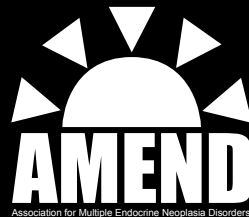


MEN 2b

Patient Information

Multiple Endocrine Neoplasia Type 2b
(also known as MEN3)



Registered Charitable Incorporated Organisation no. 1153890.

MEN SUPPORT
Tel: 01892 516076
Email: info@amend.org.uk
www.amend.org.uk

AMEND Membership,
resources and services are FREE

Contents

3	What is Multiple Endocrine Neoplasia?
4	How is MEN2b Diagnosed?
4	What Conditions are Associated with MEN2b?
6	Medullary Thyroid Cancer (MTC)
12	Phaeochromocytomas
17	Other Conditions Associated with MEN2b
18	Children and MEN2b
21	Genetic Testing Explained
24	Emotional Well-being
24	Useful Information
25	Useful Organisations
26	Glossary
28	AMEND Medical Advisory Team
29	Afterword
29	About AMEND

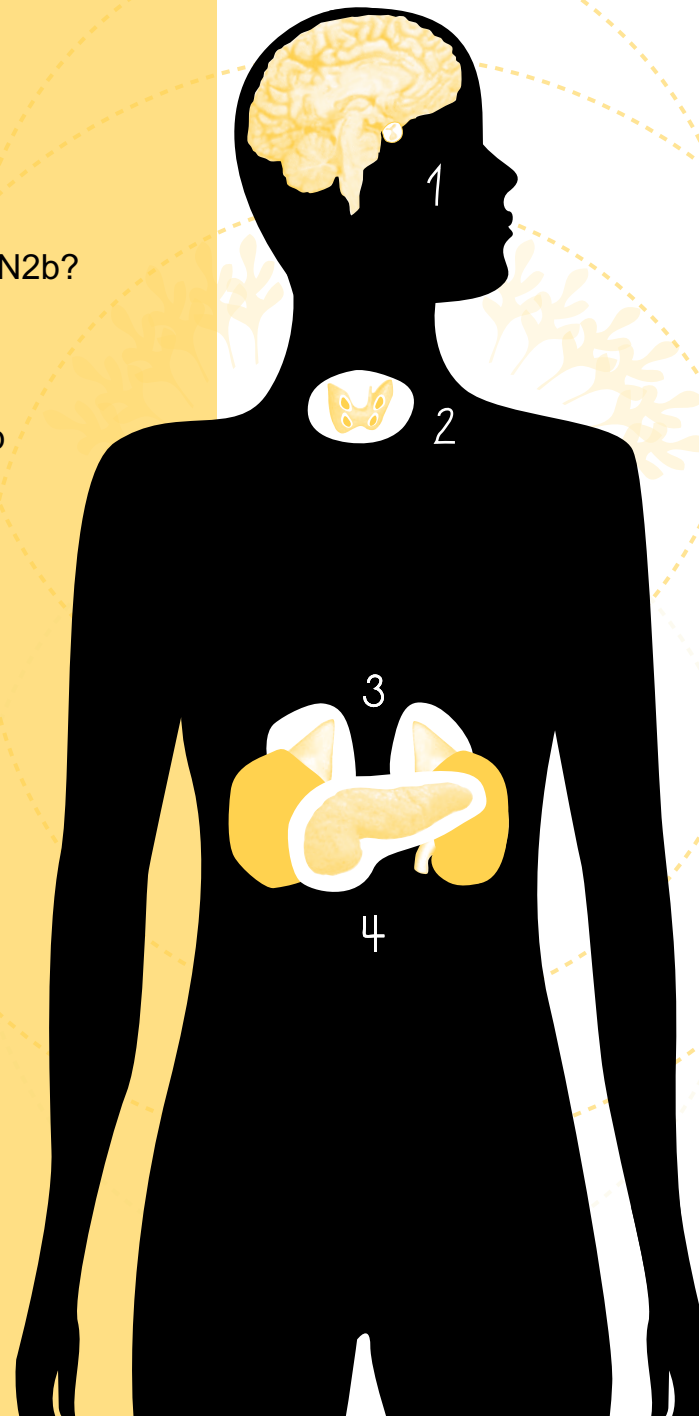
What is Multiple Endocrine Neoplasia Type 2b

Multiple Endocrine Neoplasia Type 2b is a condition which can be passed down in families. MEN2b causes more than one gland of the body's endocrine (gland) system to develop growths (tumours) known as neuroendocrine tumours (NETs). The affected glands may then make greater than normal amounts of hormones, the body's chemical messengers, which in turn cause a range of different symptoms. Each type of growth may occur alone and independently of MEN.

Multiple = more than one
Endocrine = gland system
Neoplasia = increase in growth of cells to form a tumour

MEN2b is closely related to but different from MEN2A.

1 pituitary 2 thyroid and parathyroids 3 adrenal glands 4 pancreas



How is MEN2b Diagnosed?

