Bio Factsheet

Number 28

Feedback control mechanisms

This Factsheet summarises the processes of negative and positive feedback control mechanisms and illustrates how such mechanisms help to regulate blood concentration, blood glucose concentration, the menstrual cycle, birth and body temperature.

The role and nature of feedback control in homeostasis

It is essential that the physical and chemical processes of the body are controlled. Homeostasis is the maintenance of a stable internal environment by the regulation of these processes within acceptable limits. Organisms receive oxygen, food, water, salts and warmth from the environment and return carbon dioxide and other wastes to it. Due to homeostasis, mammals and birds have a measure of independence from the external environment, whilst still existing in equilibrium with it.

Homeostasis usually involves control by a combination of negative and positive feedback. In negative feedback control, if the physiological value deviates from the mean (norm) the deviation is sensed by receptors which initiate control mechanisms to return the value to the norm. The receptors are then no longer stimulated and the control mechanisms are either reduced (damped) or completely switched off. Control mechanisms may occur either via **nerve impulses** which are rapid or via **hormones** which (with the exception of adrenaline) are slow. In positive feedback control, the control mechanism acts to push the deviating value further away from the norm. Once a certain deviation has been reached, the controlling mechanism may be damped or switched off.

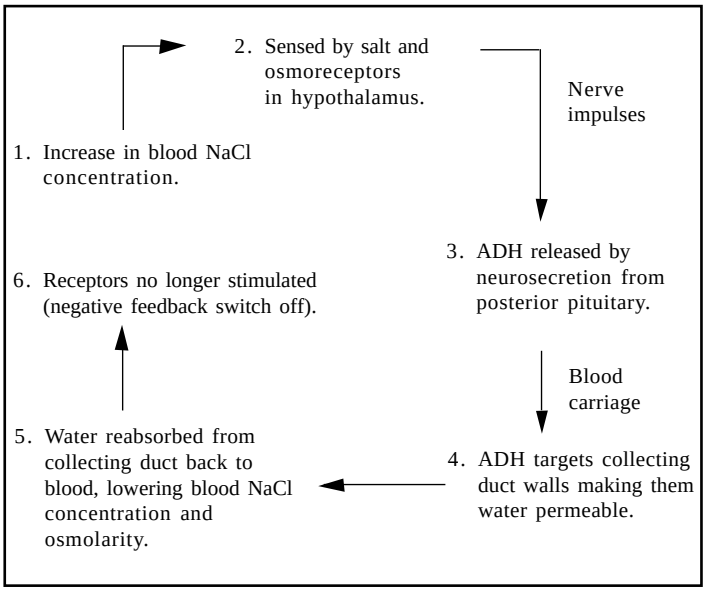
Many physiological values and processes vary in a regular fashion over a definite period of time. Most of these are daily (circadian) rhythms, such as temperature control, but some are on different time scales, such as the monthly menstrual cycle. **Endogenous** rhythms (those which originate from within), appear to follow a spontaneous internal cycle, e.g. core body temperature changes. **Exogenous** rhythms (those which are affected by external factors), appear to follow regular changes in environmental stimuli, e.g. heart rate and blood pressure changes.

Regulation of blood concentration

The counter current mechanism which operates in the loops of Henlé in the kidneys maintains a high salt concentration around the collecting ducts of the nephrons. This enables water to be reabsorbed osmotically from the collecting ducts, back into the blood, provided that the collecting duct walls are permeable to water. This permeability depends upon the presence or absence of **Antidiuretic hormone (ADH)** secreted by the posterior pituitary on the target receptors on the collecting duct walls. If ADH is absent, the walls are impermeable to water so no water can be absorbed back to the blood to dilute it, and the urine remains dilute (containing as little as 100 millimoles of NaCl per litre). If ADH is present, the walls become permeable to water and water is reabsorbed back to the blood, thus diluting it and raising the blood volume and pressure. Conversely the urine volume is reduced and its concentration is raised (to around 1200 millimoles of NaCl per litre).

The presence or absence of ADH is controlled by negative feedback. Receptors in the hypothalamus of the midbrain sense an increase in the sodium concentration and osmotic pressure (osmolarity) of the blood plasma, and transmit nerve impulses down the pituitary stalk to the posterior pituitary body. These impulses cause the release of ADH from the posterior pituitary to the blood (neurosecretion). The ADH attaches to target receptors on the collecting duct walls and makes them permeable to water which can then be reabsorbed back into the blood. As a result, the blood sodium concentration and osmolarity fall, so the receptors in the hypothalamus are no longer stimulated. ADH release is thus damped or switched off and so the collecting duct walls revert to being water impermeable. Thus, the urine becomes more dilute whilst the blood osmolarity starts to rise once more, until the ADH release is switched on again. The control mechanism of ADH is illustrated in Fig 1.

