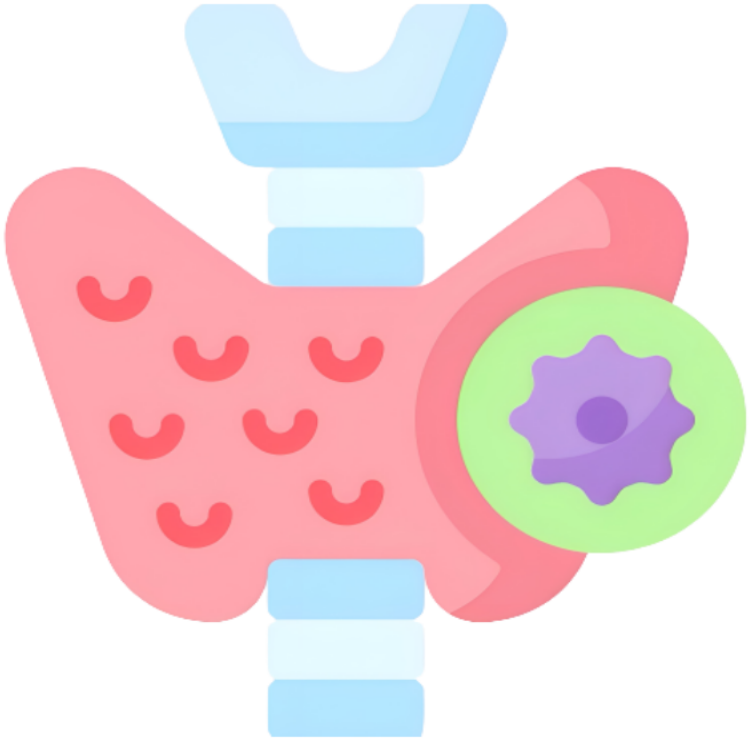
Endocrine system

Sheet No 3

physiology

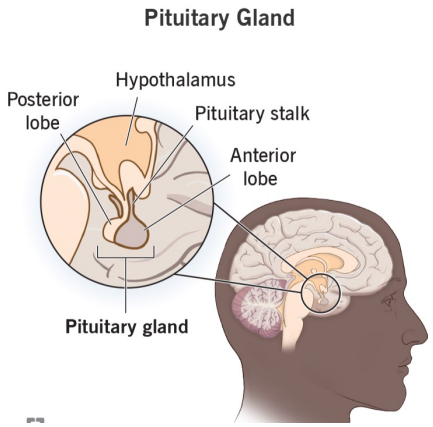


Writer: Lana Raymoony & Lubna Adnan

Corrector: Lana Raymoony & Lubna Adnan

Doctor: Salim khraisha

This sheet is short and enjoyable … try to understand & enjoy every part of it .



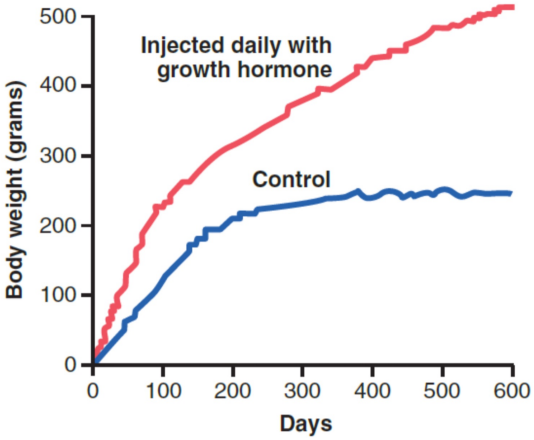
Anterior pituitary gland

o Release growth hormone (somatotropin).

o Increases the growth of the cells & number of cells which are capable to grow.

o Is established in all body cells

*It works under the influence of the growth hormone releasing factor (GHF) and is inhibited by somatostatin.



This picture shows an experiment done on two rats one is injected with GH and the other is not

rat injected with GH → significant increase in body weight

rat without GH → no significant increase in body weight

Hormones functioning with growth hormone

o The hormones which **function** together, **complement** each other.

o **Growth hormone (GH)** does not function properly unless **insulin** is present.

(growth hormone without Insulin → no growth).

