



LIVING WITH MEN2

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 – MEN 2A, MEN 2B and Familial Medullary Thyroid Cancer or FMTC, for short, in which only the thyroid gland is affected.

Gwen Catley has MEN 2A and lives near Doncaster in Yorkshire. She had her first symptoms in 2006.

GWEN CATLEY:

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

NARRATOR:

Pheochromocytoma, or Pheo for short, are adrenal tumours and occur in around 50 per cent of MEN2 patients. These are the first tumours to present in about a quarter of cases. Jo Grey is an MEN 2A patient and lives with her family near Tunbridge Wells in Kent.

JO GREY:

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 has all but finished and they 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 seven months pregnant.

My son arrived a month early after twelve 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 CATLEY:

I lost lots of weight and I could eat lots, which was fantastic. I could eat as much as anybody else though I started going to the GP just to say, look, something's not right here. And I started my period at the time as well and I was on for two months solid, even though I was on the pill. So they, they carried on doing tests. One doctor even accused me of being an alcoholic because my liver tests were showing there was something not quite right but it was alcoholic signs. And in the end it became an appointment with a doctor that actually knew the family history. Three weeks later I was diagnosed with a Pheo.

JO GREY:

I felt quite depressed and I couldn't, 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 that was abnormal for some reason. I'm not quite sure why. I slipped through the net there. When my son was about nine 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 was told that I was probably post natally 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 there's something not quite right with this woman. She's depressed because she's not very well. And 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, and that really was the breakthrough – from feeling ill, to being diagnosed, to being treated, to feeling how I am now has taken six to eight years and 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.

NARRATOR: So what are the symptoms and effects of adrenal tumours?
Professor Raj Thakker explains.

PROF RAJ THAKKER: The pheochromocytoma is sinister. This give rise to high blood pressure and can be associated with attacks of flushing; palpitations, which is fast beating of the heart; headaches; and sweating. And 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.

MR BARNEY HARRISON: For patients with MEN2 who have adrenal disease this is nearly always pheochromocytoma, a tumour of the one or both adrenal glands that can produce adrenaline. To avoid complications, the patient needs to be very well prepared before surgery with protection against adrenaline surges during surgery.

DR JOHN ADAMS: 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 pheochromocytoma 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's 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 pheochromocytoma and that will usually be alpha blockade and sometimes beta blockers as well. When patients with pheochromocytoma come for their surgery and anaesthesia, it's very important that they're managed by a team who are used to dealing with these types of conditions and that's because when the tumour is handled during the operation, there can be quite profound changes in the heart rate, blood pressure and performance of the heart. So it's important that the team knows what to do, they're 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 the blood pressure and that sometimes is the hangover effect of the medication they've been put on for the surgery. So they may require to have their blood pressure increased by special drugs and drips on the high dependency unit. So it's very important that a specialist multi disciplinary team is looking after them at that point so they can be properly assessed and managed.

JO GREY:

I was in hospital for several weeks prior to the operation, being medicated to control my blood pressure. That was a wonderful relief to, to have this 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, 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.

MR MARK LANSDOWN: Most adrenalectomys now are done with keyhole surgery, microscopic surgery, as we would call it. Most patients would have a small incision where the gland is actually removed, perhaps no more than three centimetres across, and then a number of incisions, perhaps five to ten millimetres at most, in order to insert instruments to remove the gland.

GWEN CATLEY: My surgeon was, 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, through the front. It went well. I was home about three days later.

JO GREY: I spent under 24 hours in the intensive care unit where they, they monitored blood pressure and absolutely everything. 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 then told that I should have a DNA test and also a test on my thyroid. Then my mother and son were diagnosed as well.

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?

MR BARNEY HARRISON: Treatment of patients with MEN2 nearly always will 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 glands around the thyroid.

