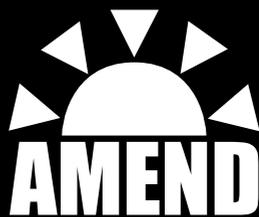


FIPA

Patient Information
Familial Isolated Pituitary Adenoma



Association for Multiple Endocrine Neoplasia Disorders

Registered Charity No. 1099796

FIPA SUPPORT
Tel: 01892 516076
Email: info@amend.org.uk
Website: www.amend.org.uk
Membership is FREE

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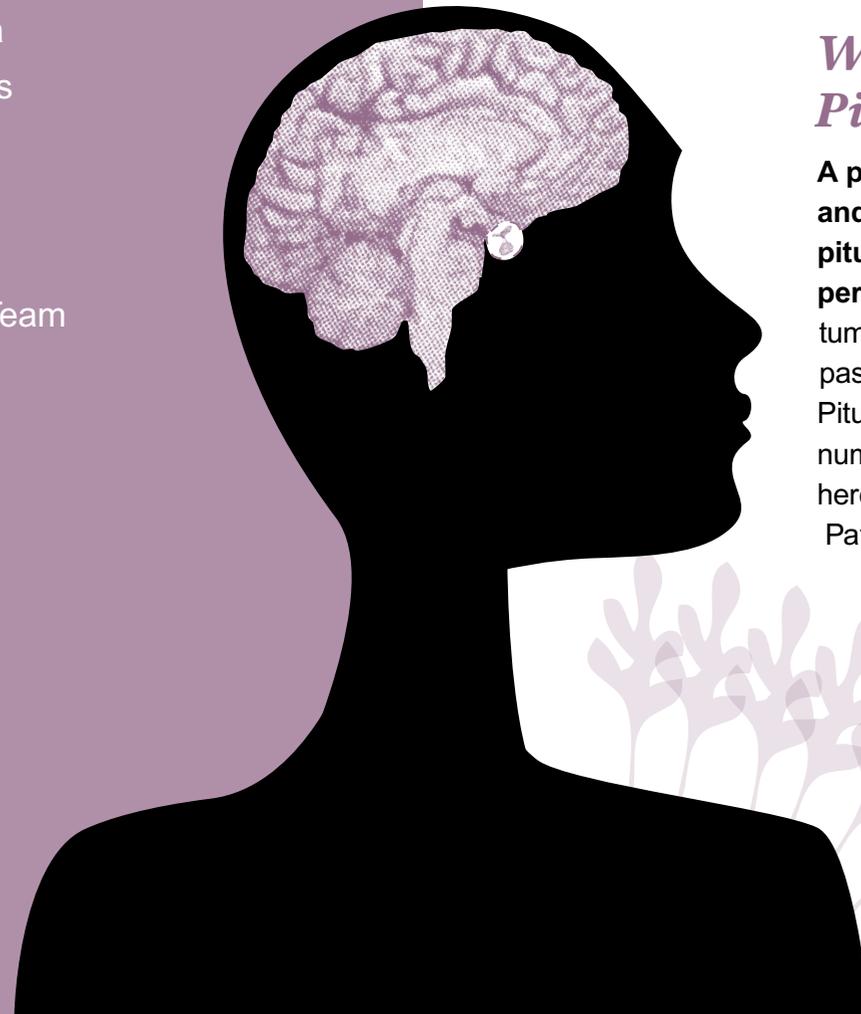
What is the pituitary gland?

The pituitary gland sits near the base of the brain behind the nose and under part of the eye nerves in a bony hollow called the sella turcica, and is roughly the size and shape of a bean. It is the master gland of the body's endocrine system, which is made up of a number of glands that release hormones (the body's chemical messengers) into the bloodstream. Pituitary hormones are important for growth and development, metabolism (turning food into energy) and reproduction.

What is Familial Isolated Pituitary Adenoma?

A pituitary adenoma is usually a slow-growing and benign (non-cancerous) tumour of the pituitary gland which occurs in about 1 person in every 1000. Only 5% (1 in 20) of these tumours are hereditary, meaning that they may be passed down through families. Familial Isolated Pituitary Adenoma (FIPA) is one of a small number of rare genetic disorders that can cause hereditary pituitary tumours.