A person may be said to have MEN2b if they have:

1. 2 or more tumours that occur in MEN2b (see Other Conditions Associated with MEN2b); or
2. Only one tumour, but there is a family history of relatives with MEN2b; or
3. A blood test which shows a change in a gene called RET

As well as endocrinologists, doctors in a range of other areas of medicine might suspect MEN2b. Paediatricians (children's' doctors) may suspect MEN2b when a young child or baby has growth or eating problems affecting development (failure to thrive), or if the child does not produce tears while crying. A dentist or doctor may suspect MEN2b when they see lumps (mucosal neuromas) in the mouth (gums and/or tongue) or the lumpy lips which are a typical

facial feature of MEN2b. Bowel doctors (gastroenterologists) may also suspect MEN2b if the cause of enlarged bowel (megacolon), constipation and/or diarrhoea is found to be the result of benign colon growths called ganglioneuromas. These conditions are dealt with in more detail later on in the book.

What Tumours occur in MEN2b?

There are two main tumours that can occur in MEN2b. These are:

1. in the thyroid gland in the neck (medullary thyroid cancer or MTC)
2. in the adrenal glands that sit on top of each kidney (phaeochromocytomas).

In addition, patients with MEN2b often have benign (not cancer) lumps on the lips, in the mouth and throughout the gut. Children with MEN2b are more likely to have feeding problems and bowel problems than other children.

The information below details the current medical monitoring programme for MEN2b patients. See specific condition sections for more details on the tests themselves.

Recommended ages for tests and thyroid surgery in MEN2b				
Codon number of the change in the RET gene	Gene testing	First calcitonin blood test and neck ultrasound	Surgery to remove the thyroid gland	Testing for adrenal tumours (phaeochromocytoma)
MEN2b (MEN3) 883, 918	As soon as possible and before age 1	As soon as possible and by between 6 months to 1 year	As soon as possible and by age 1	from age 8 and before thyroid surgery

Adapted from Harrison's Textbook of Medicine

The remainder of this information book aims to give you more detail about the conditions that occur in MEN2b and the current medical opinion on appropriate tests, treatment and medications.

Medullary Thyroid Cancer (MTC)

Almost all MEN2b patients will develop medullary thyroid cancer (MTC), sometimes within the first year of life, unless steps are taken to prevent it. The thyroid gland is found at the front of the neck. This gland makes 3 hormones; thyroxine and triiodothyronine (essential for maintaining the body's metabolism and mental and physical development), and calcitonin.

MTC starts in the C-cells of the thyroid which make the hormone calcitonin. An increase in the number of C-cells (C-cell hyperplasia) occurs before they become cancerous. In MEN2b, MTC develops at a very early age and can quickly spread to nearby lymph nodes. Even so, there may be no physical symptoms of this. As MTC grows, calcitonin levels increase.

If the thyroid and nearby lymph nodes are removed by surgery while the cancer is still contained within the thyroid (total thyroidectomy and central lymph node dissection), a patient is usually cured.

If calcitonin levels are still raised after surgery, this shows that the cancer has spread (metastatic) or has not been completely removed. In this case further surgery and other therapies may be used to control it. As yet there is no complete cure for MTC that has spread; however, it is often slow-growing and may be managed without symptoms for many years. Symptoms that develop can often be controlled by the use of radiotherapy, new drug therapies and sometimes chemotherapy (see How Is MTC Treated When It Has Spread?).

Due to the earlier detection of MEN2b made possible by a genetic test, and the high chance that a MEN2b patient will develop MTC in early childhood, surgery to remove the thyroid is done in the child's first year in order to prevent the development of the cancer (see Children and MEN2b). In older children, thyroidectomy is performed as soon as MEN2b is diagnosed.

Testing for C-cell Hyperplasia & MTC

Below are some of the tests that you may have to confirm a diagnosis of C-cell hyperplasia or MTC:

BLOOD TESTS

Baseline Calcitonin: A simple blood test to detect calcitonin levels [NB: once drawn, the blood must be taken immediately and on ice to a chilled centrifuge in the lab] Plasma calcitonin (CT) and carcinogenic antigen (CEA) levels should be measured every 3-6 months after total thyroidectomy if tests show that MTC is still present; less often if there is no MTC present.

SCANS/OTHER

Ultrasound Scan (US) with Fine Needle Aspiration (FNA): A painless scan of the neck using a probe on the skin. The images then guide the insertion of a needle to biopsy (sample) thyroid tissue.

Treating MTC

Once a diagnosis of MTC has been made, an ultrasound scan of the neck called a 'staging ultrasound' will be done. If the lymph nodes do not look larger than normal, an operation called a 'total thyroidectomy and central node dissection' is done. If any lymph nodes do look larger than normal, then further nodes will be removed at the same time as the thyroid.

