MEN 2a

Patient Information

Multiple Endocrine Neoplasia Type 2a

AMEND

Association for Multiple Endocrine Neoplasia Disorders

Registered Charity No. 1099796

USA MEN Support & Information
Tel: 707-464-7066
Email: amendusa@hotmail.com
P.O. Box 1212
Crescent City, CA 95531-1212

Membership is FREE

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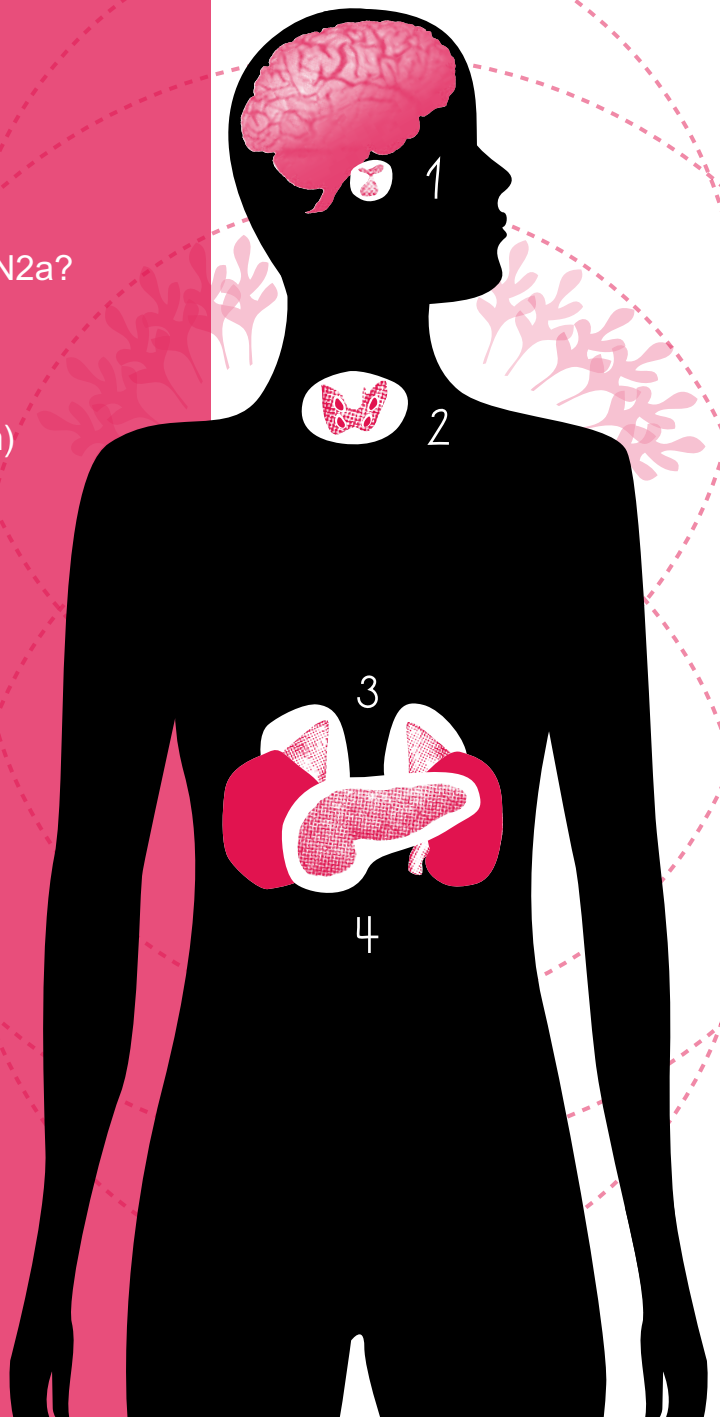


1 pituitary 2 thyroid and parathyroids 3 adrenal glands 4 pancreas

What is Multiple Endocrine Neoplasia Type 2a?

Multiple Endocrine Neoplasia Type 2a (MEN2a), also known as Sipple's Syndrome, is one of a group of genetic disorders under the name Multiple Endocrine Neoplasia, the others being called MEN1, MEN2b and FMTC (see separate Patient Information books). They are inherited disorders, which cause more than one gland of the body's endocrine (gland) system to develop growths (tumors). The affected glands may then produce abnormally increased amounts of hormones, the body's chemical messengers, which in turn cause a variety of different symptoms. Each type of growth may occur alone and independently of MEN .

How is MEN2a Diagnosed?

A diagnosis of MEN2a is made when either:

1. A patient has 2 or more MEN2-associated growths (see What Conditions are Associated with MEN2a); or
2. A patient has only one growth, but there exists a family history of relatives with MEN2a.
3. A patient has the gene change that causes MEN2a

Note: A patient may have the gene change that causes MEN2a, but not have developed any of the growths. This patient may be called a "MEN2a carrier" and should be offered medical endocrine follow-up in the same way as a patient with the MEN2a growths.

What conditions are associated with MEN2a?

