Weight loss seminar

Weight loss introduction

Done by : Saif AlJbour

Definition of weight loss

Weight loss is a decrease in body weight resulting from either voluntary or involuntary circumstances. Most instances of weight loss arise due to loss of body fat, but in cases of extreme or severe weight loss, protein and other substances of the body can be depleted.

‘(BMI)Body mass index

BMI =weight(kg) /height m^2

Classification	BMI Category (kg/m2)	Risk of Developing Health Problems
Underweight	< 18.5	Increased
Normal Weight	18.5 – 24.9	Least
Overweight	25.0 – 29.9	Increased
Obese		
Class I	30.0 – 34.9	High
Class II	35.0 – 39.9	Very High
Class III	≥ 40.0	Extremely High

Weight loss classification

- Weight loss can be classified according to three things: severity, types and the nature of lost weight.

1) according to severity:

A) mild %5 :of body weight.

B) moderate: %10-5of body weight.

C) severe %10 < :of body weight.

2) according to nature of lost weight:

A) loss of fat.

B) loss of muscles.

C) loss of water.

3)According to types:

A)voluntary or intentional weight loss.

B)involuntary or unintentional weight loss.

Voluntary weight loss

It's the loss of total body mass as a result of efforts to improve fitness and health which is achieved by adopting a lifestyle in which:

1) fewer calories are consumed than are expended.
2) increasing the physical activity in the form of exercise.

- Also it could be required for certain jobs such as modeling or athletics especially runners.
- Weight loss in overweight or obese reduces risk for diabetes, heart diseases, stroke, HTN, and many other diseases.

Involuntary weight loss

- It's defined as a noticeable drop in body weight that occurs even if the person is not trying to lose weight, that the weight does not come about because of diet or exercise.

- Weight loss of 10% of body weight over a period of 6 to 12 months is considered a significant weight loss. It can occur in anyone. However, it is most common and most serious in people who are over the age of 65.

Epidemiology

It's estimated that 15-20% of adults who are older than 65 years have unintentional weight loss if followed over 5 to 10 years. Also, up to 8% of outpatients will have unintentional weight loss.

- The strongest independent predictors of unintentional weight loss were age, smoking and poor health.
- There were no significant sex differences in weight loss incidence

Mortality

Unintentional weight loss is associated with a significant increase in risk of all-cause mortality compared with people who reported no weight change, even after adjustments for lifestyle characteristics and preexisting diseases.

On the other hand, people who lost weight intentionally showed significant benefit in all-cause mortality.

Involuntary weight loss causes

1-Gastrointestinal
2-Endocrine
3-malignancy
4-neurology
5-Cardiac
6-Pulmonary
7-substance abuse and drugs
8-HIV and other infections
9-psychiatric disorder

