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# Medical Examiners’ – Medical Manual

## Part 3 - Clinical Aviation Medicine

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### 3.4 Metabolism, Nutritional and Endocrine system

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<b>ICAO Annex 1:</b>	Chapter 6
<b>ICAO Medical Manual:</b>	Chapter 4
<b>CAR Part 67:</b>	67.103 b & f, 67.105 b & f, 67.107 b & f
<b>GD:</b>	Examination Procedures, Section 1 – Schedule 8, Section 2, Schedule 6
<b>Forms:</b>	Special Report – Diabetes, MOT 1440

## 3.4.1 Pituitary Gland Disorders

### 3.4.1.1 Considerations

The *anterior pituitary gland* produces:

**ACTH:** Over production of ACTH, usually the result of a basophil micro-adenoma, can result in Cushing's disease because of adrenal cortex overstimulation.

The symptoms and signs may include central obesity, hypertension, plethora, poor wound healing, striae, easy bruising, diabetes, osteoporosis and muscle atrophy.

The treatment is by trans-sphenoidal excision of the adenoma.

**Prolactin:** Over production of Prolactin is usually the result of a micro-adenoma (size less than 1cm) or macro-adenoma (size 1 cm or more). Large adenoma may affect the anatomy of the Sella Turcica and compress the optic chiasma.

The symptoms and signs include galactorrhoea, menstrual cycle disturbance, visual fields defects, headaches and well as low testosterone levels in males.

Prolactin levels are increased. Brain MRI and CT demonstrate the enlarged pituitary gland and its surroundings. Treatment is by Dopamine antagonists, e.g. Cabergoline, which should be taken long term. Rarely surgery is required to decompress the Sella Turcica.

It is important to note that Cabergoline and similar medication may affect behaviour in a manner that is of concern to flight safety.

**Growth hormone:** Overproduction of growth hormone results in acromegaly. The symptoms and signs include increased bone size that is most visible on hands, feet and face. Soft tissues enlargement also occurs with thicken skin, lips, tongue and ears enlargement.

The key biochemistry tests include insulin like growth factor 1 (IgF-1) level determination which may show an elevation, and GH determination following oral glucose loading which normally suppresses GH significantly but not in acromegaly. MRI will generally show the pituitary tumour.

If no tumour is seen a GHRH level may reveal the existence of a non-pituitary GHRH producing tumour somewhere else in the body. Treatment is most often surgical but also by irradiation and medication.

The **posterior pituitary gland** produces:

**Antidiuretic Hormone (Vasopressin - ADH):** Underproduction results in polyuria (Diabetes Insipidus). Fluid deprivation secures the diagnosis if the urine remains diluted despite a raise in osmolality over 295 mOsm/kg. Treatment is by titrated Desmopressin, usually administered as a nasal spray.

### 3.4.1.2 Information to be provided

On the first occasion that an applicant presents with a pituitary gland disorders:

- All specialists and investigations reports relating to the condition;
- A recent endocrinologist report, to include comments on risk of deterioration;
- Associated investigations results;
- Visual fields testing in case of pituitary macroadenoma.

On subsequent occasions that an applicant present with a history of pituitary gland disorder:

- Copy of all interim specialists and investigations reports relating to the condition;
- An endocrinologist report and associated investigations reports, as necessary. A report dated within the past 6 months will often be sufficient.

### 3.4.1.3 Disposition

- An applicant who first present with a history of pituitary gland disorder should be considered as having a condition that is of aeromedical significance.
- An applicant with a history of **ACTH** over production (Cushing's syndrome) should be considered as having a condition that is of aeromedical significance.
- An applicant with a history of overproduction of **Growth Hormone** (GH - Acromegaly) should be considered as having a condition that is of aeromedical significance.
- An applicant with a history of over production of **Prolactin** may be assessed as having a condition that is not of aeromedical significance if:
  - A previous assessment under the flexibility process has concluded favourably;
  - The adenoma is classified as micro-adenoma (< 1cm);
  - The adenoma did not result in any functional compromise such as visual field defect, other hormonal compromise and / or compression of surrounding structures;
  - The applicant is undergoing regular review by an endocrinologist and the most recent report is satisfactory;
  - The applicant is asymptomatic and complies with treatment;
  - Medication is well tolerated.

- An applicant with inappropriate secretion of **ADH** (Diabetes Insipidus) may be assessed as having a condition that is not of aeromedical significance if:
  - A previous assessment under the flexibility process has concluded favourably.
  - The applicant is undergoing regular review by an endocrinologist and a recent satisfactory report is available;
  - The applicant is asymptomatic and complies with the treatment;
  - The treatment is well tolerated;
  - The applicant's certificate is endorsed with the requirement not to exercise the licence privileges if medication has been omitted on the day.