There are three types of tumor associated with MEN2a. These occur in the thyroid in the neck (medullary thyroid cancer), the parathyroid glands that lie close to or within the thyroid (parathyroid tumors), and the adrenal glands that sit on top of each kidney (pheochromocytomas). Management of MEN2a involves two main approaches – treatment of tumors that have grown as well as medical tests that detect new tumor growth at an early stage. For example, if medullary thyroid cancer is diagnosed, the initial treatment consists of the removal of the thyroid gland and sometimes the surrounding lymph nodes. Subsequent management for the other growths associated with MEN2a consists of the monitoring of hormone levels using blood and urine tests, and scans of the neck and abdominal area, sometimes leading to treatment in the form of surgical removal of the tumor and/or affected gland. The remainder of this information book is divided up between these conditions and details the current thinking on appropriate tests, treatment and medications.

The information below details the current medical monitoring program for MEN2a patients after initial surgery to remove the thyroid gland, according to their particular codon mutation of the RET proto-oncogene (See Genetic Testing Explained). See specific condition sections for more details on the tests themselves.

Recommended monitoring program for MEN2a patients

MEDULLARY THYROID CANCER (MTC)

Plasma calcitonin (CT) levels

Annual after total thyroidectomy. Note: Some patients may be eligible to delay thyroid surgery if they do not yet have signs of medullary thyroid cancer. These patients who have not had a thyroidectomy should have their CT levels checked regularly and an ultrasound (sonogram) of their thyroid if levels begin to rise.

PHEOCHROMOCYTOMA

Codons: 634, 918

Catecholamines and/or metanephrines in 24hr urine collections Annual, from age 5.

Codons: 609, 768, 804, 891

Catecholamines and/or metanephrines in 24hr urine collections every 2 years, from age 10.

HYPERPARATHYROIDISM

Codons: 634

Plasma calcium and parathyroid hormone levels Annual.

(continued overleaf)

Codons: 609, 611, 618, 620, 790, 791

Plasma calcium and parathyroid hormone levels

every 2 years, from age 10.

Codons: 768, 804, 891

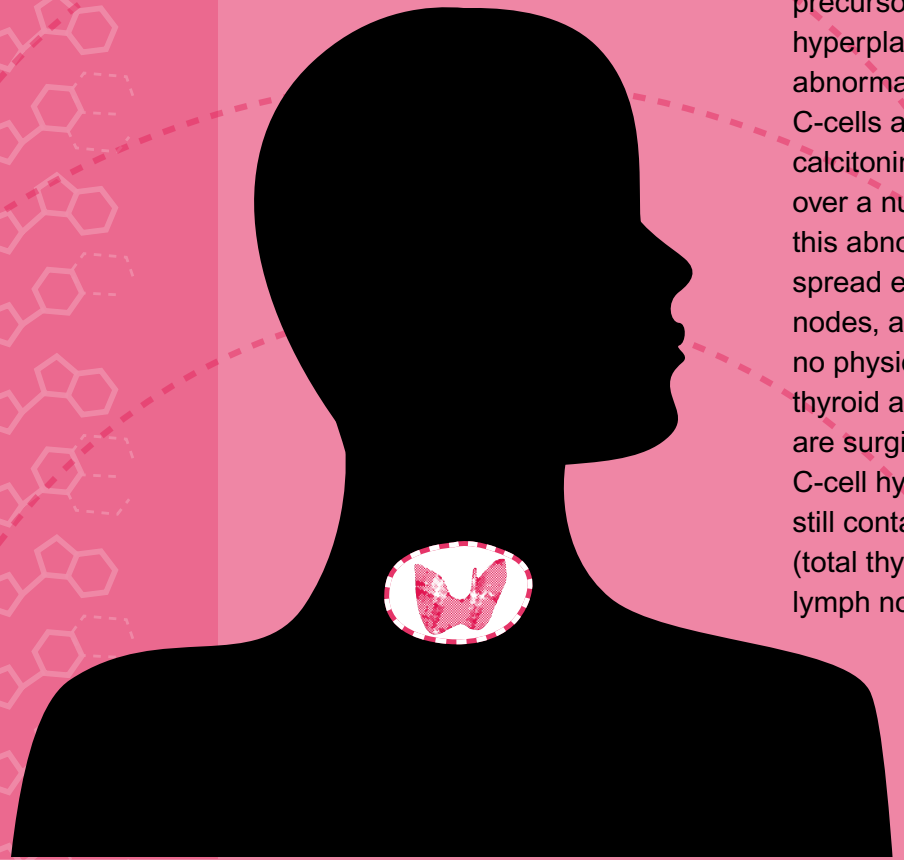
Only if showing symptoms (rare).

MEN2b & FMTC

MEN2a is closely related to FMTC, but different from MEN2b. FMTC consists of the hereditary form of MTC with a much lower risk of having any other glands being involved than MEN2a. MEN2b patients may have MTC (almost all patients), pheochromocytomas (50% of patients) but not parathyroid tumors. In addition, patients with MEN2b may have long fingers and toes and non-cancerous growths called neuromas. The neuromas can grow on the tongue, lips, and eyelids and cause a distinctive facial appearance.

Medullary Thyroid Cancer (MTC)

Almost all MEN2a patients will develop medullary thyroid cancer (MTC) if they are not treated. The age that MTC develops varies from person to person, but can sometimes be predicted based on their particular codon mutation of the RET proto-oncogene (See Genetic Testing Explained). The thyroid is located at the front of the neck. This gland produces 3 hormones; thyroxine and triiodothyronine (essential for maintaining the body's metabolism and mental and physical development), and calcitonin (which has no known action in healthy people).