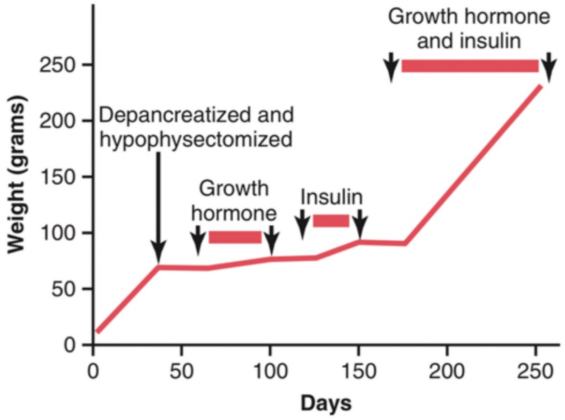
o Multiple hormones, including growth hormone (GH), insulin – like growth factors 1&2 (IGF-I and -II) ,insulin ,thyroid hormones, Glucocorticoids, androgens & estrogens contribute to the growth process in humans.

**The major hormones that are implicated as the major determinants of growth in normal post-uterine life → growth hormone (GF) & insulin-like growth factor (IGF-1). don't worry it will be covered later on

**Growth of musculoskeletal system and other tissues can be affected by deficiency or excess in hormones.

INSULIN AND GROWTH HORMONE

An experiment was conducted on a rat to observe the effect of insulin and GH on weight.



1. By excluding the effect of pancreatic and hypophyseal (pituitary) secretions we can proceed our experiment.

2. We inject the rat with GH alone → No significant change in weight (GH causes almost no growth).

3. We inject the rat with insulin alone → No significant change in weight (insulin causes almost no growth).

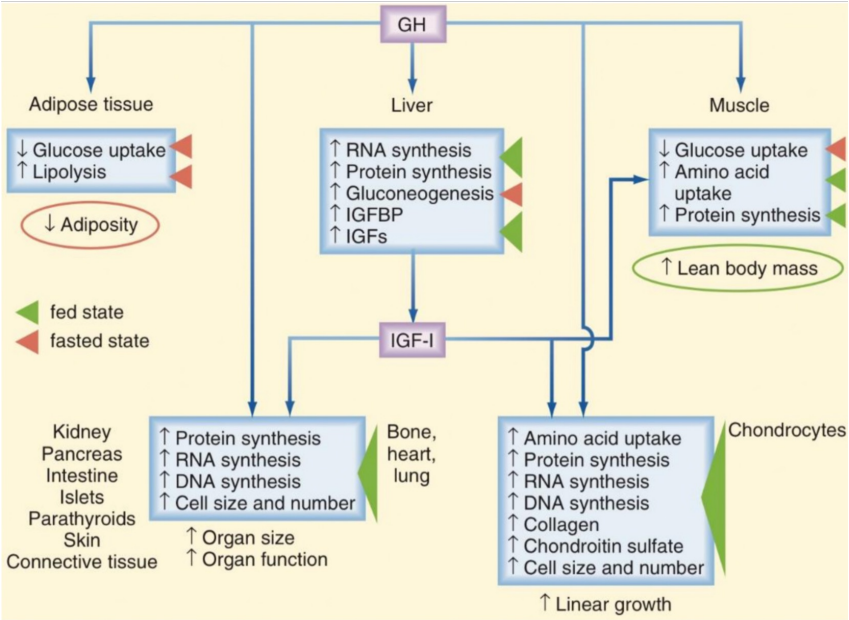
4. By injecting the rat with **both insulin and GH** at the **same time** → significant change in body weight (together they cause dramatic growth).

** GH and insulin function **synergistically** in terms of growth (which is mainly controlled by protein synthesis).

-But keep in mind that they are **counter-regulatory** (opposite) hormones in terms **of lipid and glucose metabolism**. (this will be discussed later on).

GH effects on body tissues

direct	indirect
Adipose tissue	Bones, heart, lungs
Liver	***Chondrocytes** (discussed In page 5)
muscles	Pancreas, kidney, intestines, islets, parathyroid, skin, C.T



Directly:

1. **Adipose tissue:** Decreases glucose uptake & increases lipolysis (adiposity decreases) Eventually, blood concentration of fatty acids and glucose increases.