Weight loss causes : Endocrine and gastrointestinal

Presented by..
Bushra Al- Faqeer

Endocrine and gastrointestinal causes of weight loss

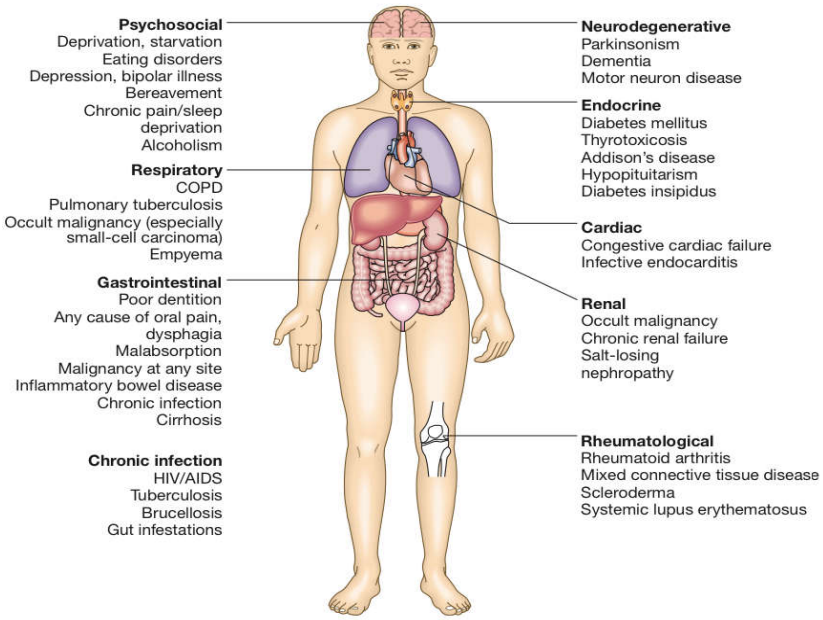
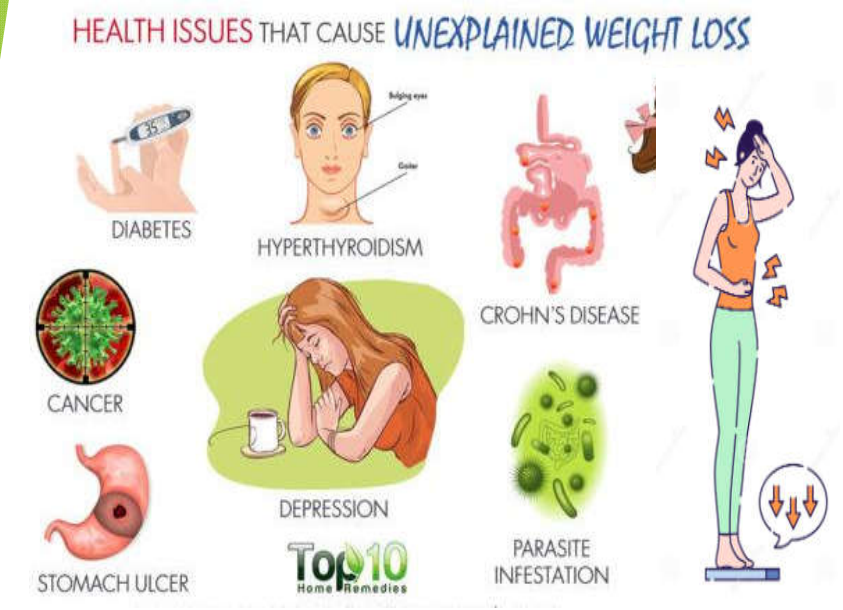
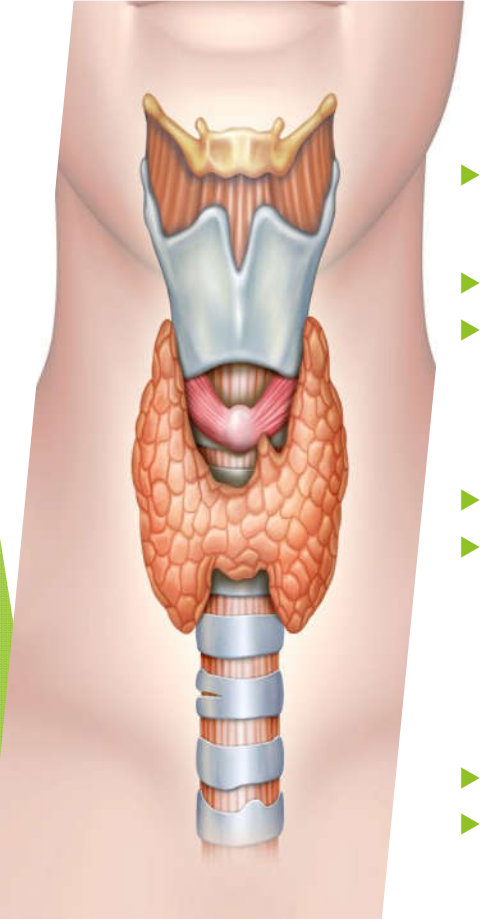


Fig. 22.23 Some important causes of weight loss.

Endocrine causes of weight loss

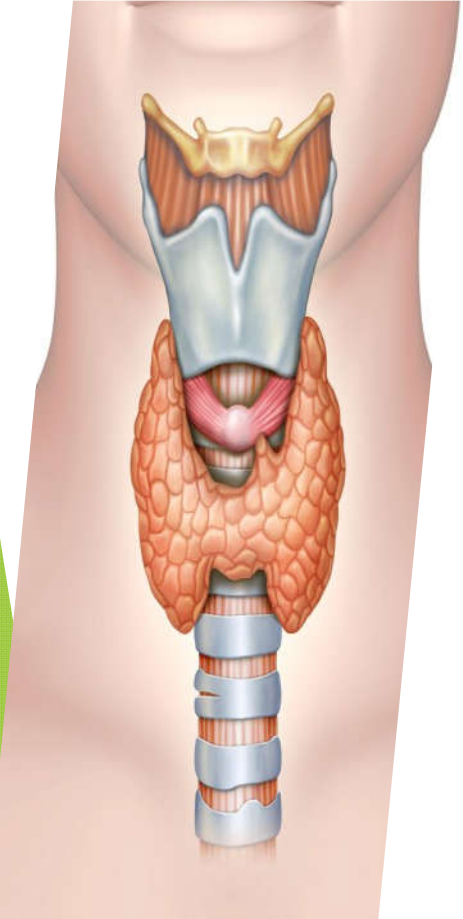


- Hyperthyroidism
- Diabetes mellitus
- Adrenal insufficiency
- Hypopitutarism
- Diabetes insipidus