MTC occurs in the calcitonin-producing cells (parafollicular or C-cells) of the thyroid. The precursor to MTC is called C-cell hyperplasia, where there is abnormal growth of the normal C-cells and overproduction of calcitonin. MTC usually develops over a number of years from this abnormal growth but can spread early on to nearby lymph nodes, although there may be no physical symptoms. If the thyroid and nearby lymph nodes are surgically removed while the C-cell hyperplasia or cancer is still contained within the thyroid (total thyroidectomy and central lymph node dissection), a patient

is usually cured. If, after surgery, calcitonin levels are still raised, or begin to rise this indicates that the cancer has spread (metastatic) or has not been completely removed, and so further surgery and other therapies are used to control it. As yet there is no definitive cure for metastatic MTC; however, it may often be managed effectively and without symptoms for many years. Symptoms that may develop can sometimes be controlled by the use of radiotherapy and sometimes chemotherapy.

Due to the possible earlier detection of MEN2a by a gene test, and the high probability that an affected patient will develop MTC, thyroidectomy is often recommended in children who carry the gene before the age of 5 in order to prevent the development of the cancer (see Children and MEN2a). This course of action may be responsible for the dramatic reduction in the number of deaths in MEN2a patients from metastatic MTC. In older children, thyroidectomy is performed as soon as MEN2a is diagnosed.

Testing for C-cell Hyperplasia & MTC

Tests 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]*

Scans

Ultrasound with Fine Needle Aspiration (FNA) A painless scan of the neck using a probe. The images then guide the insertion of a needle to biopsy (sample) thyroid or lymph node tissue.

Treating MTC

Once a diagnosis of MTC has been made, a staging ultrasound scan of the neck should be undertaken. The most common treatment for MTC is surgery. The type of surgery needed depends on whether MTC is thought to have spread to any surrounding lymph nodes. If there is no suspicion of enlarged lymph nodes, a total thyroidectomy and central node dissection is undertaken. If enlarged nodes are detected, removal of other neck lymph nodes should be undertaken at the same time.

SURGERY

Total thyroidectomy + central node dissection A small incision is made at the base of the front of the neck from which the thyroid and nearby lymph nodes can be removed. A larger incision is required if removal of the cervical lymph nodes is necessary. Eating and drinking is possible almost immediately after waking up from the operation.

Hospital Stay

Approximately 3 – 5 days

Risks

Injury to the nerves that control the vocal cords (less than 1-2%)
Unavoidable removal of, or injury to the parathyroid glands resulting in a temporary drop in calcium levels in the blood, although occasionally this may be permanent. Symptoms of low blood calcium include tingling lips, fingers and toes, and eventually cramping, all of which can be corrected with medication.

MEDICATION

Levothyroxine

This is a very well established and effective replacement for the thyroid hormones. It must be taken life-long after thyroidectomy. Tablets are taken once a day and doses are typically between 100-150mcg for adults, lower for children. Regular blood tests are required to ensure that the right dose is being prescribed.
Too large a dose may cause symptoms such as rapid heartbeat, sweating, anxiety, tremor and loss of weight
Too small a dose may cause symptoms such as lethargy, slow heartbeat, sensitivity to cold, and weight gain.
Although the above symptoms may suggest a need for a change of dosage, the same symptoms can occur in other conditions. Only a blood test (measuring the thyroid stimulating hormone or TSH level) can determine accurately whether a change in levothyroxine dose is required. Once a stable dose is achieved, as judged by blood tests, repeat tests need only be done annually.

(continued overleaf)

Calcium replacement medication

(See Treating Parathyroid Tumors, Medication)

Treating Metastatic MTC

Patients with MTC may have high blood calcitonin even after complete surgical treatment. However, although this indicates that there are MTC cells left in the body, patients with calcitonin levels that are higher than normal, remaining the same over a period of time, or slowly increasing do not necessarily need further investigation or treatment. This is because scans are unlikely to identify a site of disease outside of the neck unless calcitonin levels are significantly high: calcitonin alone is not an indication of a growing tumor. Nevertheless, in some patients, the search for metastatic disease may involve various scans (including radioactive isotope scans) and even a laparoscopy (telescopic inspection of the abdomen) followed by more surgery with radiotherapy if required.

MIBG / OCTREOTIDE THERAPY

Where surgery is no longer an option due to the extent of the disease, some specialized medical centers may use radiolabelled MIBG or Octreotide radioactive therapies, which have very few side effects, to help reduce or control the spread. However, it is only appropriate if tests suggest that the radioisotope will be taken up by the tumor. 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 lead-lined room. The treatment may need to be repeated several times at 3 or 6 month intervals. Possible side effects of radioactive isotope therapy include nausea and occasionally vomiting.

Until a complete cure is found, much of the current focus of treatment for extensive metastatic MTC is on the relief of symptoms it causes:

Diarrhea Adjustments to the patient's diet may be required, together with an anti-diarrhea medication such as Imodium, (loperamide). Some of the tumors contain somatostatin receptors, and in these instances treatment with a long-acting form of somatostatin (Octreotide or lanreotide) may sometimes be helpful. Some believe that in such cases it may also help slow down the growth of the tumor.