2. **Liver cells:** increases gluconeogenesis , protein synthesis rates, RNA synthesis & production of somatomedins (IGF-I) **IMPORTANT

3. **Muscle cells:** decreases glucose uptake (it remains in blood), increases amino acid uptake by tissues as well as protein synthesis (increases lean body mass).

Indirectly:

GH exerts much of its effects through intermediate substances called somatomedins (Insulin like Growth Factor (IGF-I)). (M.W:7500Daltons)

There are 6 types of them. Different in sequence or number of amino acids but function the same with varying potency. Somatomedins are produced predominantly by liver when GHs act on normal tissues. It increases organ size and stimulates growth and division in response to stimulation by GH .Somatomedins also stimulate production of somatostatin ,which suppresses GH release. Thus, levels of somatomedins are controlled via negative feedback through the intermediates of somatostatin and GH.

*When GH is supplied directly to cartilage chondrocytes cultured outside the body, proliferation or enlargement of chondrocytes usually fails to occur, While injecting GH into an intact animal causes proliferation & growth of the same cells. (because the effect is somatomedin mediated in terms of cartilage proliferation).

METABOLIC EFFECTS OF GROWTH HORMONE

1. **Increase** the rate of **protein synthesis**, which In returns increases the body weight.
2. **Increase** mobilization of **fatty acids** from adipose tissue & increase use of it for energy. Which leads to #3
3. **Decrease** the rate of **glucose utilization** throughout the body (decreases the entry and usage of glucose in tissues).

Net effect: GH enhances the body protein, uses up the fatty stores and conserves carbohydrates.

The increased rate of growth result mainly from the increased rate of protein synthesis. **insulin plays a major role in growth because both ,insulin and GH work synergistically in protein metabolism.

**one of the functions of GH is to increase the concentration of glucose in the blood (normalize the blood glucose level).

**Sometimes there is an abnormality, in which there is increase in the

concentration of growth hormone ⟶ Causes diabetes, This is called the **diabetogenic effect of growth hormone**

** **this effect can be achieved by at least three hormones other than GH, Including Adrenocorticotropin (ACTH), Thyroid-stimulating hormone (TSH) and Prolactin.**

***ACTH **increases** cortisol secretion by adrenal cortex, which in returns increases blood glucose concentration by increasing gluconeogenesis rate

GH causes diabetes in two ways:

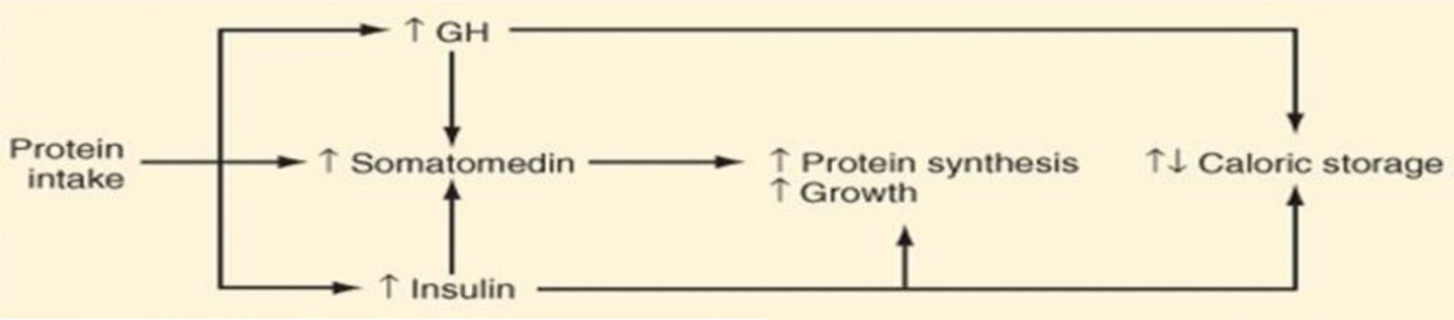
1. **Increases** blood glucose concentration which directly increases insulin.(hyperglycemia)
2. Directly increases insulin secretion from beta cells of pancreas, pancreas is over stimulated, and the cells finally burn out. the person

