he knows as much as he needs to at this stage.

Narrator: Cameron turned 11 in 2010 and all blood tests show that his early thyroidectomy may have been successful in preventing Medullary Thyroid Cancer.

MEN2B

Stephen: MEN2B is similar to MEN2A but with some added features involving skin particularly and bone structure and so if you like, it's in the same family as MEN2A but with added features which make it really quite different in many ways and it's much less common.

Raj: There may be problems with the nerve supply to the gut so these patients may get things like constipation or problems with their bowel.

(Footage of Anne and her family)

Narrator: Anne Wood and her partner Anthony O' Flaherty live in Scurry in the far North West of Scotland with her three children. One of them, Gillie, has MEN2B.

(Photographs of Gillie)

Anne: From birth he had severe constipation and although he was a purely breastfed baby, which would normally mean there would be very little constipation, he often didn't open his bowels, erm, he would open his bowels once every 4 to 6 weeks.

Anthony: The advice at the time was that it wasn't necessarily too unusual and just to monitor it.

Anne: Another quite interesting symptom was the neuromas in his mouth, these kind of little warty things, he had a big one in between his front teeth and in fact, before he had front teeth, it kind of hung down like a sort of, long gummy strand. Quite a few things on his tongue as well and we didn't really think this was a symptom of anything, we just thought, you know, this is the way he is and didn't think anything of it but in hindsight that was quite an clear symptom of MEN.

(Photograph of Gillie)

Anne: Another symptom fairly early on was, what was described as, a failure to thrive where he wasn't growing as he should have been and so in the child growth charts, he dropped from a fairly just below average kind of size, right down to below the bottom percentile.

Chris: Chris Murray is an MEN2B patient and lives near Reading. His experience with MEN2B shows a less aggressive course of thyroid disease that would be more commonly seen.

Chris: When I was a child, the physical symptoms became obvious and age 12 or so. There were certain other things, some lesions on the tongue, the thick lips that made us believe that potentially it was a thyroid problem. The diagnosis was made following some treatment at the dentist which extracted some gum and once sectioned, allowed the doctors to realise that there was a problem with the thyroid. I didn't really know what the thyroid was, what its function was and I didn't really understand the implications of what was happening, so it was all completely new to me. I'd never been ill, never been in hospital, never really had anything other than colds and flu before so it was a real shock.

(Footage of Gillie on his bike)

Narrator: As Gillie grew up, his symptoms changed and developed.

Anthony: It was getting close to Gillie starting playgroup and he was soiling himself and wetting himself a lot and we had a great struggle in managing toileting. He did start playgroup, one of the rules was that children needed to be able to look after themselves before going but there was some flexibility and certainly a great deal of support for us. Having started though, the problems continued and then that fed into meeting with the local paediatrician through the education system. She referred us onto the local consultant paediatrician.

(Footage of Anne and her family)

Anne; He started to take us on and he didn't repeat al the test, we had the notes from London but we saw him numerous times about the constipation and then he was seen by an endocrinologist who was visiting from Edinburgh and that didn't actually reveal anything the first time but we saw another endocrinologist at the second clinic. She started to get really excited about the combination of something we hadn't actually picked up as an issue with Gillie which is that he has quite big fleshy lips. We just thought that this is how he is but they are particularly big and fleshy and she talked about there being a condition which combines symptoms of mouth neuromas, big lips and bowel problems. She got quite animated taking photos of his lips on her mobile phone to show to colleagues and she tested him and the next thing we knew, we had this diagnosis.

(Footage of Anne and her family)

Anne: I think we were fortunate in that our paediatric endocrinologist who diagnosed him, had met a case of MEN in Australia and so because she had a personal experience of this, it had come to her.

(Footage of Chris picking up phone)

Chris: Within days of the tests ending, my parents sat me down, explained the situation. I went to see the general surgeon, John Farndon who was going to carry out the surgery and he explained the process, the situation and the fact that we needed to do it fairly quickly. There was potentially a risk that this might spread and therefore we needed to progress fairly quickly with surgery. Obviously, I was at school at that point so in effect, school and life was put on hold until this was resolved but within 10 days, 2 weeks, I was in hospital, in a general ward, waiting for surgery to take place.

(Footage of Chris on phone)

Chris: It was all, really a scary experience because at 12 or 13 years old, I really didn't fully understand the implications of what was about to happen to me and a simple extraction of a piece of gum suddenly led on to an awful lot more.