Fig 1. The ADH control mechanism



Regulation of blood glucose concentration

Blood glucose concentration is regulated by the islets of Langerhans which are tiny patches of endocrine tissue embedded in the pancreas. The islets contain two types of secretory cell, the beta cells, which secrete insulin and the alpha cells, which secrete glucagon. Insulin **lowers** blood glucose levels by:

1. accelerating the facilitated uptake of glucose into cells
2. accelerating the synthesis of the storage polymer glycogen from glucose in the liver and muscles

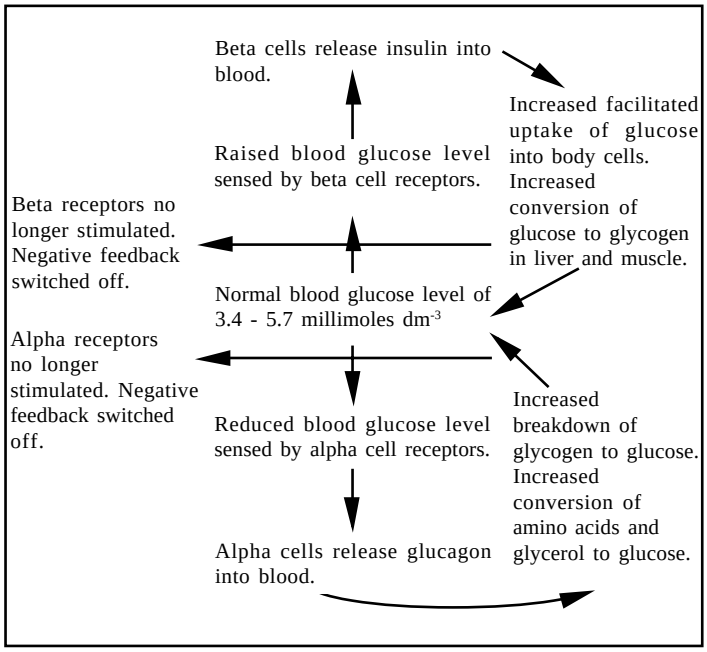
Glucagon **raises** blood glucose level by stimulating the conversion of unwanted amino acids and glycerol into glucose.

The release of insulin and glucagon is regulated by negative feedback. When the blood glucose level falls below the norm, this is sensed by receptors on the alpha cells of the islets. This stimulates the alpha cells to release glucagon into the blood, which raises the blood glucose level back to the norm and the alpha receptors become switched off. When the blood glucagon level raises above the norm, it is sensed by receptors on the beta cells of the islets. Insulin is released into the blood, which lowers the blood glucose concentration back to the norm and so the beta receptors are switched off.

Exam hint - *The receptors governing insulin and glucagon release are in the islets, not in the hypothalamus. This is a very common error made by A Level candidates.*

The insulin-glucagon control mechanism is illustrated in Fig 2.

Fig 2. The insulin-glucagon control mechanism



Regulation of the menstrual cycle

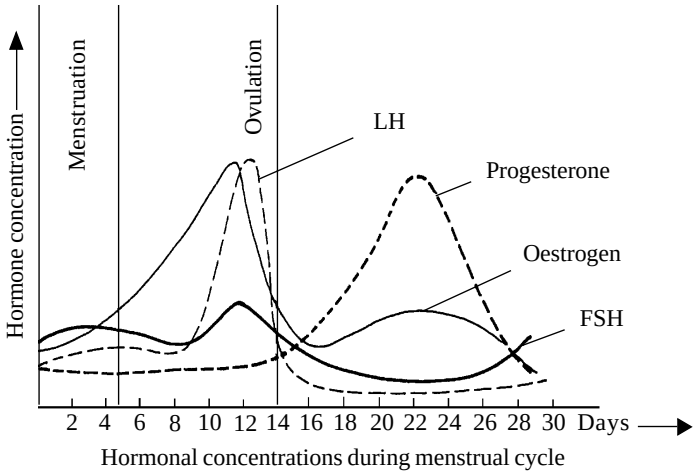
The menstrual cycle depends initially on the secretion of the hormone gonadotrophin release factor (GnRF) by the hypothalamus. Increasing blood levels of GnRF stimulates the release of follicle stimulating hormone (FSH) from the anterior pituitary gland. Increasing blood levels of FSH stimulates the development of primary follicles in the ovary into ovarian (Graafian) follicles, and also stimulates the developing follicles to secrete oestrogens. Oestrogens stimulate the repair and rebuilding of the uterus lining after its shedding during menstruation.