Patients diagnosed with FIPA are said to have



'isolated' pituitary adenomas because, unlike in some other hereditary endocrine disorders, they do not have an increased risk of developing tumours in any other glands in the body. Some pituitary gland tumours may produce abnormally increased amounts of hormones or can lead to lack of pituitary hormones, both of which in turn can cause a variety of symptoms. These symptoms are discussed later on in this booklet.

Although pituitary adenomas are usually benign, they can have implications for the health of a patient by either producing excessive amounts of pituitary hormones or lack of one or several pituitary hormones. If large enough, they can also put pressure on important structures near the pituitary gland such as the eye nerves, causing headaches and problems with vision.

It is very important to stress that pituitary tumours are not 'tumours of the brain'.

How is FIPA diagnosed?

In order to rule out other disorders that can cause hereditary pituitary adenomas, a diagnosis of FIPA is generally made when:

1. The patient has a family history of pituitary adenomas, AND
2. The patient and their family do not have any other affected glands.

If the patient or their family members have had tumours in other glands (especially other endocrine glands, such as the parathyroids, pancreas, adrenals, thyroid and testes), testing for other diseases such as Multiple Endocrine Neoplasia type 1, Carney Complex or some other rare conditions must be considered.

Families with FIPA

AIP mutation positive families

In about 20% of families with FIPA, a change can be identified in the gene called aryl hydrocarbon receptor interacting protein (AIP).

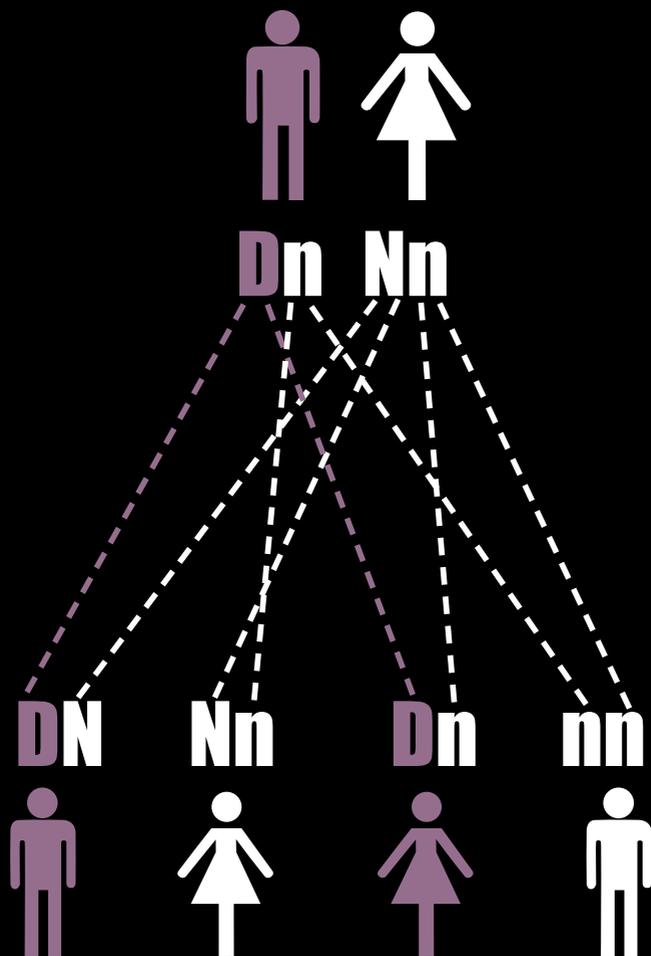
Patients with a gene change (sometimes also called a gene 'fault' or 'mutation') in the AIP gene have a predisposition to pituitary adenomas and currently it is thought that about 30% are likely to develop a pituitary adenoma in their lifetime, most occurring by the age of 30. In about half of these cases the disease develops in childhood or adolescence. Both males and females can suffer from the disease. The most common adenoma type is a growth hormone secreting adenoma causing acromegaly or, if started before the completion of puberty, excessive growth or gigantism. The second most common tumour type is a prolactinoma. Patients with an AIP gene may have adenomas which grow rapidly and respond less well to medication such as

somatostatin analogue treatment. Within the same family both types of tumours, or sometimes mixed tumours can be seen.

It is important to note, that sometimes individuals with a pituitary tumour, especially those producing growth hormone causing gigantism or acromegaly may have no apparent family history of pituitary adenomas. The family of this patient needs to be screened as other AIP mutation carriers maybe detected in such families.

