Anatomy and physiology of ageing 7: the endocrine system

Key points

1. The endocrine system regulates our physiology via a complex cascade of chemicals called hormones.
2. Hormones play an essential role in maintaining homeostasis in the body.
3. Age-related hormonal changes can lead to the build-up of body fat, lower bone density, impaired blood glucose control and sleep disturbances.
4. Age-related changes to the endocrine system increase the risk of insomnia, fractures, type 2 diabetes and cognitive changes.
5. Exercising regularly and maintaining a low percentage of body fat may slow down some of the effects of ageing on the endocrine system.

The endocrine system works in conjunction with the nervous system to regulate, and coordinate the activities of, the body’s tissues and organs. It consists of a collection of glands located in different parts of the body – the main ones being the pituitary, pineal, thyroid, parathyroids, adrenals, pancreas, ovaries and testes. These glands produce a variety of bloodborne chemical signals called hormones, which play an essential role in maintaining balance (homeostasis) in the body, helping to ensure that variables such as blood glucose and electrolytes are kept within normal ranges.

Pituitary gland and somatopause

The pituitary gland, often referred to as the master gland, produces several major hormones and regulates the activity of many other endocrine glands. It is split into a posterior portion, which is formed from neural tissue extending from the hypothalamus, and an anterior portion, which is formed from epithelial cells derived from the roof of the oral cavity.

The anterior pituitary secretes growth hormone (somatotropin), which promotes the growth of bone, muscle and most of the major internal organs. In early childhood, somatotropin is secreted in relatively small amounts, but during the teenage years there is a marked increase in serum somatotropin levels corresponding to the growth spurt of puberty. Around the age of 25-30, somatotropin secretion begins to decline in both men and women. In men it is estimated to halve every seven years – although there appears to be much variation between individuals (Gentili, 2015).

The decline in somatotropin secretion in later years is often referred to as the somatopause and is associated with a variety of physiological changes (Jonas et al, 2015; Veldhuis et al, 2005), including:

- A general reduction in protein synthesis;

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Abstract
Glands in the endocrine system produce a range of hormones that regulate our body’s activities by keeping substances such as blood glucose and electrolytes within their normal ranges. Like all other body systems, the endocrine system undergoes age-related changes that negatively affect its functioning. As a result of these changes, older people are more prone to disturbed sleep patterns, have a reduced metabolic rate, lose bone density, accumulate body fat, and show increases in blood glucose. As a consequence, they are at higher risk of health issues such as insomnia, fractures, type 2 diabetes and cognitive decline. This seventh article in our series about the effects of age on the body describes what happens, with advancing age, to endocrine glands and hormone production.

Citation
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Pineal gland and sleep disturbances
The pineal gland is slightly smaller than a pea and resembles a small pine cone—hence its name. Found in the diencephalon, towards the centre of the brain, it synthesises the hormone melatonin from the neurotransmitter serotonin. The pineal gland functions like an internal body clock: during the day, when there is a lot of light, melatonin secretion is inhibited, but as the day draws to a close and light diminishes, melatonin secretion increases, preparing the body for sleep.

As we age, the pineal gland undergoes a process of calcification, detectable even in young children. Melatonin levels progressively decrease: 60-year-olds have 80% less melatonin in their blood than teenagers. Some drugs commonly prescribed to older people, such as beta blockers and non-steroidal anti-inflammatory drugs, can decrease melatonin levels even further.

Decreased melatonin levels are linked to an increased prevalence of sleep disturbances and, in some people, may ultimately lead to geriatric insomnia (Rubenik and Konturek, 2011). Since sleep is essential for cognitive function, sleep disturbances can exacerbate age-related changes in the brain.

There is some evidence that exposure to bright light—either sunlight or artificial light—in the morning increases the speed of sleep onset by triggering an earlier release of melatonin in the evening. Similarly, the therapeutic use of prolonged-release melatonin has been shown to improve sleep onset time, sleep quality, morning alertness and quality of life in people aged 55 and over who have insomnia (Wade et al, 2007).