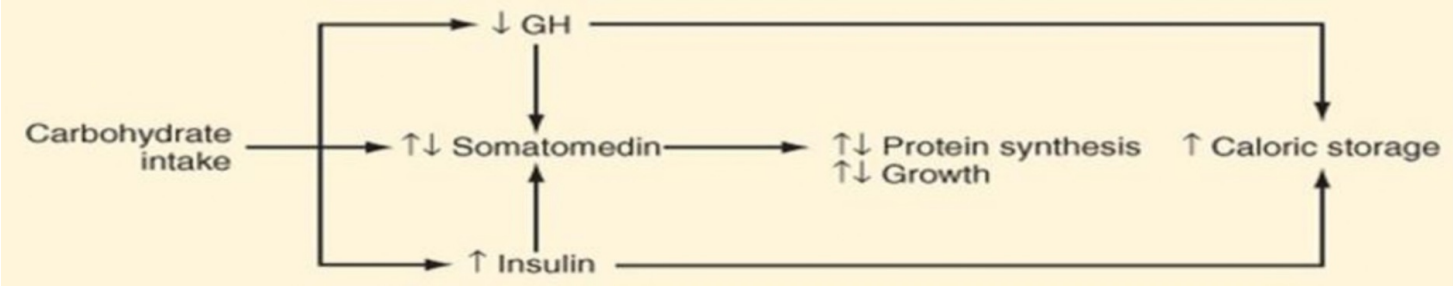
develops diabetes mellitus.

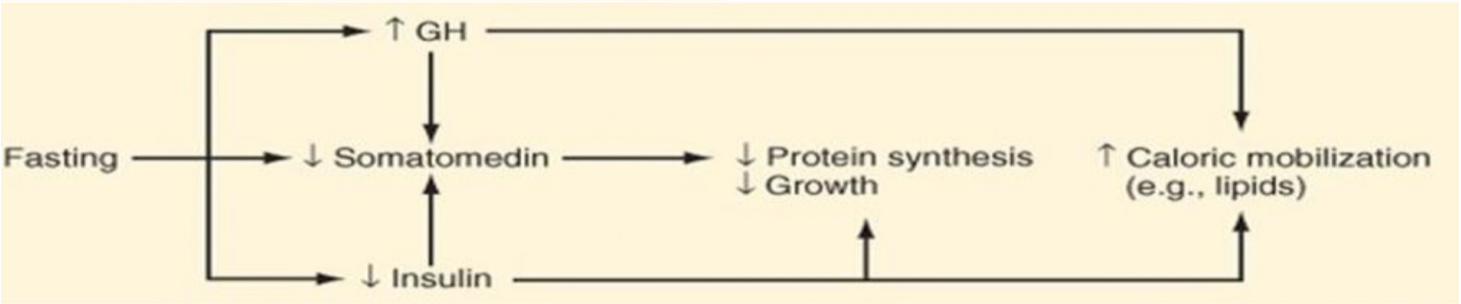
***Effect of GH in enhancing fat utilization by increasing lipolysis:**

1. Increases the free fatty acids in the blood by increase the lipolysis.
2. Fatty acids concentration increases in body fluids.
3. Under the excessive release of GH, great amount of fat is mobilized.

Therefore, a lot of acetoacetic acids (ketone bodies) are formed by the liver and released into the body fluids, thus causing (ketosis). Which is called **ketogenic effect** of GH(burning fat as a fuel)







** (IMPORTANT) keep in mind that GH , somatomedin & Insulin synergies to promote growth by **protein intake**, while **carbohydrates intake** increases levels of insulin only (the only hypoglycemic hormone in body) in order to transport glucose into the cells. While GH is decreased, somatomedin is not affected. **In Fasting**, GH increases(we need to increase glucose and F.A levels in blood), insulin and somatomedin decreases.

GH levels differ depending on:

Growth hormone is secreted in a pulsatile pattern or called diurnal rhythm, increasing and decreasing. The precise mechanisms that control secretion of growth hormone are not fully understood, but several factors related to a person's state of nutrition or stress are known to stimulate secretion**.**

1. **Age (developmental rhythm) :** GH levels are at their highest during Puberty and decline with aging.