SURGERY

Total thyroidectomy + central node dissection - a small cut is made at the base of the front of the neck from which the thyroid and nearby lymph nodes can be removed. A larger cut is needed if the cervical lymph nodes need to be removed as well. Eating and drinking is possible almost straight away after waking up from the operation.

Hospital Stay - you will probably stay in the hospital for around 3 to 5 days in total.

Risks - thyroid surgery is generally safe, but there are some possible risks that you need to be aware of.

Injury to the nerves that control the vocal cords (less than 1-2%) may affect the voice.

Unavoidable removal of or injury to the parathyroid glands may occur which might result in a temporary drop in calcium levels in the blood. Sometimes this may be permanent. Symptoms of low blood calcium include tingling lips, fingers and toes, and eventually cramping. All these symptoms can be corrected with medication.

Often there are no obvious symptoms of very mild low calcium although some subtle signs are shown in the table right:

MEDICATION AFTER SURGERY

Thyroid replacement medication

Levothyroxine: Levothyroxine (or Thyroxine) must be taken lifelong after thyroidectomy. Tablets are taken once a day and doses are based on the body weight of

Symptoms of HYPOcalcaemia

- calcium	- - calcium	- - - calcium
<ul style="list-style-type: none"> Tingling of the face and extremities (fingers and toes) Pins and needles in the face and extremities (fingers and toes) <p>These symptoms may be worse when crossing one's legs or sitting on the toilet for example.</p>	<p>all of the previous plus:</p> <ul style="list-style-type: none"> Muscle cramps Clawing of hands or feet (tetany) Chvostek's sign - twitching of the face, mouth or nose when the facial nerves just in front of the ear are tapped Trousseau's sign - spasm of the hand and fingers when a blood pressure cuff is applied and pumped up to a pressure sufficient to block the hand's blood supply 	<p>all of the previous plus:</p> <ul style="list-style-type: none"> Convulsions irregular heartbeat Difficulty breathing <p>Over a long period of time, low calcium can lead to:</p> <ul style="list-style-type: none"> osteoporosis cataracts

the individual (typically between 100-150mcg for adults, lower for children). You will need regular blood tests to make sure that you are on the right dose. A dose that is too big may cause symptoms such as rapid heartbeat, sweating, anxiety, shaking and weight loss. A dose that is too small may cause symptoms such as tiredness, a slow heartbeat, sensitivity to cold, and weight gain.

Although the above symptoms may suggest a need to change your dose, the same symptoms can occur in other conditions. Only a blood test measuring the thyroid stimulating hormone (TSH) level can help doctors be sure whether a change in dose is needed. Once your ideal dose is found, as judged by blood tests, repeat tests only need to be done once a year.

Calcium replacement medication

Vitamin D (alphacalcidol, ergocalciferol, calcitriol)

Vitamin D may be given in a capsule form to help the body absorb calcium from the diet.

Calcium Carbonate (Calcichew, Adcal)

This is a chalk-like tablet that has to be chewed or sucked. This is often used as a short term “top-up” after surgery, but is not always needed life-long. If the patient begins to suffer from headaches, nausea and vomiting, this may show that these tablets are no longer needed.

Magnesium supplement

This may be in the form of an injection or a tablet (e.g. magnesium glycerol-phosphate), but is rarely needed long-term.

How is MTC Treated if it has Spread?

Patients with MTC may have high levels of calcitonin in the blood even after surgery. However, although this shows that there are MTC cells left in the body, patients with calcitonin levels that are higher than normal, staying the same over a period of time, or slowly increasing, often do not need further tests or treatment. This is because scans are not always able to find a site of disease outside of the neck unless calcitonin levels are very high: calcitonin alone is not proof of a growing tumour. Even so, in some patients, the search for metastatic disease may involve various scans, including radioactive isotope scans, followed by treatment with more surgery or radiotherapy if needed. C-cells also produce a substance called carcinoembryonic antigen (CEA) which is measured together with calcitonin.

MIBG / OCTREOTIDE THERAPY (radioactive isotope therapy)

Where surgery is no longer an option due to the extent of the disease, some expert medical centres may use radioactive therapies called octreotide or MIBG radioactive therapies. These have very few side effects and can help to reduce or control the spread. However, they are only used if tests show that they will be taken up by the tumour. The agent is attached to a radioactive substance, and is given through a vein by slow injection. The patient remains radioactive for a few days and therefore must be nursed in a special room alone. The treatment may need to be repeated several times at 3 or 6 month intervals. Possible side effects of MIBG / Octreotide therapy include feeling sick, and sometimes vomiting.

Until a complete cure is found, much of the current focus of

treatment for extensive metastatic MTC is on the relief of the symptoms it causes:

Diarrhoea: A change to the patient’s diet may be needed, together with medicine such as Imodium which can help to control it. In some cases diarrhoea can also be relieved by treatment with a long-acting form of somatostatin (octreotide or lanreotide) although this is not the case for everyone. Some believe that in such cases it may also help slow down the growth of the tumour.