## 3.4.2 Thyroid Gland Disorders

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### 3.4.2.1 Considerations

Thyroid gland disorders that are of aeromedical concern consist of hypothyroidism, hyperthyroidism (thyrotoxicosis), thyroid cancer and occasionally large goitres with obstructive symptoms. Cancer will be discussed in the oncology chapter.

**Hypothyroidism** may be result of impaired production of TSH in the context of pituitary disease. Thyroiditis, surgical ablation and radio-iodine ablation are far more common causes. In these latter situations the TSH is always elevated before the T4 is reduced. In pituitary disease the TSH will not be significantly elevated and T4 determination is necessary.

Symptoms may include fatigue, weight gain, dry skin and bradycardia. Constipation is not uncommon as is periorbital puffiness. Myxoedema, heart failure and rarely coma may occur.

Treatment is via lifelong thyroid replacement, titrated until clinical and biological stability are achieved, as demonstrated by normalisation of the TSH (and T4 in the case of pituitary disease). The usual daily dose of Thyroxine is around 100 to 150 mcg. The rare omission of medication should not result in any acute impairment. This makes this treatment acceptable in the aviation context. Lifelong, twice yearly, TSH biochemical surveillance is required, to include T4 in the case of pituitary disease, once stability is achieved.

**Hyperthyroidism** is often due to autoimmune Grave's disease or a toxic nodular goitre, or occasionally medication, including iodine.

In Grave's disease the antibodies attach to the TSH receptors causing the release of thyroid hormone from the gland. Toxic nodular goitre and toxic adenoma also result in excessive thyroid endocrine activity. TSH will be decreased and T4 / freeT4 and T3 / freeT3 are increased.

Symptoms may include Insomnia, tremor, weight loss, nervousness, lethargy and palpitations including atrial fibrillation. Eye changes including redness, lid retraction and proptosis may result in heterophoria or diplopia in severe cases. Beta-blockers (Propranolol or Metoprolol) are effective in giving rapid relief of palpitations and tremor. Carbimazole or Propyl Thiouracil control thyroid hormone overproduction but can take 2-3 weeks to respond. Therapy for 12 months or so is often required. There is at least a 50% relapse once medication is stopped.

More definitive therapy includes total thyroidectomy or radioiodine ablation, both resulting in hypothyroidism which is permanent after surgery and often permanent after radio iodine. This generally requires lifelong surveillance and treatment.

**Goitre:** The presence of goitre not causing functional impairment, such as obstruction of airways or swallowing is of little aeromedical significance provided that thyroid endocrine function is not impaired and malignancy has been excluded.

### 3.4.2.2 Information to be provided

On the first occasion that an applicant presents with a history of thyroid disease;

- GP notes for the past 12 months;
- All related specialist reports;
- All related investigations reports;
- All related biochemistry results, to include a recent thyroid function test result.

On subsequent occasions that an applicant presents with a history of thyroid disease:

- Interim specialist reports;
- Interim investigations reports;
- Interim GP notes in the case of thyrotoxicosis;
- Recent thyroid function test result.

### 3.4.2.3 Disposition

- An applicant who presents with a history of **hyperthyroidism** should be considered as having a condition that is of aeromedical significance.
- An applicant who presents with a history of **hypothyroidism that is not treated** should be considered as having a condition that is of aeromedical significance.

An applicant who presents with **hypothyroidism** treated may be considered as having a condition that is not of aeromedical significance if:

- There is no history of thyroid cancer, unless specialist opinion considers the cancer to be cured;
  - The hypothyroidism is not caused by hypothalamic or pituitary disease;
  - The hypothyroidism is the result of resolved thyroiditis, or
  - The hypothyroidism is the result of thyroidectomy; or
  - The hypothyroidism is the result of radioiodine ablation;
  - If thyrotoxicosis has occurred the condition no longer requires suppressive medication and is considered to be cured and unlikely to relapse;
  - If thyrotoxicosis has occurred, there has been no ophthalmic symptoms, unless a special eye report indicates absence of aeromedically significant heterophoria;
  - The TSH is within normal limits:
  - The applicant is asymptomatic and compliant with medication;
  - The certificate is endorsed with the requirement for surveillance every six months, TSH determination. (This is to include T4 in the case of pituitary disease).

### 3.4.3 Adrenal Gland Disorder – Addison Disease

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#### 3.4.3.1 Considerations

The principal condition of concern is failure of the adrenal gland cortex. The cause is most often autoimmune; tuberculosis or other infectious processes are less likely.

Symptoms generally consist in progressive weakness, weight loss, anorexia, vomiting. Occasionally decompensation can be abrupt (Addisonian Crisis) in the context of an acute illness. In this case, shock may be present (usually without hypoxaemia), hypotension and possibly death. Hyperkalaemia and hyponatremia may occur together, with possible related ECG changes, but are not always present. Addison disease may be accompanied by hyperpigmentation.