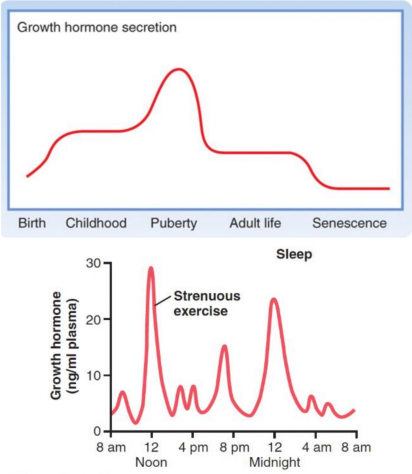


Figure 76-6. Typical variations in growth hormone secretion throughout the day, demonstrating the especially powerful effect of strenuous exercise and also the high rate of growth hormone secretion that occurs during the first few hours of deep sleep.

2. **Sleep-wake rhythm:**

Highest during strenuous exercise and at

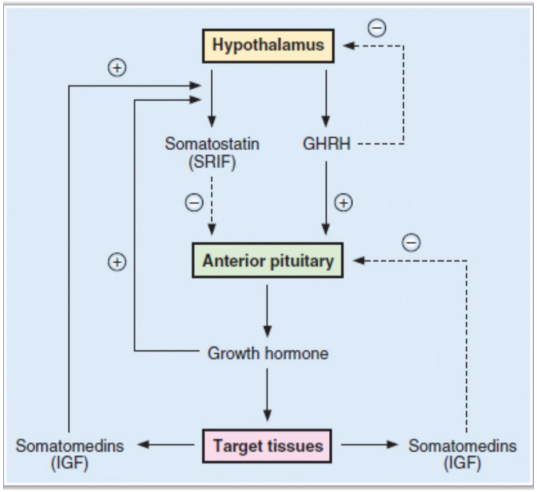
Midnight (during deep sleep).

Negative feedback control of GH release:

• GHRH inhibits its own secretion directly. (ultra-short loop).

• By stimulating the secretion of somatomedin which stimulates somatostatin secretion (which in turn inhibits the release of GH)

• by stimulating the secretion of somatostatin directly



FEEDBACK MECHANISMS FOR CONTROL OF FOOD INTAKE

- Eating is a habit

- When you feel full "satisfied", you stop eating, **how?**

The inside surface of stomach has receptors (Stretch receptors).

When filled …. The food touches the receptors … it becomes stimulated …. You feel satisfied.

if your stomach is too large, you must eat a lot to let the food touch these receptors … so, eat normally.

- **Stretch receptors** in the stomach activate sensory afferent pathway

of vagus nerve and inhibit food intake.

Peptide YY ,CCK (cholecystokinin) & insulin are gastrointestinal hormones that are released by the ingestion of food and suppress further eating.

Ghrelin is released by the stomach and intestines especially during fasting and stimulates appetite , secreted by oxyntic cells in stomach, peak before eating & fall rapidly after a meal. It stimulates the release of GH.

Leptin (adipose tissue hormone) is produced in increasing amounts by fat cells as they increase in size, it inhibits food intake.

Factors that stimulate or inhibit GH secretion

Stimulate GH secreation	Inhibit GH secreation
Decreased blood glucose	Increased blood glucose
Decreased blood free fatty acids	Increased blood free fatty acids
Increased blood amino acids (arginine)	Aging
Starvation or fasting, protein deficiency	Obesity
Trauma, stress, excitement	GH inhibitory hormone (somatostatin)
exercise	GH exogenous
Testosterone, estrogen	Somatomedins (IGF'S)
Deep sleep (stage II & IV)	
Growth hormone-releasing hormone	
ghrelin	

HORMONES OF PUTITARY

ANTERIOR LOBE	POSTERIOR LOBE
Tropic :ACTH,FSH,LH,TSH	Oxytocin
NON Tropic: MSH,GH &Prolactin	ADH (Vasopressin)

Abnormalities of GH secretion

- **Hypofunction secretion:**

1. **Panhypopituitarism :** decreased secretion of all pituitary gland hormones (anterior lobe and posterior lobe) causes:

- Extensive destructive tumors (usually Craniopharyngioma).
- Postsurgical
- Granuloma or trauma

a) **ADH deficiency** :

causes central **diabetes insipidus** which is a condition characterized by large amount of diluted urine (can reach 20 liters), increased thirst with normal glucose levels. ADH increases water absorption and eventually decreases urine volume so in the absence of adequate amount of ADH urine osmolarity will decrease (Diluted urine) and urine volume will increase (loss of water as urine will increase leading to Polydipsia "Increased thirst"). The color of the urine in case of diabetes insipidus is pale without taste because it is diluted, in contrast to diabetes mellitus which has sweet taste and normal urine color varying from light yellow to dark yellow depending on fluid intake

b) **Oxytocin deficiency**:

Deficiency of oxytocin is not problematic because baby delivery can occur without it. However, delivery process can be difficult that is why we now use substitute drugs for oxytocin deficiency.