Flushes: medicines used to control ulcers called H2 blockers (cimetidine or ranitidine) may sometimes be used to help ease flushing.

Painful bone metastases: external radiation therapy can sometimes provide rapid relief when MTC has spread to the bone. In all cases, pain medicine may be prescribed.

Other Therapies for Metastatic MTC

A class of drugs called Tyrosine Kinase Inhibitors (TKIs) and Multi-Kinase Inhibitors (MKIs) are becoming available for use in metastatic MTC where other treatments do not work. These drugs are not cures, but may in some people help to slow or stop the spread of MTC as well as to relieve some of the side effects of high calcitonin levels. The drugs (cabozantinib and vandetanib) are expensive and are therefore currently only available through the Cancer Drugs Fund (CDF). Specialists have to apply to the CDF to use them. You should discuss this option, the possible side effects and other issues about these therapies with your specialist. TKIs and MKIs are not always suitable for everyone.

Research into MTC is ongoing. There are other drugs in the pipeline that are currently being tested on animals and humans. To view the various human clinical trials, please visit the Research section of the AMEND website.

Phaeochromocytomas ('fee-oh-cromo-sy-tomers')

Phaeochromocytomas (phaeos - 'fee-ohs') are tumours of the adrenal glands. In MEN they are almost always benign (not cancer). The body's two adrenal glands are normally each about the size of a whole walnut, and sit just on top of the kidneys. Phaeos grow in the inner part of the adrenal gland (the medulla) and make larger than normal amounts of a group of hormones called catecholamines (such as adrenaline). Phaeos may grow for many years without causing severe symptoms, but they can start to do so due to stressful events such as childbirth or surgery. Even though phaeos are almost always benign in MEN, they are still a danger to the patient due to the sudden larger than normal amounts of hormones they make. They have been known to cause strokes, heart failure and premature death if they are not diagnosed and treated. Once a patient is known

to have MEN2b, regular tests should find a phaeo well before any symptoms develop.

Possible symptoms of a phaeo may include all or some of the following:

sudden severe headaches, palpitations, breathlessness, excessive sweating, high (or rarely low) blood pressure (either all the time or every so often), shaking,

pale appearance, tiredness, depression, anxiety, and feeling sick with or without being sick.

Testing for Phaeochromocytomas

24 hour Urine Collections for Catecholamines & Metanephrines

A collection of a patient's urine over 24 hours to measure quantities of catecholamines and metanephrines in the body. Raised levels suggest that a phaeo is present. Different labs use different methods so the bottles used to collect urine may or may not contain acid to help preserve it. In all cases the bottle should not be put in a fridge during the test.

Plasma Metanephrines

More and more often now, blood tests for metanephrines and normetanephrines are being used to check if a phaeo is present. A special diet to avoid coffee, chocolate, and other foods should be followed to make sure that the test is accurate. For this test you will need to lie still for 30 minutes before the blood is drawn.



SCANS/OTHER

MRI / CT Scans

You will be asked to lie still in a donut or tube-like machine for up to 1 hour. You may be asked to hold your breath for a short time every so often and may be given an injection of a contrast fluid during the scan to highlight certain areas of interest within the body.

Radioactive Isotope Scan (MIBG)

These special scans are often performed in Nuclear Medicine Departments of large or university hospitals. The process can take two days, although the scan itself will only take about 1 hour on each day. Before the scan, the hospital may supply you with tablets (potassium iodide) to take before the scan to protect your thyroid gland (even if you no longer have one!)

Day 1: you will be asked to lie still under a large camera-like scanner and general pictures will be taken. You will then be given an injection of radioactive material to highlight areas of activity in your abdomen.

Marks are then placed on your abdomen and further scans done.

Day 2: lining the machine up using the marks on your body, a further scan will be done to record which areas are still lit up by the radioactive material.

How are Pheos Treated?

Treatment for pheochromocytomas is surgery. The tumour and the adrenal gland where it grows are both removed. If only one gland is affected then only that gland will be removed at that time. This is because removing both adrenal glands will leave the patient needing corticosteroid drugs for the rest of their life to replace the hormones made by the glands. Doctors prefer to delay this type of drug treatment for as long as possible as the medication has its own potential drawbacks (see Bilateral Adrenalectomy).

Alpha-Blockade

As soon as a phaeo is

diagnosed, a drug is given to help make the blood pressure as stable as possible (alpha-blockade).

This is needed because a phaeo can cause sudden high blood pressure. Alpha-blockers (phenoxybenzamine or doxazosin) have side effects including feeling dizzy, a dry mouth and a stuffy nose. Your doctors may enquire about these symptoms because it tells them that the drug is working. Men may also find that they cannot ejaculate during sex. Patients can take these drugs at home for the time before surgery. The side effects of the drugs decrease during this time as the body absorbs more salt and water to fill up the blood vessels, but the patient may still feel tired and become easily breathless and dizzy. The drugs are stopped after the tumour has been removed.