The diagnosis of primary adrenal failure is confirmed by low plasma cortisol (usually less than 100 nanomol/L, blood taken around 8 - 9 am), as well as lack of response to ACTH (Synacten test) with elevated ACTH level. CT imaging may be necessary and sometimes confirms an atrophic adrenal gland.

#### 3.4.3.2 Information to be provided

- All specialist reports relating to the condition;
- A recent endocrinologist report;
- GP notes for the past 12 months;
- Renal function and electrolytes, plasma Renin and ACTH;
- BP taken at least twice lying and standing;
- Evidence of the applicant understanding their conditions;
- Action plan in case of illness.

#### 3.4.3.3 Disposition

- An applicant with a history of Addison disease should be considered as having a condition that is of aeromedical significance.

A **Class 1** applicant with well controlled and stable disease may possibly be issued a medical certificate under the flexibility process. A “Not Valid for Single Pilot Air Operations Carrying Passengers” restriction and other restrictions are likely to apply.

A **Class 2** applicant with well controlled and stable disease may possibly be issued a medical certificate under the flexibility process. Some restrictions may apply.

**Note:** Certificate holders on Prednisone or Hydrocortisone long term need ‘sick day’ rules. They need to understand that in the context of illness, particularly diarrhoea and vomiting where absorption of steroids is not reliable, they are in danger of adrenal crisis. They need supplementary oral or I.V. steroid cover if unwell. A medical alert bracelet is warranted. Licences holders must readily remove themselves from duty, even if only slightly unwell.

## 3.4.4 Diabetes Type II

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### 3.4.4.1 Considerations

The increasing prevalence of diabetes type II is raising alarm bells from a population health perspective. Unfortunately pilots and Air Traffic Controllers are not immune to this trend. Immobility, excessive food intake, soft drinks and alcohol consumption in more than small amounts contribute to the development of obesity.

In type II diabetes endogenous Insulin is present, frequently with hyperinsulinaemia, but also frequently with a degree of insulin deficiency. There is insulin resistance.

Diabetes type II is an insidious disease that can progress with few or no symptoms, leading eventually to microangiopathy and serious complications. Regular General Examination for the purpose of certification and the associated blood investigations required under the General Directions should identify applicants with diabetes early, well before safety relevant complications arise.

The aviation safety risks relate to:

- Intrinsic risks from the diabetes mellitus. These are possible visual and cognitive symptoms, including fatigue whereby poor glycaemic control results in severe hyperglycaemia; and
- Long term intrinsic risks from diabetes, with end organ damage to the heart, kidneys, eyes and nerves; and
- Iatrogenic risks due to medication. The main concern being the risk of hypoglycaemia resulting in cognitive impairment, and possibly coma.

**The diagnosis of diabetes** in NZ is made according to the [New Zealand Society for the Study of Diabetes \(NZSSD\)](#).

The NZSSD guidelines are reproduced here:

- HbA1c  $\leq$  40 mmol/mol and, if measured, fasting glucose  $\leq$  6 mmol/L is normal
- In symptomatic individuals an HbA1c  $\geq$  50 mmol/mol and, if measured, a fasting blood glucose  $\geq$  7.0 mmol/l or a random glucose  $\geq$  11.1 mmol/l, is sufficient to establish the diagnosis of diabetes. Diabetes confirmed.
- In asymptomatic individuals the same criteria apply but, to confirm the diagnosis of diabetes, a confirmatory test (preferably HbA1c) is needed on a separate occasion. Two results above the diagnostic cutoffs, on separate occasions are required for the diagnosis of diabetes.
- Those with an HbA1c of 41-49 mmol/mol and, if measured, a fasting glucose concentration of 6.1 - 6.9 mmol/l, are categorized as 'pre-diabetes' or impaired fasting glucose (also called 'dysglycaemia' or 'borderline diabetes'). Patients with values in this range should be advised on diet and lifestyle modification (and from the age of 35 have a full cardiovascular risk assessment and appropriate management). HbA1c measurement should be repeated after 6-12 months.



Meeting these diagnostic criteria should result in a clear diagnosis of diabetes. A full cardiovascular risk assessment and appropriate CV and glycaemic management should follow. Additionally entry into microvascular screening programmes (retinal photography, microalbuminuria, eGFR, foot checks) should be commenced.

**The American Diabetes Association (ADA)** also recommended abolishing the use of the oral glucose tolerance test. **The WHO** has so far retained the glucose tolerance test.