High oestrogen levels in the blood around the time of ovulation have two effects. Firstly, they inhibit the further release of GnRF and hence of FSH by negative feedback. Secondly they cause the anterior pituitary to release increasing amounts of luteinising hormone (LH) - this is a good example of positive feedback.

LH stimulates ovulation, in which the ovarian follicle ruptures to release the secondary oocyte into the ovarian (fallopian) funnel. It also stimulates the remains of the follicle in the ovary to develop into the corpus luteum (yellow body) which then starts to secrete the hormone progesterone as well as oestrogen. Together, oestrogen and progesterone maintain and develop the uterine wall further.

If fertilisation does not occur, the increasing levels of these hormones eventually inhibit the further release of LH by negative feedback. Without the maintaining effect of LH, the corpus luteum degenerates and so the concentrations of oestrogen and progesterone fall and their maintaining action on the uterine wall is lost. Thus, the uterine wall breaks down, resulting in the menstrual flow of cells and blood out through the vagina. Fig 3 illustrates the changes in hormonal concentrations which occur during the menstrual cycle.

Fig 3. Hormonal concentrations during the menstrual cycle.



Days 8-12
Increasing oestrogen concentrations stimulate LH release by positive feedback.

Days 16-22
Increasing oestrogen and progesterone concentrations inhibit any further release of LH by negative feedback.

Regulation of the birth process

Throughout pregnancy, high concentrations of progesterone secreted by the placenta inhibit contractions of uterine muscle and thus prevent birth and maintain the pregnancy.

Towards the end of pregnancy, from about week 36 in humans, the placenta starts to age. This has two main effects which increase as time passes, resulting in birth at around 40 weeks (humans). The two effects are:

1. The development of foetal anoxia (insufficient oxygen) which causes foetal discomfort resulting in struggling and kicking. This increases the mechanical stimulation on the uterine wall sending nerve impulses to the hypothalamus. When these reach a certain intensity the hypothalamus sends nerve impulses to the posterior pituitary, causing the release of the hormone oxytocin into the blood. This hormone stimulates the contractions of uterine muscle. As the intensity of nervous stimulation increases, so does the output of oxytocin (positive feedback).

2. The ageing placenta produces progressively less progesterone until eventually it no longer inhibits uterine contractions which then commence, initiating the birth process. Secretion of oestrogen from the foetus also occurs at this time which also stimulates uterine contractions (positive feedback). The placenta also secretes substances known as prostaglandins which also stimulate uterine contractions and stimulate oxytocin release from the posterior pituitary (positive feedback).

Eventually the amnion ruptures, releasing the 'waters' and the foetus is then in direct contact with the uterine wall. This greatly increases mechanical and thus nervous stimulation, resulting in further increases in oxytocin output by positive feedback. The oxytocin also causes dilation of the cervix, so that eventually the uterine contractions push the baby out. Following the birth of the baby, the high concentration of oxytocin in the blood causes more powerful uterine contractions to expel the bleeding placenta from the damaged uterine wall. The release of oxytocin then falls back into a lower level by negative feedback, since the mechanical stimulation of the uterine wall is no longer present.

Regulation of body temperature

Precision temperature control is only found in endothermic animals such as mammals and birds, which can maintain their body temperatures within narrow limits by balancing their heat production with their heat loss. The regulation of temperature is due to a thermostat in the hypothalamus which becomes activated if the temperature varies from a set point (37°C in humans). The thermostat contains two centres, one promoting heat loss and one promoting heat gain. These centres receive information from temperature receptors (thermoreceptors) in the skin which sense the surface temperature of the body, and in the hypothalamus which senses the core blood temperature.

If the skin or blood temperatures fall below the set point, the heat promoting centre of the hypothalamus is stimulated. This sends impulses through the sympathetic nerves, which stimulate responses leading to an increase in temperature. These responses include:

- Vasoconstriction of arterioles in the skin so that less heat is lost from the blood by radiation and conduction through the skin.
- Contraction of the erector pili muscles to raise the hairs. This traps a thicker layer of air which is a good insulator thus preventing heat loss.
- Release of adrenaline and noradrenaline from the adrenal medulla which stimulates an increase in cell metabolism, thus increasing heat production.
- An increase in striated muscle tone which causes shivering, generating heat.