In addition to alpha-blockade, a few patients may need beta-blockers too (propranolol / atenolol). These should only be prescribed when alpha-blockade is complete.

SURGERY

How the surgery will be done will depend on the size of the tumour, and which gland or glands are being removed.

Right Hand (RH) Adrenalectomy

- removal of the right side adrenal gland only.

Left Hand (LH) Adrenalectomy

- removal of the left side adrenal gland only.

Bilateral Adrenalectomy

- removal of both adrenal glands at the same time.

Most tumours can be removed by key-hole surgery (laparoscopic surgery) through a series of small cuts in the belly or in the back. Larger tumours may be removed through a larger single cut in the belly.

Some patients with tumours in both glands at the same time (bilateral) may be able to have a type of surgery which leaves a part of the outer rim of the gland behind. This needs a surgeon who is experienced with this type of surgery. You should discuss the pros and cons of this with your surgeon and medical team.

HOSPITAL STAY

Before surgery for alpha-blockade – you may need to stay in hospital for up to 7 days before surgery to make sure that the drugs are working well and that all your fluid levels are good.

After surgery – you will usually spend 2-4 days in hospital after key-hole surgery, and longer after open surgery.

Risks

Sudden surges in blood pressure during removal of the tumour could cause stroke and heart failure. However, these risks have been greatly reduced since the use of alpha-blockade and other potent drugs began.

MEDICATION AFTER SURGERY

After both adrenal glands have been removed hydrocortisone and fludrocortisone must be taken for life. These medications replace the hormones cortisol and aldosterone which are made by the adrenals. The drugs take over keeping blood sugar levels normal, aiding recovery from

injury and stress, and keeping the balance of salts and water content of the body normal.

Hydrocortisone (a corticosteroid) *Hydrocortone*

These tablets must be taken every day for life. Doses are usually split during the day. Doses may vary but often 10mg is taken early morning with 5mg at lunch and 5mg in the evening. A double dose should be taken at times of illness. At times of extra stress, such as surgery, injury, severe vomiting and diarrhoea, extra hydrocortisone (100ml IV or IM) injected in liquid form (efcortisol or solucortef) is needed straight away. The injection helps to stop the risk of shock which leads to loss of blood pressure and death. For this reason, all patients should carry an emergency injection kit. After both adrenal glands have been removed, they should be shown how to self-inject before they leave the hospital.

Fludrocortisone (a corticosteroid) *Fludrocortone*

These tablets must also be taken

once a day for life. Tablets are taken early in the morning and doses may vary.

Regular blood tests are very important to check the levels of these drugs. This must be overseen by an experienced endocrinologist.

The Addison's Disease Self Help Group (ADSHG) supports patients with Addison's Disease who also need lifelong steroids. They are a fantastic source of information on how to deal with life on steroids (see Useful Organisations)

Other associated MEN2b Conditions

GANGLIONEUROMAS

Ganglioneuromas are benign tumours (not cancer) of areas of nerve tissue in the gut. They occur in almost all MEN2b patients and can grow anywhere from the mouth down to the rectum.

These tumours often cause no symptoms, but those along the gut may cause a swollen belly,

and a change in shape of the bowel (megacolon) that can cause diarrhoea or constipation. These problems may be seen in early childhood in some MEN2b patients and may sometimes require surgery.

Ganglioneuromas in and around the mouth (mucosal neuromas) are the cause of the swollen lips and lumps on the tongue and/or gums often seen in MEN2b patients. Some growths can be removed, especially if they cause problems with brushing teeth. A similar tumour (neuroma) can also occur along the eyelids of patients with MEN2b.

MARFANOID HABITUS

MEN2b patients are often tall and thin with long fingers and toes. This is due to common abnormalities affecting muscles and/or bones (marfanoid habitus). Orthopaedic issues like these can also include foot and hip abnormalities, hypermobile joints and scoliosis. People with MEN2b do not have Marfan Syndrome.

Children and MEN2b

Deciding to have children

There is a 1 in 2 (50%) chance that a child born to someone with MEN2b will also have MEN2b (see Genetic Testing Explained).

If a child is known to carry the gene change, testing and treatment plans may be set up from the start. In this way, conditions may be found and treated before serious symptoms develop. Testing during pregnancy (PND) is available if the gene change is known. Pre-implantation Genetic

Diagnosis (PGD) is also available through the NHS to potential parents with MEN who want to start a family. PGD uses the IVF process but embryos are screened and only the ones that do not have MEN2b are re-implanted in the mother's womb.

If families are considering PND or PGD, they should ask for a referral to one of the 23 UK clinical genetics centres before they become pregnant. PND or PGD is a personal choice and often depends on the family's experience of MEN2b.

Pregnancy and MEN2b

Before becoming pregnant, women with MEN2b should be tested for phaeochromocytoma. An undiagnosed phaeochromocytoma can cause a life-threatening crisis during birth.