Flushes Anti-ulcer medications called histamine receptor blockers (H2 blockers such as cimetidine or ranitidine) may occasionally be prescribed to help ease flushing.

Painful bone metastases Painful bone metastases may be suitable for external radiation therapy, which can provide rapid relief. In all cases, pain medications may be prescribed.

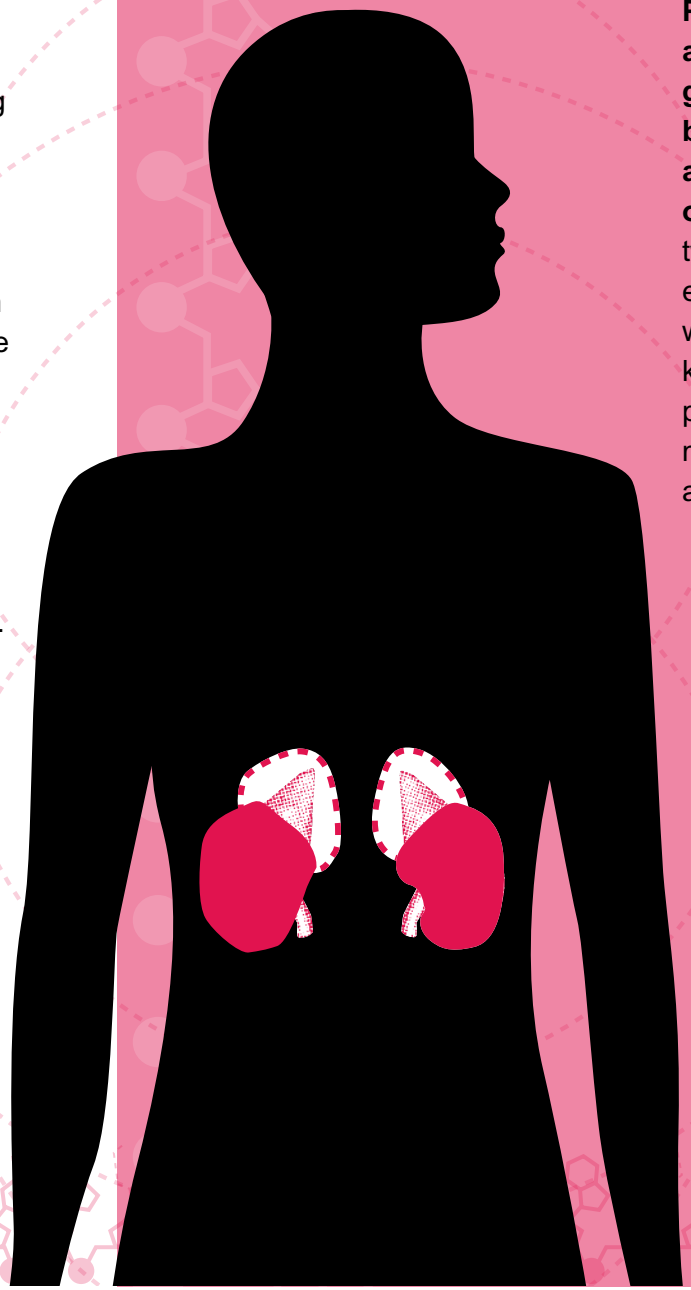
The Future for Metastatic MTC Treatment

Research into treatments for MTC is currently focused on human trials which are testing the effectiveness of a group of drugs called tyrosine kinase inhibitors (TKIs). These have been shown to work in the laboratory by stopping the uncontrolled cell division of MTC, or even making cells self-destruct. Early trials revealed that between 20 to 50% (from 1 in 5 up to 1 in 2) of patients saw a reduction in the size of their tumors (termed a response to therapy).

In April 2011, the FDA approved the use of the TKI vandetanib as a front line treatment for patients with metastatic MTC. Although complete responses are rare, tyrosine kinase inhibitors can potentially provide long-term

disease control. For many patients with progressive advanced MTC, participation in clinical trials may be recommended but you should seek further information regarding this from your specialist. For patients who are unable to enroll in a clinical trial, an oral tyrosine kinase inhibitor (taken by mouth) is likely to be of more benefit than chemotherapy or MIBG/Octreotide therapies.

There are also other drugs under trial which may directly interfere with the growth factors involved in maintaining tumor growth, but such agents are also only currently available in clinical trials.



Pheochromocytomas

Pheochromocytomas (pheos) are tumors of the adrenal glands that are almost always benign (non-cancerous) in MEN and occur in about 1 in 2 (50%) of MEN2a patients. The body's two adrenal glands are normally each about the size of a whole walnut, and sit just on top of the kidneys. Pheos occur in the inner part of the adrenal gland (the medulla) and produce excess amounts of a group of hormones called catecholamines (including adrenalin). Pheos may grow for many years without causing severe symptoms, but they can be activated by events such as childbirth or surgery.

Although when occurring in MEN patients they are almost always benign (non-cancerous), these tumors present a danger to the patient due to the sudden quantities of hormones they produce, which have been known to cause strokes, heart failure and premature death.

Unless a patient is already known to have MEN2a, pheos may be difficult to diagnose as the symptoms may be very varied and often occur episodically in sudden "attacks". Once a patient has a diagnosis of MEN2a, the monitoring program should identify a pheo before severe symptoms develop.