#### 3.4.4.2 Information to be provided

- A recent HbA1c determination result;
- Recent pre and post prandial capillary glucose determination results through the day (5 results) on three different days, if the applicant is treated with a Sulphonylurea, or other oral agents capable of inducing hypoglycaemia;
- Download and statistical analysis of glucometer data, if treated with Insulin or if using such a device;
- Renal function, electrolytes, blood lipids, urinary Albumin and Albumin/Creatinine ratio determination results, undertaken within the last 12 months, or more recent results if considered reasonably necessary by the ME;
- Blood lipids determination undertaken in accordance with the GD “Timetable for Routine Examination”;
- A special report – Diabetes;
- A specialist report if using Insulin, Sulphonylurea or other agents capable of inducing hypoglycaemia;
- A retinal screening result, undertaken within the past two years;
- GP notes for the past 12 months unless treated by diet and/or or Metformin only.

#### 3.4.4.3 Disposition

- An applicant with diabetes type II, controlled by the use of any agent capable of inducing hypoglycaemia, (i.e. Sulphonylurea, Insulin), should be considered as having a condition that is of aeromedical significance;
- An applicant with diabetes type II, that is not well controlled or resulting in end organ damage, should be considered as having a condition that is of aeromedical significance;
- An applicant with diabetes type II, well controlled by the use of a Biguanide only (i.e. Metformin), may be considered as having a condition that is not of aeromedical significance if there is no evidence of end organ damage and provided conditions of surveillance are imposed (refer Part 67). The applicant must be compliant with medication. The cardiovascular risk should be assessed in accordance with the applicable General Direction;

- An applicant with diabetes type II, well controlled by diet, may be considered as having a condition that is not of aeromedical significance if there is no evidence of end organ damage. The cardiovascular risk should be assessed in accordance with the applicable General Direction.

## 3.4.5 Diabetes Type I

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### 3.4.5.1 Considerations

Diabetes type I is an autoimmune disease associated with T-cells and HLA factors. Insulin production decreases rapidly. Early in the disease, appropriate measures may lead to a honeymoon period during which treatment is no longer necessary. Progression to the requirement for administration of exogenous insulin is however inevitable.

The loss of endogenous control of insulin production leads to difficulties and unpredictability in regulating the blood glucose. The main aviation safety risk relates to hypoglycaemia, with associated impaired cognition and possible coma. Brisk glycaemic variation and hyperglycaemia over 15 mmol/L can affect vision and have other deleterious functional results, including on cognition.

The diagnosis is made on the same blood glucose / HbA1c criteria as for diabetes type II (refer 3.4.4.). Age, the presence of obesity and other factors assist in determining what is the type of diabetes. Diabetes type I generally has an onset before the age of 30 and obesity is often absent. This contrasts with the commonly over 40 age for diabetes type II and the frequently found obesity.

It is sometimes difficult, at least initially, to be sure of the type of diabetes and caution must be exercised if labelling diabetes as being type II. This is particularly true for younger or lean individuals who may not [yet] require Insulin treatment but require more intense surveillance.

The aviation safety risks relate to:

- Intrinsic risks from the diabetes mellitus. These are possible visual and cognitive symptoms, including fatigue whereby poor glycaemic control results in severe hyperglycaemia, no to mention the possibility of ketoacidotic decompensation and coma; and
- Long term intrinsic risks from diabetes, with end organ damage to the heart, kidneys, eyes and nerves; and
- Iatrogenic risks due to Insulin. The main risk being hypoglycaemia leading to general and cognitive impairment, and possibly coma. Progress has been made with blood glucose monitoring (continuous monitoring) and Insulin dosage estimation and administration (Insulin pumps).

Currently CAA consider the risk of hypoglycaemia to be generally excessive for any form of certification.

However, the Director has issued a very small amount of Class 2 medical certificates to applicants who have demonstrated excellent glycaemic control, such that the risk of hypoglycaemia has been considered to be sufficiently low.

Restrictions and a raft of operational conditions have been imposed in such cases.

### 3.4.5.2 Information to be provided

- All related specialist reports;
- A recent endocrinologist report;
- A recent HbA1c determination result;
- Pre and post prandial capillary blood glucose determinations through the day (at least 5 results) on three different days if the applicant is not yet treated by Insulin (honeymoon period) and not using a glucometer;
- Download and statistical analysis of glucometer data, if treated with Insulin or if using a glucometer;
- Renal function, electrolytes, blood lipids and urinary Albumin and Albumin/Creatinine ratio determination results undertaken within the last 12 months;
- Blood lipids determination results, undertaken in accordance with the GD “Timetable for Routine Examination”;
- A special Report – Diabetes;
- A retinal screening result, undertaken within the past two years;
- GP notes for the past 12 months unless treated by diet and/or or Metformin only.

### 3.4.5.3 Disposition

- An applicant with type I diabetes should be considered as having a condition that is of aeromedical significance.