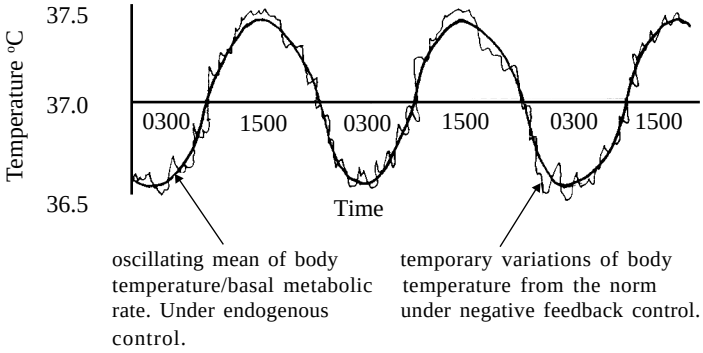
As the body temperature rises back to the set point, the heat promoting centre is no longer activated. Thus no further impulses are generated and the adjusting mechanisms are damped or switched off by negative feedback. If the skin or blood temperature rises above the set point, the heat losing centre of the hypothalamus is stimulated. This sends impulses, mainly through parasympathetic nerves, which stimulate responses leading to a decrease in temperature. These responses include:

- Vasodilation of arterioles in the skin so that more heat is lost from the blood by radiation and conduction through the skin.
- Relaxation of the erector pili muscles to lower the hairs so that less insulating air is trapped.
- Increasing activity of the sweat glands (actually under sympathetic control) releasing sweat which evaporates, thus cooling the skin by removing latent heat of vaporisation.

As the body temperature falls back to the set point, the heat losing centre is no longer activated. Thus no further impulses are generated and the adjusting mechanisms are damped or switched off by negative feedback. The norm or set point of body temperature actually fluctuates between set limits (between 36.5 and 37.5°C) over a 24 hour period. The temperature is highest at around 1500 hrs and lowest around 0300 hrs and is a result of a similar fluctuation in basal metabolic rate which generates heat as a by-product. This is an example of a circadian rhythm which is endogenous, although the precise internal reason for it is unknown. Fig 4 illustrates daily changes in body temperature.

Exam hint - *Students usually learn and revise their Biology notes topic by topic - often in the same order that they were taught them. However, feedback control mechanisms is a good example of a topic which requires students to be able to integrate in-depth knowledge of several different parts of a syllabus. This is, therefore, a popular topic on synoptic papers.*

Fig 4. The circadian rhythm of body temperature



During infections, the body temperature may be temporarily controlled by positive feedback. Diseased organisms often produce certain toxins called pyrogens (heat makers) which have the effect of raising the norm of body temperature, and the temperature is raised above the norm by positive feedback. This is of value, since the higher temperature may inhibit the enzymes of the bacteria or viruses, preventing their growth, whilst the enzymes of the host are less affected and can continue to work. Once the bacteria or viruses die and stop producing pyrogens, the control of body temperature reverts to the normal negative feedback.

Practice Questions

1. Read through the following passage, then write on the dotted lines the most appropriate word or words to complete the account.

   Blood glucose concentration is regulated by …… feedback involving hormones secreted by the ……. embedded in the pancreas. These contain ……. cells which detect a reduced blood glucose concentration and as a result secrete …….. This hormone returns the blood glucose concentration to the norm by stimulating the conversion of …… to ……..
   The ……..cells detect a raised blood glucose concentration and then secrete the hormone …… which returns the value to the norm. It does this by stimulating the conversion of …….. to ……..... and by stimulating the ……..uptake of …… into respiring cells. (12 marks)

2. The table below contains information relating to the actions and control of different hormones. Complete the missing information in the empty boxes.

hormone	secreted by	action	feedback control
		stimulates uterine muscle contraction in birth	
	anterior pituitary	stimulates growth of ovarian follicle	
	corpus luteum		negative
oestrogen		stimulates growth and repair of uterine wall	

(9 marks)