Also, milk production is not much affected because of the presence of other factors affecting milk ejection and delivery.

Gonadotropic hormones normal function: Follicle-stimulating hormone (FSH): stimulates development of ovarian follicle and regulates spermatogenesis in the testis. Luteinizing Hormone (LH): causes ovulation and formation of the corpus luteum in the ovary, stimulates production of estrogen and progesterone by the ovary, stimulates testosterone production by the testis.

c) **Gonadotropins deficiency**:

the function of the primary sexual organs (ovaries and testis), which is the production of ova and sperms respectively and the secretion of hormones, is affected by the deficiency of the gonadotropins.

In Males: decreased libido (sexual desire), Aspermia, Loss of some facial and body hair.

In females: Decreased libido, Amenorrhea (no menstrual cycle)

Child: Delayed puberty.

Note that in all cases **gonadotropin hormones are deficient, why is that?

Out of the hormones of the pituitary gland, Gonadotropins are the hormones secreted with the least percentage (3%-5%) and if you take a section in the pituitary gland you will find the distribution of gonadotropin secreting cells (Gonadotrophs) is the least.

d)TSH deficiency: Hypothyroidism.

e) **ACTH deficiency**: Adrenal cortical insufficiency. The production of glucocorticoids and androgens is affected, especially cortisol.

f) **MSH** (Melanocyte Stimulating Hormone): its deficiency causes pallor (paleness).

• **Growth Hormone (somatotropin)**: Its deficiency causes **dwarfism** (short stature). Usually their

mentality (intelligence) is normal, but their fertility might be sometimes affected; they are

sometimes infertile. They also suffer from muscle loss, microsplanchnia (the abdomen is small compared to the thorax)

2. **Severe anterior pituitary deficiency**: deficiency of all anterior pituitary hormones (no posterior)

3. **Moderate anterior pituitary deficiency**: deficiency in all anterior pituitary hormones except STH (GH) ,it is normal.
   MSH&ACTH are partially deficient, Gonadotropin &TSH are deficient.

4. **Mild anterior pituitary deficiency**: from the anterior pituitary hormones only Gonadotropins hormones (FSH& LH) are deficient, the others are normal.

GH over secretion can cause two abnormalities which differ depending on the time when GH hormone begins to over secrete and their clinical manifestations .

Gigantism: excessive growth and height above average caused by Over secretion (genetic – not tumor) of growth hormone **before adolescence (**before fusion of growth plate which occurs in some point after puberty).

- All body tissues will grow rapidly These people height ranges from 8-9

feet (1feet = 30.48cm), they are more than 2.5m tall. Their extremities have normal proportions compared to their height.

- Giant people suffer from **Hyperglycemia** and 10% of them may develop **diabetes mellitus**.

**Extra Note: Since Giantism causes hyperglycemia, the beta cells of the islets of Langerhans in the pancreas become hyperactive and thus they become prone to degeneration. Beta cells produce insulin, and diabetes is due to the pancreas not producing enough insulin, therefore, by the degeneration of beta cells, not enough insulin will be produced and diabetes mellites may develop.

If they were not treated, they will usually suffer from panhypopituitarism,that is because gigantism is usually caused by a tumor of the pituitary gland that grows until the gland is destroyed.

acromegaly: (the adult form of the disorder)

(tumor after adolescence) caused by a tumor in

pituitary gland, it doesn't cause excessive height

(because it occurs after the fusion of the growth plate .), but the soft tissue can continue growing, so the bones get thicker . Enlargement marked in the small bones of the hands, feet, and in the membranous bones, including the cranium, nose, forehead, supraorbital ridge, the lower jaw bones, and portions of the vertebraeAlso many soft tissues in organs like liver, tongue and **kidneys** become greatly enlarged.

** the most important thing you need to know is that Gigantism occurs when the growth hormone over-secretion occurs before puberty (adolescence), while in Acromegaly, over-secretion occurs after puberty.

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Gigantism

Acromegaly (thickening of bones)