GWEN CATLEY:

From my last scan they had thought that there was nothing wrong with the, the thyroid glands. They were looking completely normal. But with the MEN 2A 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 GREY:

I was more scared of having my thyroid removed than I was of having my stomach cut open and I think it's 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 and that sort of thing. And 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 - it wouldn't be painful – and that was easy. I had quite an experienced surgeon on the thyroid front.

NARRATOR:

So what is the surgical procedure?

MR MARK LANSDOWN:

So most thyroidectomys will be done through a scar on the front of the neck, approximately four or five centimetres, 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 up towards the ear or make a separate scar in order to remove those nodes safely.

For those older patients who present with medullary thyroid cancer or who when they're investigated by virtue of their family history 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 the lymph nodes that area adjacent to the thyroid, going from between the carotid 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.

MR BARNEY HARRISON: There may be patients who have isolated spread of their medullary thyroid cancer to, for example, a bone, and that metastasis and 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 upper 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 – and this should be rare – or to inadequate parathyroid gland function after surgery which leads to a low calcium. And this can be treated with calcium and vitamin supplements after operation.

PROF RAJ THAKKER: For the thyroid tumours, the majority of the carcinomas, it is best to have them taken out very, very early. If it's MEN 2A we will say as soon as is possible, certainly in early childhood.

DR STEPHEN GILBY: 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 the development of medullary carcinoma of the thyroid.

MR BARNEY HARRISON: 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.

NARRATOR: Each child of an MEN carrier has a 50 per cent or one in two chance of inheriting MEN. Detecting MEN2 in early childhood provides an opportunity for early preventative or curative treatment.

JO GREY:

In true 50:50 inheritance style that goes with MEN, I've got two children, one of whom does have MEN 2A and the other one who doesn't. The one who does, my youngest, my son, he's the first boy in the family that we know of to, to have MEN and he has already has his thyroid removed. He had this done at age three 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. He was very unaware of what was going on. It looked like almost 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 go and see him and I was just, I was just absolutely amazed that he was fine and he was just waking up and 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.

He is aware that he has something called MEN 2A 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 seven and he knows as much as he needs to at this stage.

NARRATOR:

Cameron turned eleven in 2010 and all blood tests currently show that his early thyroidectomy may have been successful in preventing medullary thyroid cancer.

DR STEPHEN GILBEY:

MEN 2B is similar to MEN 2A but with some added features involving skin, particularly, and bone structure. So, if you like, in the

same family as MEN 2A but with added features which make it really quite different in many ways. And it's much less common.

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

NARRATOR: Anne Wood and Anthony O'Flaherty live near Scourie in the far northwest of Scotland with their three children. One of them, Gillie, has MEN 2B.

ANNE WOOD: From birth he had severe constipation and although he was a purely breast fed baby, which would normally mean there would be very little constipation, he often didn't open his bowels for, he would often open his bowels once every four to six weeks.

ANTHONY O'FLAHERTY: The advice at the time was it wasn't necessarily too unusual and just to monitor it.

ANNE WOOD: Another quite interesting symptom was the neuromas in his mouth which are 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 kind of long, gummy sort of strand really. Quite, quite a few things on his tongue as well and we didn't really think this was a symptom of anything. We just thought this is, you know, this is the way he is and didn't think anything of it. But with hindsight that was actually quite a clear symptom of MEN.

And 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 he, he, in the child growth charts he dropped from a fairly just below average kind of size right down to below the bottom centile.

NARRATOR: Chris Murray is an MEN 2B patient and lives near Reading. His experience with MEN 2B shows a less aggressive course of thyroid disease that would be more commonly seen.

CHRIS MURRAY: When I was a child the, the physical symptoms became obvious at age twelve or so. There were certain other things, some lesions on the tongue, the thick lips that made us believe that it was, potentially, 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, 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.

NARRATOR: As Gillie grew up his symptoms changed and developed.

ANTHONY O'FLAHERTY: 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. There was, 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 there. And, having started though, the problems continued and that then fed into meeting with the local community paediatrician through the education system and she referred us onto the local consultant paediatrician.