The thyroid gland and metabolism
The thyroid gland plays a major role in controlling metabolism and adjusting blood calcium levels. The hormones it secretes regulate a number of physiological processes, including:
- The metabolism of carbohydrates, fats and proteins;
- Thermoregulation;
- Digestion;
- Muscle and nerve activity;
- Maintaining skin thickness and integrity;
- Maintaining normal bone density.

Changes to metabolic rate
The thyroid secretes the iodine-containing hormones T4 (tetraiodothyronine, which is also known as thyroxine) and T3 (triiodothyronine), which largely control cellular metabolism. T4 is released in greater quantities than T3, the typical ratio being 15:1. T4 is then rapidly converted into the more biologically active T3, which is around three times more potent in terms of increasing the metabolic rate.

The clearance of T4 by the liver decreases with age, but this is offset by a gradual decline in T4 secretion, so T4 serum levels tend to remain constant. However, there is a clear age-related decrease in the levels of serum T3, as well as of thyroid-stimulating hormone (TSH) produced by the pituitary gland (Peeters, 2008; Chahal and Drake, 2007). This may contribute to the gradual reduction in basal metabolism that is apparent in many people in middle and old age (in which the decline in lean muscle mass described above also plays a role).

With advancing age, autoimmune reactions against one’s own thyroid gland are commonly seen. Indeed, the presence, in older people, of antibodies specific to thyroid tissue is so common that it is often considered a normal age-related change. A high concentration of such antibodies may herald the onset of autoimmune hypothyroidism, a disease affecting up to 5% of the population.
over-60s and associated with low metabolic rates, a tendency to put on weight and low core temperature. Since this condition is autoimmune in nature, women are at greater risk of developing it (this is true for most autoimmune diseases); up to eight times more women than men experience autoimmune hypothyroidism.

The results of thyroid function tests should be assessed carefully in older people, as common long-term conditions (such as chronic obstructive pulmonary disease, hypertension, diabetes and arthritis) and dieting can lead to reductions in circulating thyroid hormones, particularly the more active T₃. This phenomenon of reduced thyroid function in the absence of thyroid disease is referred to as non-thyroidal illness. Similarly, many drugs used to treat long-term conditions in older people (for example, lithium and glucocorticoids) can suppress thyroid function or reduce the activity of circulating thyroid hormones, leading to a reduction in metabolic rate (Peeters, 2008).

Changes to calcitonin secretion
The thyroid gland also plays a role in calcium homeostasis. When we consume foods rich in calcium, it releases calcitonin, which inhibits the activity of osteoclasts - bone cells that break down bone tissue (bone is a dynamic tissue continually being built and broken down). By inhibiting osteoclast activity, calcitonin indirectly increases bone density.

Few studies have examined the effects of ageing on calcitonin production in humans. The most comprehensive study, dating back to 1980, demonstrated an age-related decline in calcitonin production in 50 healthy women aged between 20 and 69 years (Shamonki et al, 1980). This decline may partially explain the reduction in bone mass seen in most women as they grow older. However, a later study has contradicted these findings, showing that although women appear to have lower levels of calcitonin secretion than men, there is no clear age-related decrease in serum calcitonin concentration (Tiegs et al, 1986).

Parathyroid glands and hyperparathyroidism
The posterior portion of the thyroid is the location of four tiny parathyroid glands, which secrete parathyroid hormone (PTH) whenever blood calcium levels fall. Since a normal concentration of calcium is essential to many physiological processes (including muscle contraction, nerve conduction and blood clotting), the reserves of calcium stored in the skeleton need to be mobilised. PTH triggers the release of calcium from the bones into the blood by indirectly stimulating osteoclasts.

Several studies have shown that most people, as they grow older, have significantly increased levels of circulating PTH (Portale et al, 1997). This hyperparathyroidism may well be one of the main causes of the reduction in bone density commonly seen in middle and old age. Recent studies have also shown a potential link with other pathologies, particularly age-related cognitive decline and dementia (Braverman et al, 2009).