AIP mutation negative families

In the remaining 80% (8 in 10) of families with FIPA, the gene change that causes the disorder is currently unknown. In these cases, the disorder most often starts in adulthood. Males and females are equally affected. The two most common tumour types are growth hormone and prolactin secreting adenomas, followed by non-functioning adenomas. Within a particular family the types of adenomas can be the same or different.



In this case, the father's altered gene (D) was inherited by 2 of his 4 children. Not all subjects who inherit the gene will develop disease and currently it cannot be predicted which carrier subject (marked with dark silhouette here) will develop the disease in the future.

Pattern of inheritance

We all have two copies of each gene, receiving one copy from our mother and the other from our father. Patients with FIPA have one normal and one abnormal copy of the AIP gene. There is a 50% (1 in 2) risk that any child, whether male or female, will inherit the faulty gene from an affected parent. There is currently no way of knowing if this child will be more or less severely affected than the parent. Not everyone who inherits the genetic change will necessarily go on to develop a pituitary tumour (the disease has 'incomplete penetrance'). Current research suggests that about 1 in 3 of those who inherit the AIP gene abnormality actually go on to develop a pituitary adenoma. In families with FIPA but no AIP mutation an even lower percentage of patients develop pituitary adenoma.

Genetic Testing

In families with a confirmed AIP gene change, all first degree relatives (parents, siblings, children) with a chance of inheriting the gene should be offered genetic counselling and screening by a DNA test (a simple blood test). The relatives who carry an abnormal copy of the gene should also be seen by an endocrinologist, as assessment of growth pattern,

some further blood tests and an MRI scan can help to determine if these carriers have a pituitary adenoma. If the results of these tests are normal, the patient should be reviewed once per year. Children may be offered a genetic test as the disease can manifest in childhood with the earliest reported patient diagnosed with a pituitary tumour at the age of 6. Based on current data it is suggested that screening starts around 4 years of age.

In patients with FIPA but without an AIP mutation, relatives do not need to be tested for the AIP gene. However, a sample of their DNA may be useful in studies that are trying to find the gene responsible for FIPA in these families. Any relatives that have a chance of inheriting the unknown gene should consider seeing an endocrinologist for blood tests and an MRI scan, though the review of children can usually be delayed until they are 16 years old. Currently, there has not been enough data collected to prove or disprove the risks and/or benefits of screening families without an AIP mutation.

Genetic testing and counselling is available for FIPA. A referral for genetic testing is usually made through your family doctor or specialist. Further information and contacts can be found on www.fipapatient.org.

Types of Pituitary Adenoma

Pituitary adenomas can be classified by their size or by the type of hormones they may produce. Microadenomas are less than 10mm in diameter (10mm is the maximal size of a normal pituitary gland), and

macroadenomas are more than 10mm. Please see the table below for descriptions of the different types of adenoma which can occur in FIPA and the hormones and symptoms they may produce.

TYPE OF TUMOUR	ACTION OF TUMOUR	POSSIBLE SYMPTOMS	OTHER INFORMATION
Somatotrophinoma	Overproduces growth hormone (GH or somatotrophin) causing acromegaly with or without gigantism	Causes a condition known as 'acromegaly', which is characterised by changes in appearance such as a large jaw, increasing size of hands and feet, sweating, headaches and joint pains. If it starts in children or adolescents it can cause extreme growth (gigantism). Visual disturbances if the tumour is large. Large tumours may also put pressure on the rest of the pituitary gland and stop it working.	Most common pituitary tumour in FIPA
Prolactinoma	Overproduces the hormone prolactin	Women: lack of periods, lactation (breast milk production) without pregnancy, poor libido, and may lead to infertility. Men: low testosterone, causing fatigue, erectile failure and infertility. Headaches and visual disturbances if the tumour is large. Large tumours may also put pressure on the rest of the pituitary gland and stop it working.	A common type of adenoma in FIPA
Non-functioning	Usually no overproduction of a hormone but often lack of one or several pituitary hormones	Headaches and visual disturbances due to local pressure. Large tumours may also put pressure on the rest of the pituitary gland and stop it working.	Moderately common type in FIPA
Corticotrophinoma	Overproduces the hormone adrenocorticotrophin (ACTH) causing Cushing's disease	Causes a condition known as Cushing's disease by producing the over-production of cortisol in the adrenal glands, which can cause weight gain, reddening of the face and neck, excess growth of body and facial hair, change of body shape, and raised blood pressure. Headaches and visual disturbances if the tumour is large. Large tumours may also put pressure on the rest of the pituitary gland and stop it working.	Rarely seen in FIPA
TSH-producing	Overproduces thyroid stimulating hormone (TSH) causing hyperthyroidism	Causes the thyroid to become overactive, resulting in fast or irregular heartbeat, fatigue, difficulty sleeping, weight loss, frequent bowel movements, and irritability. Headaches and visual disturbances if the tumour is large. Large tumours may also put pressure on the rest of the pituitary gland and stop it working.	These are very rare tumours and are extremely rare in FIPA