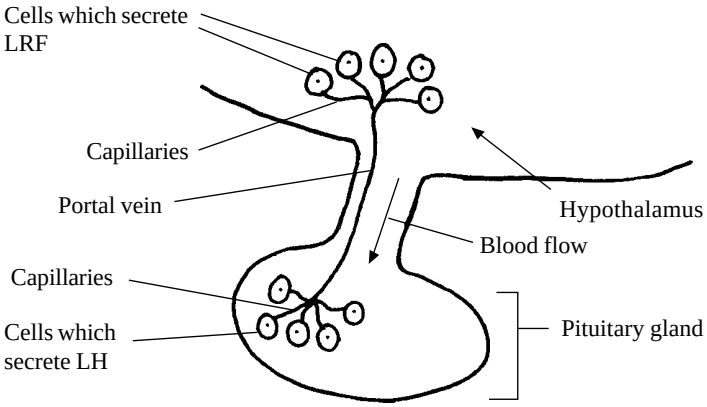
3. By referring to the physiological mechanisms involved give an explanation of the following:

(a) Eating an ice cream on a hot day may actually cause the skin temperature to rise. (5 marks)

(b) Drinking ½ litre of strong coffee may cause the production of 1 litre of dilute urine. (Remember that caffeine is an inhibitor of ADH release). (5 marks)

(c) Doing shift work at nights may cause a loss of efficiency amongst the work force. (5 marks)

4. The secretion of LH is controlled by LH releasing factor (LRF), a small peptide produced in the hypothalamus. Here LRF is secreted directly into capillaries which join to form a short portal vein which runs to the anterior pituitary. In the pituitary this portal vein branches into another capillary network which supplies the cells which secrete LH. This system is illustrated in the following diagram.



(a) How does the transport of LRF to its target cells differ from the transport of a typical hormone such as LH to its target cells? (2 marks)

(b) What advantage may be gained from the LRF transport system? (2 marks)

(c) LRF can be synthesised industrially and triggers LH secretion by binding to receptors on the surface of LH secretory cells. Explain the physiological basis of the suggestion that synthetic LRF could be used as a contraceptive. (3 marks)

Answers

Semicolons indicate marking points.

1. negative;
islets (of Langerhans);
alpha;
glucagon;
glycogen/amino acids;
glucose;
beta;
insulin;
glucose;
glycogen;
facilitated;
glucose;

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2.

hormone	secreted by	action	feedback control
oxytocin	posterior pituitary	stimulates uterine muscle contraction in birth	positive
FSH	anterior pituitary	stimulates growth of ovarian follicle	negative
progesterone	corpus luteum	maintains uterine wall	negative
oestrogen	ovarian follicle	stimulates growth and repair of uterine wall	negative

3. (a) Ice cream in stomach cools core blood temperature;
sensed by thermoreceptors in hypothalamus;
heat promoting centre is stimulated;
impulses through sympathetic nervous system cause;
erection of hair thus trapping insulating air which warms the skin/ arteriole vasoconstriction so less heat lost from skin/suppression of sweating so no heat lost by latent heat of vaporisation;
Thus skin temperature warms up (consequential mark only);

(b) Water from coffee absorbed into blood increasing blood volume/ pressure/causing dilution;
sensed by osmoreceptors in hypothalamus;
nerve impulses sent to posterior pituitary to reduce ADH release;
but caffeine also absorbed into blood completely inhibits ADH release;
thus no water reabsorption in collecting ducts so a large volume of dilute urine is excreted;
increase in blood pressure also causes increase in glomerular filtration rate thus also increases urine formation;
comment on caffeine interfering with negative feedback loop;

(c) Normal circadian rhythm of body temperature is under endogenous/ internal control;
this causes the lowest body temperature/metabolic rate in the early hours of the morning/around 0300hrs;
thus mental and physical activities of the body function least efficiently at this time;
this causes night shift workers to be less efficient/more prone to accidents;
also when they try to sleep during the day it is difficult since their metabolism is at a peak/normally more alert during the day;
it takes several weeks to adapt/circadian rhythm by 12 hours;

4. (a) LRF taken directly from LRF secretory cells to target cells in portal vein blood;
LH released into general circulation/thus diluted by whole blood volume/disperses through whole body before reaching its target;

(b) Shorter distance to travel so quicker; less needs to be produced since probably all of it reaches the targets/higher concentration reaches target cells;

(c) LRH pills would stimulate the continual production of high concentration of LH;
although this high concentration of LH may allow an initial ovulation it would then maintain the luteal phase of the menstrual cycle;
thus as long as the pill was taken, further development of follicles could not occur;