The pancreas and diabetes risk
The endocrine regions of the pancreas (islets of Langerhans) regulate blood glucose levels. Beta cells in the islets secrete insulin in response to increased blood glucose – for example, after a carbohydrate-rich meal. Insulin binds to receptors present on most cells, triggering the uptake of glucose from the blood. Once inside the cells, glucose is either metabolised immediately to release energy, or stored and converted into glycogen.

Alongside race, genetic predisposition and a high body mass index, ageing is one of the many risk factors linked to the development of type 2 diabetes (Knight and Nigam, 2017). ageing human cells become less sensitive to the effects of insulin. The most likely cause appears to be a reduction in the number of insulin receptors at the surface of cells. This gradual insulin resistance goes hand in hand with an increase in blood glucose concentrations.

As shown in a study of 6,901 non-diabetic people (Ko et al, 2006), fasting blood glucose levels rise by around 0.15mmol/l for each decade of life after the age of 20. Whether this rise is a normal age-related change or a sign of diabetes in its early stages is not always clear, but it is certainly seen in many older people with no other symptoms of diabetes.

With advancing age, the insulin-producing beta cells become less sensitive to the level of glucose in the blood, so higher blood glucose levels are needed to trigger insulin release. Since older people’s cells are less receptive to insulin, the pancreas often responds by producing more, leading to increased insulin levels in the blood (hyperinsulinaemia). This can put excessive stress on the beta cells, leading to their exhaustion.

Age-related depletion of the beta cell population in the pancreas also occurs as a result of increased programmed cell death (apoptosis) and a diminished ability of the pancreas to produce new cells. Beta cell exhaustion and depletion result in a drop of insulin secretion of up to 0.5% per year of life. Additionally, the clearance of insulin by the liver increases with age, so there is less insulin available to interact with cells and promote glucose uptake.

These age-related changes to insulin production, clearance and response contribute to the creation of a diabetogenic environment. This may partially explain why the risk of developing type 2 diabetes increases with age (Brown, 2012).

Abdominal fat
The accumulation of abdominal fat is a common feature of ageing, particularly in people who have a poor diet and/or a sedentary lifestyle. Many age-related changes to the endocrine system contribute to this accumulation of adipose tissue, including the somatopause, autoimmune hypothyroidism, insulin resistance, and reduced circulating sex hormones.

This abdominal fat accumulation is linked to heart disease, high blood pressure and type 2 diabetes. These conditions may occur in isolation or together in the form of metabolic syndrome (Gong and Muzumdar, 2012).

The adrenal glands
The two adrenal glands are located above the kidneys and each consists of two main regions: the adrenal medulla (inner region) and the adrenal cortex (outermost layer).

Adrenal medulla and adrenaline
The adrenal medulla is the location of chromaffin cells, which secrete the catecholamines adrenaline (epinephrine) and noradrenaline (norepinephrine). These are the ‘fight or flight’ hormones that prepare the body for activity when it is threatened or in a state of excitement. The effects of adrenaline and nor-adrenaline include:

- Increased heart rate;
- Increased vasoconstriction in the skin and gut;
- Increased blood pressure;
- Increased blood flow to the major skeletal muscle groups;
- Increased blood flow to the brain;
Enquiry:  The elderly experience a number of age-related changes in the endocrine system, including increased cortisol production, decreased aldosterone secretion, and changes in parathyroid hormone and calcitonin levels. These changes can lead to increased blood glucose levels, exacerbated hyponatraemia, and reduced bone density.

Research: An age-related increase in cortisol secretion has been reported, with highest values in the morning. Aldosterone secretion decreases with age, which contributes to the loss of cells from the hippocampus, resulting in hippocampal atrophy.

Evidence: Researchers have found an age-related increase in cortisol secretion between the ages of 20 to 80 years (Chahal and Drake, 2007). Studies have shown that age-related increases in cortisol may also be linked to memory loss and sleep disorders (Chahal and Drake, 2007; Wolf et al, 2005).

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