Testing for Pituitary Tumours

Diagnosis of pituitary adenomas involves clinical assessment, testing the field of vision, measuring hormone levels and a pituitary MRI scan (or sometimes a CT scan).

Initial blood tests to measure pituitary function are performed for serum prolactin, thyroid function, LH and FSH, testosterone, oestradiol, growth hormone, IGF-I and morning cortisol.

Additional tests may be necessary depending on the type of adenoma including:

SOMATOTROPHINOMAS (GROWTH HORMONE-SECRETING ADENOMAS)

Oral glucose tolerance test:

taking a drink of glucose followed by simple blood tests over 2-3 hours.

PROLACTINOMAS (PROLACTIN-SECRETING ADENOMAS)

It is important to rule out other possible causes of high prolactin levels such as an underactive thyroid or the influence of certain medications you may be taking.

CORTICOTROPHINOMAS (ACTH-SECRETING ADENOMAS)

Dexamethasone suppression

blood test (overnight or 2 days):

take a steroid tablet or tablets followed by simple blood and/or urine tests.

24-hour urine collections: simple collections of urine over the course of a day to measure cortisol levels. Circadian rhythm studies: look at how levels of the hormone cortisol vary in the blood over the day and night.

Salivary cortisol testing: used in some centres.

Additional scans and tests might be necessary to diagnose patients adequately.

Treating Pituitary Tumours

Treatment may be in the form of medicine or surgery depending upon the type of tumour, its size and response to drug therapy. Sometimes, small tumours can be treated with tablets or injections, although surgery is often needed. In other cases (rarely) radiotherapy may be needed. The aim of all treatments for pituitary tumours is to stop or reduce the abnormal secretion of hormones and the symptoms they cause and reduce the tumour size.

Somatotrophinomas

Treatment will depend upon several factors, but surgical removal (transsphenoidal surgery) of the tumour is the most common treatment. It is possible to treat the tumour with medication called a somatostatin analogue in the form of an injection (e.g. octreotide, brand name Sandostatin, and lanreotide, brand name Somatuline) to reduce the production of growth hormone. Sometimes, these do not work, in which case pegvisomant (brand name Somavert), a growth

hormone receptor antagonist, may be successful instead. Sometimes radiotherapy may also be used in order to reduce adenoma growth and growth hormone levels.

These treatments aim to stop or reduce adenoma growth and the secretion by the tumour of the abnormally high levels of growth hormone. With treatment many symptoms improve dramatically, although some of the changes cannot be reversed. The Pituitary Foundation is a good source of further information on acromegaly or any of the pituitary adenomas (see Useful Organisations).

Prolactinomas

The most common treatment is with medication called a dopamine agonist in the form of a tablet (e.g. bromocriptine, brand name Parlodel; cabergoline, brand name Dostinex; or quinagolide, brand name Norprolac) to reduce the production of prolactin and reduce tumour volume. Doses vary according to the size of the tumour and the amount of prolactin it produces. In some cases, surgery (transsphenoidal surgery), radiotherapy, or both may be needed.

ACTH-Producing

The most common treatment is surgical removal (transsphenoidal surgery) of the tumour from the pituitary gland, followed by radiotherapy if this is not completely successful. Medical treatment with ketoconazole (brand name Nizoral) or metyrapone (brand name Metopirone) can be used if necessary. Sometimes, radiotherapy is needed and occasionally the removal of both adrenal glands is recommended.

TSH-Producing

The most common treatment is surgical removal (transsphenoidal surgery) of the tumour. If necessary radiotherapy or injections of a somatostatin analogue such as octreotide (brand name Sandostatin) or lanreotide (brand name Somatuline) can be used.