ANNE WOOD: And he started to take us on. And he didn't repeat all the tests. We had the notes from London but we saw him numerous times about the constipation. And then we were seen by a, 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, the second clinic, and she started to get really excited

about the combination of something we hadn't actually picked up was an issue with Gillie at all, which was he had 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 combined symptoms of mouth neuromas, big lips and bowel problems. And she was, she got quite animated, taking photos of his lips on her mobile phone and, to show to colleagues and she tested him and the next thing we knew was that he had this diagnosis.

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'd had a personal experience of this it had, it had come to her.

CHRIS MURRAY:

(Hello.) 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, 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 in general was put on hold until, until this was resolved but within ten days, two weeks I was in hospital in a general ward waiting for surgery to take place.

It was all quite a scary experience because at twelve or thirteen 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, to an awful lot more.

The recovery time was probably a couple of weeks at home with elastoplasts and the like covering my neck and the, the actual scar still remains very slightly. You can just, just see where it, 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, so it was all a daunting experience as a child and it took me some time to recover mentally more than, more than physically.

ANTHONY O'FLAHERTY: The paediatrician 'phoned. He asked if we would like to come in and see him or would we like to receive news over the 'phone. He was very sensitive. He told us on the 'phone that he had MEN 2B. As I remember, he avoided the word 'cancer' or he played it down. He said that there is a potential for cancerous growths.

ANNE WOOD: I was confused as to whether, is MEN cancer or does MEN lead to cancer? And, you know, just trying to get our head around it, it seemed extremely complex.

ANTHONY O'FLAHERTY: The big C word – it's a very emotive word and he played it down and so we played it down too. We didn't really, we didn't really connect with perhaps the rarity of it and also the potential difficulties.

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

ANTHONY O'FLAHERTY: Gillie's coped very well with the, the whole issue really. The operation, the thyroidectomy went very well. It was 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 WOOD: Immediately afterwards he was on calcium supplements to regulate his levels and there was regular blood tests to test his calcitonin levels because the question was, had, had the cancer spread?

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 this showed that he still has active cancer cells somewhere in his body.

In MEN 2B 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 MEN 2B patients.

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

CHRIS MURRAY: At the time, I think, the internet wasn't an option so I was reliant on, on my father who, who did a bit of research through his medical connections to find out more about the illness. And myself, 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. So, 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 that it was MEN 2B, the whole scenario of what was going to happen in the future. And then, of course, the link came out with the adrenal glands that potentially at some point in the future, maybe a year, it maybe 20 years, it may be never, that there would be some, potentially some problem with the adrenal glands to deal with further down the line.

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

CHRIS MURRAY:

It became obvious that the adrenals were becoming a problem and, and once tests had proved that this was the case and that the pheochromocytoma was diagnosed fairly quickly afterwards, it was necessary to bring my blood pressure down to a level where surgery on the adrenals becomes safe.

The, again, similar to the thyroid surgery, in many way the tests and the lead up to the surgery was, was worse than the surgery itself. At that time, we were hoping it was going to be laparoscopic surgery rather than normal surgery. This, thankfully, did become the case and I had a very, very quick and short stay in hospital and I had four or five very small scars instead of one very big scar and within four or five days I was at home on new drugs as well as the existing thyroxin with very, very minimal symptoms from the surgery.

ANNE WOOD:

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

NARRATOR:

Anne and Anthony want to present a positive message in contrast to some of the difficulties they could face with MEN 2B. They promote self education and a proactive attitude with medical professionals to help them to ensure the best possible outcome for Gillie.

ANTHONY O'FLAHERTY:

Parents generally know their kids best, particularly when it's to do with bodily functions, the day to day muck that you have to get into and that's quite often not necessarily respected by, by, by the experts. And 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, to elucidate it in the way that the doctor might, but not to forget that we have a lot of information and that it needs to be listened to.

ANNE WOOD:

Our hope is that he lives happily ever after and if he wants to have children that they don't have the disorder and, and that'll be the end of MEN 2B in our line of family.

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.