(Footage of Chris in his garden)

Chris: The recovery time was probably a couple of weeks at home with Elastoplasts and the like covering my neck and the actual scar still remains very slightly; you can just see where the surgery took place. I think the biggest problem I had was the fact that I was still relatively young, still had no concept of surgery at that point and so it was all a daunting experience as a child and it took me some time to recover mentally more than physically.

Anthony: The paediatrician phoned and asked if we would like to come in and see him or if we would like to receive news over the phone. He was very sensitive. He told us on the phone that he had MEN2B. As I remember, he avoided the word 'cancer' or he played it down. He said that there was a potential for cancerous growths.

Anne: I was confused as to whether MEN was cancer or did MEN lead to cancer, you know, just trying to get our heads around it, it seemed extremely complex.

Anthony: The big 'c' word is a very emotive word; he played it down so we played it down too. We didn't connect with perhaps the rarity of it and also the potential difficulties.

Anne: We were told immediately that he would be having an operation to have his thyroid taken out and they were going into planning that immediately. So there was a sense of urgency about it so there wasn't any time to worry or kind of dwell, you know, it was action time and we just kind of went with it really.

Anthony: Gillie's coped very well with the whole issue really, the operation, the thyroidectomy went very well, very smooth and he came away from that experience having had an adventure. He was very well cared for. He had a lot of positive attention and that was also good for him.

Anne: Immediately afterwards, he was on calcium supplements to regulate his levels and there were regular blood tests to test his calcitonin levels because the question was, "Had the cancer spread?"

(Footage of Gillie with siblings/family)

Narrator: Examination of Gillie's extracted thyroid tissue showed that the gland already contained Medullary Thyroid Cancer. Gillie's calcitonin level is closely monitored and in 2010, they showed that he still has active cancer cells somewhere in his body. In MEN2B, the earlier the thyroid is removed, the better the outcome. Current international guidelines recommend the removal of the thyroid in the first year of life in diagnosed MEN2B patients.

Anne: Having direct contact with our paediatric endocrinologist is absolutely what we want and anybody else that we ask is going to defer to her anyway so we have been very fortunate in being able to contact her directly with any questions or issues that we have. We've planned his journey through this together, all the way.

(Chris at his computer)

Chris: At the time, the internet wasn't an option so I was reliant on my father who did a bit of research through his medical connections to find out more about the illness and me; I asked my biology teacher at school who I got on well with, for some more information about the calcitonin side of things and what that meant for me. Slowly but surely, I managed to gather enough information to get me by, to understand what the thyroid situation was and then as it became evident it was MEN2 B, the whole scenario of what was going to happen in the future. Then of course, the link came out with the adrenal glands that potentially at some point in the future; maybe a year, it may be 20 years, it may be never, that there would be potentially some problem with the adrenal glands to deal with somewhere down the line.

(Footage of Chris at home)

Narrator: Sure enough, Chris did end up with adrenal tumours.

Chris: It became obvious that the adrenals were becoming a problem and once tests proved that this was the case and that the Phaeochromocytoma was diagnosed, fairly quickly afterwards, it was necessary to bring my blood pressure down to a level where surgery on adrenals becomes safe. Again, similar to the thyroid surgery in many ways, the tests and the lead up to the surgery was worse than the surgery itself. At the time we were hoping it was going to be laparoscopic surgery rather than normal surgery and thankfully this did become the case and I had a very quick, short stay in hospital.

(Chris taking medication)

Chris: I had 4 or 5 very small scars instead of one very big scar and within 4 or 5 days, I was at home on new drugs as well as the existing thyroxine with minimal symptoms from the surgery.

Anne: We've also seen the geneticist who has also tested the rest of the family and we've all come out negative so Gillie is a sporadic case on his own.

(Gillie with his family)

Narrator: Anne and Anthony want to present a positive message in contrast to some of the difficulties they could face with MEN2B. They promote self education and a proactive attitude with medical professionals to help to ensure the best possible outcome for Gillie.

Anthony: Parents generally know their kids best, particularly when it's to do with bodily functions and the day to day muck that you have to get into and that's not necessarily respected by the experts. We too easily put the medical people up there on the pedestal but we actually come to appointments; we come to meetings with such a breadth of knowing, we might not be able to elucidate it the way the doctor might but not to forget that we have a lot of information and that it needs to be listened to.

Anne: Our hope is that he lives happily ever after and that if he wants to have children that they don't have the disorder and that'll be the end of MEN2B in our line of family.

(Footage of Anne playing musical instruments with her boys)

Narrator: But the reality for Anne and Anthony is that the residual cancer somewhere in Gillie's body could, at some point, progress. Then the challenge will be to locate it and if possible remove it before it spreads.

CREDITS