Potential symptoms of a pheo may include all or some of the following: sudden migraine-like headaches, palpitations, breathlessness, excessive sweating, high (or rarely low) blood pressure (sustained or episodic), trembling, pale appearance, lethargy, depression, anxiety, and nausea with or without vomiting.

Testing for Pheochromocytomas

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 the presence of a pheochromocytoma. Depending on the laboratory to which they are sent, collection bottles may or may not contain acid as a preservative, but they should not be refrigerated during the test.

Plasma Metanephrines

Increasingly, plasma (blood) metanephrine and normetanephrine tests are being used to identify the presence of pheochromocytomas. This test should be performed after the patient has been lying quietly for about 30 minutes to avoid a false positive result.

MRI / CT Scans You will be asked to lie still in a donut or tube-like machine for up to 1 hour, sometimes periodically being required to hold your breath and often partway through being given an injection of contrast to highlight specific areas of interest within the body.

Radioactive Isotope Scan (MIBG) Radioactive isotope scans that are usually only performed in Nuclear Medicine Departments in the larger 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 potassium iodide tablets, which you must take prior to 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.
Day 2: a further scan will be done to record which areas are still absorbing the radioactive material.
Once a pheochromocytoma is diagnosed, treatment with alpha-blockade and later on sometimes beta-blockade (see Treating Pheochromocytomas) is started in order to control the rise in blood pressure and thereby prevent strokes, heart attacks and death.

Treating Pheochromocytomas

Treatment for pheochromocytomas is the surgical removal of the affected adrenal gland. If only one gland is affected then only that gland will be removed at that time. This is because removal of both adrenal glands means that the patient will be reliant on lifelong replacement corticosteroid drugs. The preference is to delay this type of drug treatment for as long as possible due to the medication's own potential drawbacks (see Bilateral Adrenalectomy).

Alpha-Blockade

Considerable pre-surgical preparation called 'adrenoceptor blockade' is required in all cases as a functioning pheo makes the patient's blood pressure extremely unstable. Blood pressure is stabilized using blood pressure medications called Alpha- and sometimes Beta-blockers (eg. phenoxybenzamine and atenolol or propranolol respectively).

Alpha-blockade is started as an outpatient. Alpha-blockers may have several side-affects, including dizziness, a dry mouth and a stuffy nose. Phenoxybenzamine may also cause the inability for men to ejaculate during sex. A positive side affect is that this medication will stop the symptoms and high blood pressure (hypertension) "attacks" caused by the pheo. The overall aim is to induce 'orthostatic' hypotension in the patient (i.e. where the blood pressure falls on standing). When this is achieved beta-blockers may be added and the patient may rest at home for several days or even weeks prior to surgery. The symptoms lessen during this time, as the body absorbs more salt and water to fill up the blood vessels, although the patient may still feel tired and become easily breathless and dizzy. Alpha-blockade is not continued after the successful removal of the tumor.

SURGERY

Surgical technique depends upon the experience of the surgeon, the size of the tumor, and which gland(s) 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 tumors can be removed laparoscopically (i.e. “key-hole surgery”) through a series of small incisions in the abdomen or sometimes through a single incision through the back. Larger tumors may be removed through a larger single incision in the abdomen.

Hospital Stay

Pre-surgery for alpha-blockade up to 7 days to ensure complete alpha-blockade and fluid replacement.

Post-surgery Usually 2-4 days after laparoscopic surgery, and longer after open surgery.

Risks

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

If surgery is not possible or alpha-blockade is not well tolerated by the patient, new drugs called tyrosine hydroxylase inhibitors such as metyrosine (Demser) may be used either with or without alpha-blockers in order to control the release of hormones from the tumor and minimize symptoms.

Some patients with tumors occurring in both adrenal glands at the same time (bilateral) may be suitable for cortical sparing adrenalectomy, where the unaffected outer rim of the gland is preserved in order to avoid additional medication needs. However, this requires careful discussion with an experienced surgeon in terms of risk and benefit.

If both adrenal glands are removed, the patient will have to take life-long replacement steroid medication. The Addison’s Disease Self Help Group (ADSHG) supports patients with Addison’s Disease who similarly require lifelong steroid replacement medication. They are a fantastic source of information on managing life on steroids after bilateral adrenalectomy in MEN2 (see Useful Organizations).

The two main drugs that a patient must take after bilateral adrenalectomy are hydrocortisone and fludrocortisone. They replace the cortisol and another hormone called aldosterone, which are normally produced by the adrenal glands. The drugs take over in the maintenance of normal blood sugar levels, the promotion of recovery from injury and stress, and the regulation of the balance of mineral salts and water content of the body. Interestingly, the hormone adrenalin, which is also produced by the adrenal glands, does not need to be replaced.

MEDICATION

Hydrocortisone (a corticosteroid)
Hydrocortone, Efcortesol

Tablet for everyday use, usually taken in split doses (e.g. 10mg + 5mg + 5mg) early morning, lunchtime and in the evening although doses and times are variable. Doses should be doubled during times of illness. At times of extra stress (i.e. surgery, injury, severe vomiting and diarrhea) an injection of extra hydrocortisone (100ml IV or IM) is required immediately to eliminate the risk of hypovolaemic shock leading to loss of blood pressure and ultimately death. For this reason, all bilateral adrenalectomy patients should be issued with an emergency hydrocortisone injection kit and be shown how to give themselves an injection before they leave hospital.