Doses of medications already being taken may need to be changed during pregnancy. For example, mothers who have had both adrenal glands removed and who are taking corticosteroid medications will need extra doses for the birth. They will also need more regular blood tests to check levels, and more regular antenatal checks.

DNA Testing for Children

Children of a parent with a known MEN2b gene change can be offered a genetic test to find out if they also carry the gene. This is usually offered soon after birth. The test may be done using a blood sample or in some cases, using a cheek scraping or saliva sample. You should discuss this with a genetic counsellor at your Regional Genetics Services Centre.

Talking to Your Children About MEN2b

AMEND produced an information leaflet on this subject in 2012. You can download this for free from our website (www.amend.org.uk) or in hardcopy on request. The leaflet suggests ways in which to broach the subject of your family's MEN2b with your children, along with how much to tell them according to their age.

Explaining MEN2b to Your Children

Thanks to an award from the UK Big Lottery Fund, AMEND commissioned a Medikidz™ comic on MEN2, called 'Medikidz Explain Multiple Endocrine Neoplasia Type 2: what's up with Cameron?'. Aimed at 8-12 year olds, the comic explains MEN2A and MEN2b as simply as possible in an engaging way and is a tool to help you explain the disorder to children in this age group. The comic is free and available through your specialist or directly from AMEND. An entertaining and accessible web animation aimed at ages 5 years and up is also available to view in the children's area of the AMEND website or on our YouTube Channel (AMEND3).

Treatment and Testing Recommendations in Children

Medullary Thyroid Cancer (MTC)

Baseline Calcitonin A simple blood test to detect changes in the thyroid (C-cell hyperplasia or the presence of MTC)

Phaeochromocytomas (uncommon before age 10)

Plasma (blood) metanephrines / normetanephrines 24 hour urine collections (annual or 6 monthly): Young children in particular often find the novelty of weeing into a bottle for a day rather exciting, which makes urine tests relatively easy to do.

For a child carrying a known MEN2b gene mutation, total thyroidectomy to prevent the development of medullary thyroid cancer is recommended in the first year of life.

A phaeochromocytoma detected on screening will require removal.

A geneticist will be able to advise you on this. In the hands of an experienced surgeon and team, many children cope much better with surgery than some adults.

Older Children

Children diagnosed with MEN2b at an older age should be tested straight away due to the strong chance of having MTC. They will need to have tests for pheos before thyroid surgery takes place.

Blood Tests

There are many adults who find blood tests difficult, so no parent should be surprised if their child shows an intense dislike to them as well. For small children, many hospitals use Ametop or Emla Cream ("magic cream") covered by plasters to numb the hands and/or arms ready for the test. The cream takes up to an hour to work during which time the child may focus on the area and become distressed. In these cases, it is sometimes quicker and easier either not to use the cream at all or to use a topical anaesthetic spray instead. A phlebotomist experienced in doing children's blood tests is essential to ensure as few repeated jabs and tests and thereby as little distress for the child as possible.

Genetic Testing Explained Chromosomes and Genes

In each cell of the body there are 23 pairs of chromosomes that contain our genes. We inherit one chromosome from each pair from each parent. This means that we inherit one copy of each gene from each of our parents, thereby giving us two copies.

In most people there are two normal functioning MEN2b genes (RET or RET proto-oncogene). In patients with MEN2b one of this pair has a change (sometimes called a 'mutation'). The most common gene change in MEN2b is called 'M918T'.

The gene change can be passed down to a child from either parent, but in most people with MEN2b, it started in that person for the very first time (new or de novo mutation). However, once someone with MEN2b has children they can pass on either the normal gene or the gene with the change. This is random like

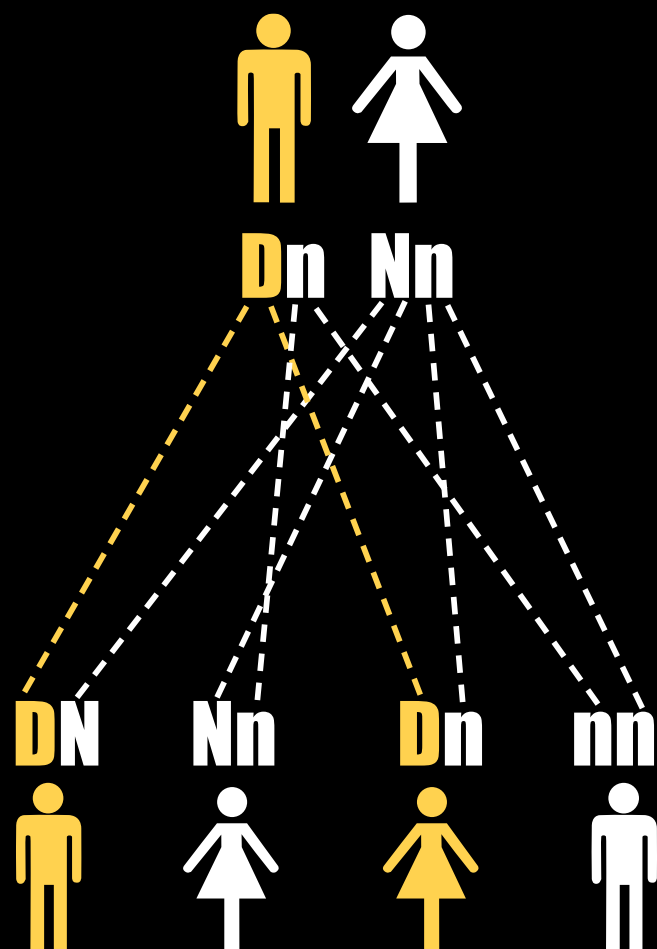
tossing a coin. Each child of an affected parent thus has a 1 in 2 or 50% chance of inheriting the faulty RET gene (coloured yellow over page). This child would then be at risk of developing the tumours of MEN2b. It also means that there is a 50% chance that the child would inherit a normal copy of the gene, and would therefore not inherit MEN2b. This method of inheritance is called autosomal dominant inheritance.