Non-functioning adenomas

Usually treated with surgery, but sometimes careful observation could be considered. Radiotherapy can be used to reduce tumour growth.

SURGERY

Transsphenoidal Resection:

this is the most common surgical method for the removal of a pituitary tumour. It is a relatively small operation carried out under general anaesthetic. The surgeon makes a small cut front of the upper teeth behind the upper lip, or inside the nose. This way the surgeon can reach the pituitary gland without having to operate on the main part of the head. Patients are up and eating normally by the following day.

Hospital stay

approximately 2-5 days.

Recovery time

recovery time from surgery is approximately 1-4 weeks, though improvement of symptoms may take several weeks or months.

Risks

diabetes insipidus (an inability to concentrate the urine; not diabetes mellitus which is a disorder of the glucose household) can occasionally occur postoperatively. Symptoms include increased thirst and the need to pass urine more often than normal. If the condition becomes permanent, it

can be treated using a drug called desmopressin. In some instances, after treatment, some patients may require long-term medication to replace other hormones (such as sex hormones, thyroid hormone, or corticosteroids), or may require additional treatment in the form of radiotherapy, or a somatostatin analogue (e.g. octreotide or lanreotide).

RADIOTHERAPY

This may be used to reduce the size, growth potential and activity of a pituitary tumour that has not been treated adequately by surgery or medical therapy. Alternatively, it may be used after surgery to decrease the chance of the tumour regrowing. Radiotherapy can be either a single setting treatment (radiosurgery) or repeated treatment usually given for 5 days a week over 5 weeks, giving 25 treatments altogether. Careful planning is necessary for the treatment. This is quite painless, and each treatment is usually over in half an hour and most patients can carry on with their normal life throughout, but may find they tire easily.

Useful Information

Free Prescriptions: in the UK, you are entitled to free prescriptions for all your medicines if you need to take lifelong insulin for diabetes mellitus or suffer from a pituitary disorder that requires one or more of the following drugs:

- Hydrocortisone
- Thyroxine
- Desmopressin
- Testosterone
- Oestrogen replacement
- Growth hormone

You will need to obtain a Prescription Charge Exemption Certificate by filling in a form (FP92A) which is available from your doctor, hospital, or pharmacist. Your doctor will sign the form and send it on, and you will later receive your exemption certificate which you must show to your pharmacist when collecting medicines.

Medicalert®: AMEND recommends that anyone taking lifelong medicines 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. Contact AMEND for an order form and brochure or join online at www.medicalert.org.uk. Other medical identification products are available.

Useful Organisations

AMEND
International patient group providing free information and support to anyone affected by multiple endocrine neoplasia disorders and associated endocrine tumours as well as running a Research Registry and Fund
Tel: +44 (0)1892 516076
Email: info@amend.org.uk
www.amend.org.uk

FIPA Patients
Based at Bart's and The London Medical School in London, please contact this registered charity if you are interested in donating specifically to FIPA research
Tel: +44 (0)20 7618 1720
Email: info@fipapatient.org
www.fipapatient.org

The Pituitary Foundation
UK charity providing information and support to people living with pituitary disorders, including patients, their relatives, friends and carers
Tel: +44 (0)870 774 3355
Email: helpline@pituitary.org.uk
www.pituitary.org.uk

AMEND 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 John Connell**, Dean of Medicine, University of Dundee;
 - **Professor Ashley Grossman**, University of Oxford, Oxford Centre for Diabetes, Endocrinology & Metabolism;
 - **Mr Barney Harrison**, Endocrine Surgery, Royal Hallamshire Hospital, Sheffield
 - **Dr Fiona Laloo**, Consultant Clinical Geneticist, St Mary's Hospital, Manchester;
 - **Mr Tom Lennard**, Professor of Surgery, University of Newcastle upon Tyne Medical School
 - **Mr David Scott-Coombes**, Department of Surgery, University Hospital of Wales, Cardiff;
- Special Medical Advisor**
- **Professor Márta Korbonits**, Department of Endocrinology, Bart's and The London Medical School, London

AMEND Editorial Team

- **Mr Callum Hackett**, Assistant MEN1 Representative (Author)
- **Mrs Jo Grey**, CEO (Editor)

Afterword

This book has been written for patients by 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 FIPA. It is not for use in self-diagnosis. It contains detailed information on tests, surgery and potential symptoms associated with FIPA. 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 have 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.

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