Fludrocortisone (a corticosteroid)
Fludrocortone

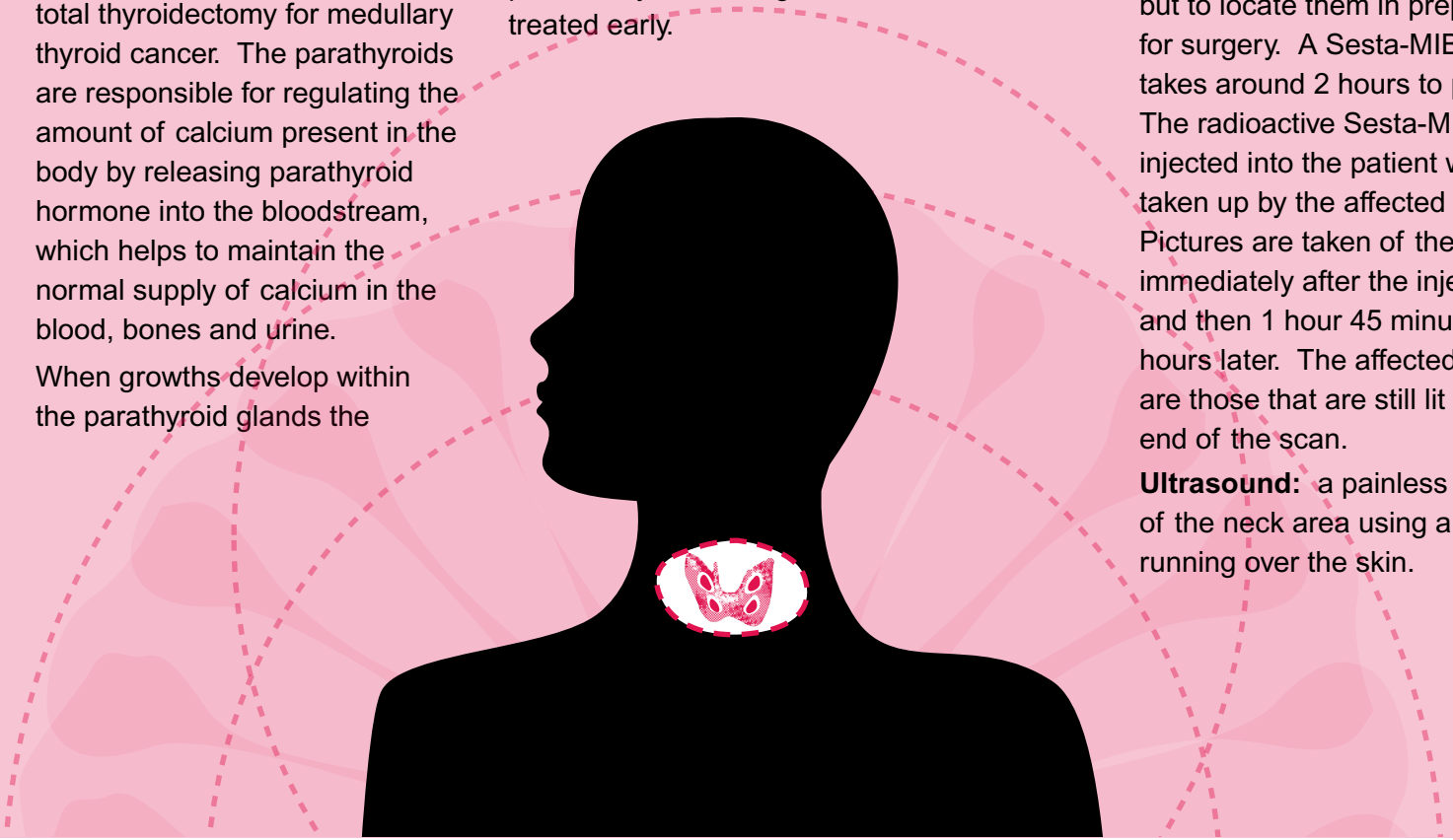
Tablet taken once a day, early in the morning. Doses may vary. Replacement doses of corticosteroids must be regularly and carefully determined by an experienced endocrinologist. Regular monitoring through blood tests is required.

Parathyroid Tumors

Growths in the parathyroid glands resulting in hyperparathyroidism (high level of parathyroid hormone or PTH) occur in less than 1 in 4 (25%) of MEN2a patients.

The parathyroid glands lie just next to or are sometimes contained within the thyroid in the neck and as such are often unavoidably removed during total thyroidectomy for medullary thyroid cancer. The parathyroids are responsible for regulating the amount of calcium present in the body by releasing parathyroid hormone into the bloodstream, which helps to maintain the normal supply of calcium in the blood, bones and urine.

When growths develop within the parathyroid glands the body is fooled into releasing calcium from the bones into the bloodstream and if left untreated can cause osteoporosis (brittle bones), so a bone density scan is sometimes recommended. Another problem associated with parathyroid growths is too much calcium in the urine, which may lead to kidney stones. Nowadays, however, most patients have very few of these symptoms, particularly when diagnosed and treated early.