What are codons and why do they matter?

There are a number of different changes at different positions in the RET gene. The position of the change (eg codon 918) may help to predict the course of disease in a person. In some cases this can also help doctors to plan tests and treatments.

Genetic Testing

This special blood test is recommended to confirm a diagnosis of MEN2b. The genetic test reads through the RET gene to identify any changes. Once



MEN2b has been confirmed in a person by gene test, it is then possible for their children (and in some cases, their other families members) to have a genetic test to see if anyone else has inherited the gene change or not. There are a number of issues surrounding predictive genetic testing particularly in relation to children. As such, all patients should be seen and counselled by a consultant clinical geneticist.

There is an ethical argument for healthcare professionals that would allow them to test a child suspected of having MEN2b, even if the parents refuse to do so. This is because it is possible that testing and early treatment can be life-saving for that child.

Those who are shown to have inherited the gene can be comforted by the fact that testing and treatment plans will show as early as possible when treatment is required. Thanks to this early detection by genetic test, complications from advanced medullary thyroid cancer, and high

blood pressure, stroke and heart failure due to phaeos may be greatly reduced.

Genetic testing and counselling is available at 23 regional genetic centres throughout the UK (www.bsgm.org.uk). A referral to a genetic centre is made through your GP or specialist.



Emotional Well-being

Living with a rare genetic disorder is not always easy. Some people cope better than others, but most people will have periods of low mood at some point along the way. It is now better recognised that overall health depends upon both physical and emotional health. For this reason, AMEND offers a free telephone counselling service to registered members. In addition, AMEND's Counsellor is sometimes available for face-to-face sessions at our free events. See our website for more details. In 2015, AMEND began a project to look at the psychological impact of living with MEN. The project includes the development of some specific resources that we are sure patients will find useful. The range of leaflets includes 'Dealing with Diagnosis' and 'Living with Uncertainty'. They are available to download for free from the Resources section of our website or in hard copy on request. A series of podcasts

and an introductory video on the relaxation method, Mindfulness, have also been developed as part of this project and are free to access via our website and YouTube Channel (AMEND3).

Useful Information

Free Prescriptions: In the UK, if you are to take lifelong hydrocortisone or levothyroxine, you are entitled to free prescriptions for all medicines. You should obtain a FP92A application form from your doctor and complete parts 1 and 2. Your doctor will then sign it and send it on. You will then receive a Medical Exemption Certificate, which you must show to your pharmacist when collecting medicines. You can find more information on Medical Exemption Certificates on the following website: www.nhsbsa.nhs.uk/HealthCosts/2095.aspx

MedicAlert Emblem®: AMEND recommends that anyone taking life-long medications obtain and wear a MedicAlert® identification

emblem. The emblem contains summarised information of your medical condition and a 24-hour Helpline number for emergency medical staff to call in order to obtain detailed information on your medical condition from the MedicAlert database. This enables emergency medical staff to give appropriate treatment in full knowledge of your underlying condition and current medications. Emblems come in a range of styles so that there is something for everyone, even children. Telephone AMEND for an order form and brochure or join online at www.medicalert.org.uk. Other medical identification products are available.

Useful Organisations

The British Thyroid Foundation

Tel: 0870 770 7933
www.btf-thyroid.org.uk

Addison's Disease Self Help Group (ADSHG)

Tel/Fax: 01483 830673
www.adshg.org.uk

Teenage Cancer Trust

Tel: 020 7612 0370
www.teenagecancertrust.org

Butterfly Thyroid Cancer Trust

Tel: 01207 545469
www.butterfly.org.uk

Hypopara UK

Tel: 01342 316315
www.hypopara.org.uk

Glossary

Adrenal Glands a pair of walnut-sized organs found above the kidneys that make stress hormones

Autosomal Dominant

Inheritance when the child of a parent with a genetic condition has a 50% or 1 in 2 chance of inheriting that condition from the affected parent