Tests for Parathyroid Tumors

Blood Tests

Blood Calcium (serum calcium): a simple blood test

Parathyroid Hormone (PTH):

a simple blood test

Scans

Sesta-MIBI of neck area: These scans may be performed, not to diagnose affected parathyroids, but to locate them in preparation for surgery. A Sesta-MIBI scan takes around 2 hours to perform. The radioactive Sesta-MIBI is injected into the patient where it is taken up by the affected gland(s). Pictures are taken of the area immediately after the injection, and then 1 hour 45 minutes to 2 hours later. The affected glands are those that are still lit up at the end of the scan.

Ultrasound: a painless scan of the neck area using a probe running over the skin.

Treating Parathyroid Tumors

Treatment is by surgical removal of the affected gland(s). In MEN2a, all patients will have to undergo a total thyroidectomy (see treating MTC) at which time the parathyroids may unavoidably be removed as well. If all of the parathyroid glands are affected, a patient will have all of them removed (total parathyroidectomy).

At the time of a total parathyroidectomy, some surgeons choose to transplant part of a normal gland back into the body (usually into the neck or arm). This parathyroid transplant may help to control the body's calcium levels, and if in time this gland develops a tumor itself, it may be easier to remove.

In the event of total parathyroidectomy, the patient will need lifelong calcium replacement medication with a form of Vitamin D (see Medication). Decisions regarding these issues will be discussed with you when you see your surgeon.

SURGERY

The surgeon makes a 4-5cm incision at the base of the neck through which the affected gland(s) are removed. It is possible for the patient to be up and about, eating and drinking the same or next day.

Total parathyroidectomy: removal of all glands

Partial parathyroidectomy: removal of an individual gland

Hospital Stay

Usually a few days

Risks

The most common side effect of surgery is treatable episodes of low calcium (hypocalcemia), which causes tingling fingers, toes and lips and sometimes cramping, and requires immediate top-off replacement medication. There is also a possible but rare risk of nerve damage which might affect the voice.

MEDICATION

Vitamin D
(alphacalcidol, ergocalciferol, calcitriol)

Vitamin D supplements in a capsule form, which aid absorption of calcium from the patient's diet. Taken once a day, this is often the only life-long medication required after total parathyroidectomy.

Calcium Carbonate
(Calcichew, Adcal)

This is a chalk-like tablet that has to be chewed or sucked. This is often used as a temporary calcium top-off after surgery, but is not necessarily required life-long. Too large a dose or an indication that this supplement is no longer needed may become apparent if the patient begins to suffer from headaches, nausea and vomiting.

Magnesium supplement

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

Children and MEN2a

Deciding to have Children

There is a 1 in 2 (50%) chance that a child born to someone with MEN2a will also have MEN2a. If a child is known to carry the altered gene, testing and treatment programs may be established from the outset, and conditions addressed and managed before serious symptoms develop.

Pre-natal (during pregnancy) testing (PND) is available if the mutation has been identified within the family. A relatively new technology called Pre-implantation Genetic Diagnosis (PGD) is also now available to potential parents with MEN. This technique uses the IVF process but embryos are screened and only healthy ones re-implanted in the mother's womb.

If families are considering PND or PGD, they should seek a referral to genetic counselor before they become pregnant. PND or PGD is a personal choice, often depending upon the family's experience of the disease.

Pregnancy and MEN2

Before planning a pregnancy, mothers with known MEN2 should have screening for pheochromocytoma. An un-diagnosed pheo can present as a life-threatening crisis during delivery.
Existing medications may need to be adjusted during pregnancy – i.e. mothers who have had bilateral adrenalectomy and so are already on corticosteroid replacement will need extra steroid cover for birth, regular blood tests for levels, and more regular antenatal checks.

DNA Testing for Children

Children of a MEN parent with an identified MEN2a gene mutation can be offered a genetic test to determine if they also carry the gene. This may be offered soon after birth or at 4-5 years old. You should discuss these options with a genetic counselor.

Treatment and Testing Recommendations

Medullary Thyroid Cancer (MTC)

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

Pheochromocytomas *(uncommon before age 10)*

Plasma (blood) metanephrines / normetanephrines
24 hour urine collections (annual or 6 monthly);
young children in particular find the novelty of peeing into a bottle for a day rather exciting, which makes urine tests relatively easy to do.
For a child carrying a known MEN2a gene mutation, total thyroidectomy to prevent the development of medullary thyroid cancer is recommended from the age of 4, depending upon the precise mutation. A pheochromocytoma detected on screening will require removal. The geneticist will be able to advise you on this. In the hands of an experienced surgeon and team, many children cope much better with this surgery than some adults. Older children of recently diagnosed cases should be investigated right away due to the high incidence of MTC in MEN2.

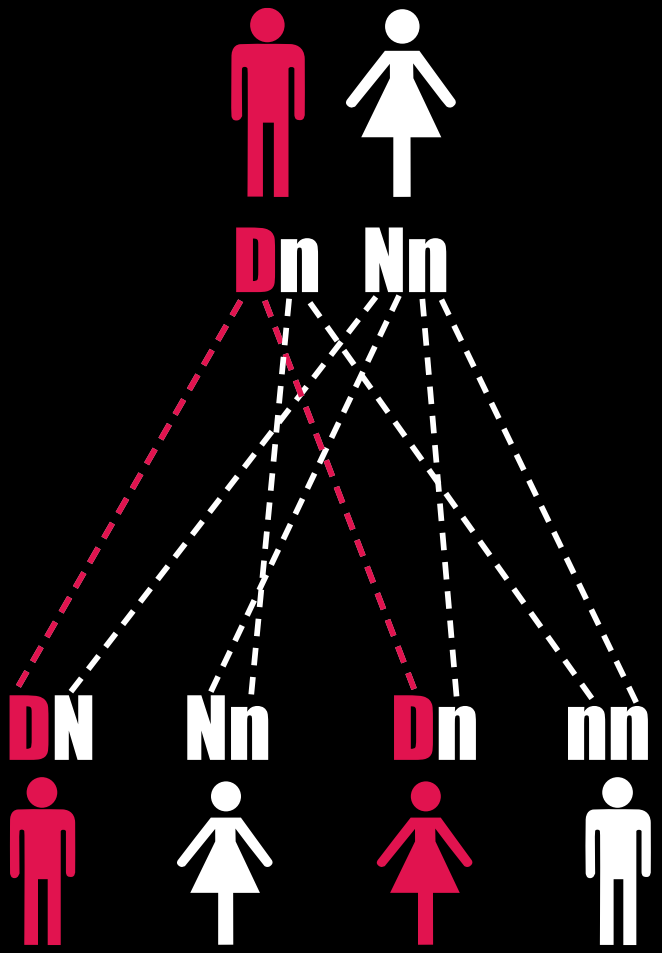
Blood Tests

There are many adults who find blood tests difficult, so no parent should be surprised if their child develops 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 a must to ensure as few repeated pokes 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 MEN2 genes. The name of the MEN2 gene is "RET" (or sometimes referred to as the RET proto-oncogene). In patients with MEN2, one of this pair has a genetic error. This can be inherited from either parent (inherited or familial) or can start in an individual for the first time (new mutation or sporadic).
When someone with MEN2 has children they can pass on either the normal gene or the faulty gene. This is entirely random, like tossing a coin. Each child therefore has a 1 in 2 or 50% chance of inheriting the faulty gene (colored red overleaf), and is therefore predisposed to the tumors of MEN2. This method of inheritance is called autosomal dominant inheritance.



Genetic Testing

It is possible in some families to have a genetic test to see whether someone has inherited the genetic error. However, the first step is to have a blood sample tested from someone with MEN2a in the family. With this initial test (mutation screen), the result may not be received for some weeks, and, indeed, the genetic error is not always found. If the genetic error is found, a blood test (predictive genetic testing) may then be offered to other members of the family. The results from predictive genetic testing are received normally within several weeks. There are a number of issues surrounding predictive genetic testing particularly in relation to children and as such, all patients should be seen and counseled by a consulting genetic specialist. If the genetic error cannot be found or if a blood sample from an affected person cannot be obtained then predictive genetic testing cannot be done. Having children tested is a very individual decision, however; if children of a known MEN2a parent are tested, those unaffected can rest assured that no further investigations are required. Those who have inherited the gene can be comforted by the fact that testing and treatment patterns will determine as early as possible when intervention is required. Thanks to this early detection by DNA test, complications from advanced medullary thyroid cancer, high blood pressure, stroke and heart failure due to adrenal tumors, and kidney stones as a result of parathyroid tumors, may be drastically reduced. Genetic testing and counselling is available by a referral through your GP or endocrinologist.

In the MEN2 gene, the mutation can occur in one of several different areas called codons. Research has determined that mutations of different codons can relatively accurately predict to what extent and at what age the MEN2 conditions will manifest themselves. Ultimately, this knowledge enables doctors to tailor testing and treatment programs to the patient's needs accordingly.

Useful Information

MEDICALERT®: AMEND recommends that anyone taking lifelong medications obtain and wear a MedicAlert® identification emblem. The emblem contains summarized 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. Contact AMEND for an order form and brochure or join online at www.medicalert.org

FEDERAL REGULATIONS: In 1996, the Health Insurance and Portability Act (HIPPA) and in 2008 the Genetic Information Non-discrimination Act (GINA) made it illegal for employers and insurance companies to discriminate against anyone based on their medical genetics.

Useful Organizations

ThyCa – Thyroid Cancer Survivors' Association, Inc.
www.thyca.org

Addison's Disease Self Help Group (ADSHG)
www.adshg.org.uk

The Pheo-Para-Alliance
917-318-3560
www.pheo-para-alliance.org

The Pheo Para Troopers
www.pheoparatroopers.org

The American Cancer Society
1-800-227-2345
www.cancer.org

AMEND Medical Advisory Team

USA: Ms Thereasa Rich, Dr Constantine Stratakis, Dr Samuel Wells, Dr Electron Kebebew
UK: Professor Rajesh Thakker, Dr Caroline Brain, Professor John Connell, Professor Ashley Grossman, Mr Barney Harrison, Dr Fiona Lalloo, Mr Tom Lennard, Mr David Scott-Coombes
Australia: Professor Bruce Robinson

Afterword

This book has been written for MEN patients by MEN patients with the help of a medical advisory panel. 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 MEN2a. It is not for use in self-diagnosis. It contains detailed information on tests, surgery and potential symptoms associated with MEN2a. 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 doctor. 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.

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