Calcitonin a hormone made by the C-cells of the thyroid gland that has no known action in healthy people

Catecholamine a class of stress hormones made by the adrenal glands

CEA short for carcinoembryonic antigen; a substance that can be measured as a marker for MTC

Chemotherapy cancer treatment using chemicals

Chromosomes cell structures that contain genes

Codons sections of genes where mutations may occur to cause disease

De novo a new gene change that starts in that person and which has not been passed down from a parent

DNA short for deoxyribonucleic acid; the carrier of genetic information, stored in every cell in the body

Endocrine Glands organs in the body that make and release hormones which affect the activity of other organs

Ganglioneuromas benign growths (not cancer) found in areas of nerve tissue

Gene structures made of DNA. A change in normal gene structure results in a mutation (i.e. RET gene mutation in MEN2)

Hormones chemical messengers in the body which drive different processes by controlling the function of many different organs

Hypercalcaemia a state of having too much calcium in the blood

Hypocalcaemia a state of having too little calcium in the blood

Marfanoid Habitus unusual

muscle and/or bone presentation which causes longer than normal limbs, fingers and toes and taller than average height

Medulla the central part of an organ

Megacolon an enlargement of the diameter of the bowel which can affect its function

Metanephrines a substance in urine which is measured to help diagnose a phaeochromocytoma

Mucosal Neuroma small benign growths which can occur in the lips, mouth, or on the tongue in MEN2b

Neoplasia abnormal level of growth in cells to form a tumour

Neuroendocrine tumours a body system consisting of nerve and gland cells that produce hormones and releases them into the bloodstream

Osteoporosis a condition caused by having hypocalcaemia over a long time period making bones break more easily than normal

Pancreatitis painful swelling of the pancreas

Parathyroid Glands four small organs found in the neck that make parathyroid hormone (PTH)

Phaeochromocytoma a growth in the inner part of an adrenal gland which makes greater than normal levels of stress hormones

PGD short for preimplantation genetic diagnosis; the screening out of embryos with a genetic disorder prior to implantation using an IVF-like procedure

PND short for prenatal diagnosis; the testing of a baby for genetic disorders before it is born

Radiotherapy a form of cancer treatment that uses X-ray radiation to destroy cancer cells

RET the name of the gene that, if containing a change, can cause MEN2A, MEN2b and FMTC

Thyroid Gland a butterfly-shaped organ found in the neck that makes and releases hormones called thyroxine and triiodothyronine

Ulcer a painful sore on or inside of the body

AMEND UK Medical Advisory Team

- **Professor Rajesh Thakker**, University of Oxford, Oxford Centre for Diabetes, Endocrinology & Metabolism;
- **Dr Caroline Brain**, Consultant Paediatric Endocrinologist, UCLH & GOSH, London;
- **Professor Ashley Grossman**, University of Oxford, Oxford Centre for Diabetes, Endocrinology & Metabolism;
- **Mr Barney Harrison**, Department of Endocrine Surgery, Royal Hallamshire Hospital, Sheffield
- **Dr Fiona Laloo**, Consultant Clinical Geneticist, St Mary's Hospital, Manchester;
- **Mr Tom Lennard**, Professor of Surgery, The Medical School, University of Newcastle upon Tyne
- **Mr David Scott-Coombes**, Department of Surgery, University Hospital of Wales, Cardiff;

Afterword

This book has been written for MEN patients by MEN patients with the help of a medical advisory team. The aim of this book is to answer those questions, sometimes in great detail, that one may come across during a lifetime of living with MEN2b. It is not for use in self diagnosis. It contains detailed information on tests, surgery and potential symptoms associated with MEN2b. However, it is possible that not all of this information will be relevant to you. This book is not intended to replace clinical care decisions and you should always discuss any concerns you may have carefully with your specialist. Every care has been taken to ensure that the information contained in this book is accurate, nevertheless, AMEND cannot accept responsibility for any clinical decisions.

About AMEND

AMEND is a Charitable Incorporated Organisation registered in England and Wales (number 1153890). It provides support and information services to families affected by multiple endocrine neoplasia and related endocrine tumours. AMEND encourages research into the conditions by awarding annual medical prizes and research awards. It hosts regular free patient information events every year and runs social media forums connecting patients from around the world.

© Association for Multiple Endocrine Neoplasia Disorders (AMEND), July 2015
1st Edition May 2005; Review due 2017

Written by Jo Grey (AMEND CEO) with the help of the AMEND Medical Advisory Team, and 2015 Intern, Lauren Winsor
Design by Up The Hill www.up-the-hill.co.uk

Gunning Fog Index: 12.68

This update was made possible thanks to a patient group grant from the Society for Endocrinology (www.endocrinology.org)



Please visit our website for more information on AMEND or to make a donation:

www.amend.org.uk

Find us on Facebook

Follow us on Twitter
(@AmendInfo)

Scan with your smartphone to go to our website:



Notes