Overview of the thyroid gland : Anatomy , function and types of hyperthyroidism

- **The thyroid gland:** is an endocrine gland found in the neck, it is responsible for regulating the body's metabolic rate via hormones it produces(T3,T4).
- **Anatomical Location**
- The thyroid gland is located in the anterior neck and spans the C5-T1 vertebrae. It consists of two lobes (left and right), which are connected by a central isthmus anteriorly – this produces a butterfly-shape appearance.
- **Function**
- The thyroid gland is one of the main regulators of metabolism. T3 and T4 typically act via nuclear receptors in target tissues and initiate a variety of metabolic pathways. High levels of them typically cause these processes to occur faster or more frequently. Metabolic processes increased by thyroid hormones include:
- Basal Metabolic Rate
- Gluconeogenesis



Protein synthesis

Glycogenolysis

Lipogenesis

Thermogenesis

This is achieved in a number of ways, such as increasing the size and number of mitochondria within cells, increasing Na-K pump activity and increasing the presence of β-adrenergic receptors in tissues such as cardiac muscle.

Types of hyperthyroidism:

Hyperthyroidism : is overactivity of the thyroid gland, which results in a number of symptoms and signs. It can be primary or secondary:

Primary hyperthyroidism the pathology is within the thyroid gland itself .(high T3,T4, low TSH).

Secondary hyperthyroidism is when the thyroid gland is stimulated by excessive thyroid-stimulating hormone (TSH) in the circulation.(high TSH and high levels of both T3,T4).

Patients with hyperthyroidism experience a **fast heartbeat, increased appetite, anxiety, sensitivity to heat, and sudden weight loss.**

Hyperthyroidism most commonly occurs in three ways:

thyroiditis, or
an inflammation of the thyroid.

a thyroid nodule
that produces too much T4 hormone.

an autoimmune
condition known as Graves' disease.

Thyroid hormones help the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should.
Weight loss is a classic symptom of hyperthyroidism.
Most patients have hyperphagia.
Some younger patients with mild hyperthyroidism eat enough to actually gain weight.
In older patients, however, hyperthyroidism often causes anorexia with accelerated weight loss.

WHAT IS THE RELATIONSHIP BETWEEN THYROID AND WEIGHT?

Patients with hyperthyroidism are found to have high BMRs.
Metabolism is determined by measuring the amount of oxygen used by the body over a specific amount of time. If the measurement is made at rest, it is known as the basal metabolic rate (BMR).

BMR: The amount of energy needed while resting in a neutrally temperate environment when the digestive system is inactive.

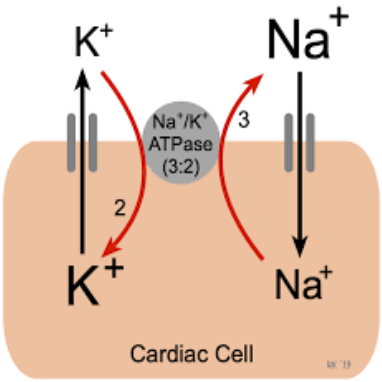
- **Furthermore, weight loss is related to the severity of the overactive thyroid.**

- **For example, if the thyroid is extremely overactive, the individual's BMR increases which leads to increased calories needed to maintain the body weight. If the person does not increase the amount of calories eaten to match the excess calories burned, then there will be weight loss.**

- **The effects of thyroid hormone (T3) on various organ systems are as follows:**
- **Basal metabolic rate (BMR): One of the most significant and pronounced effects of thyroid hormone is increased oxygen consumption and a resulting increase in BMR and body tempreture.**

- **Thyroid hormones increase oxygen consumption in all tissues except the brain, gonads, and spleen by inducing the synthesis and increasing the activity of the Na+-K+ ATPase. The Na+-K+ ATPase is responsible for primary active transport of Na+ and K+ in all cells; this activity is highly correlated with and accounts for a large percentage of the total oxygen consumption and heat production in the body.**

- Thus, when thyroid hormones increase Na+-K+ ATPase activity, they also increase oxygen consumption, BMR, and heat production all of these effects explain the weight loss in patient with thyrotoxicosis.



Metabolism:

- Ultimately, increased oxygen consumption depends on increased availability of substrates for oxidative metabolism.
- Thyroid hormones increase glucose absorption from the gastrointestinal tract and potentiate the effects of other hormones (e.g., catecholamines, glucagon, growth hormone) on gluconeogenesis, lipolysis, and proteolysis.

- Thyroid hormones increase both protein synthesis and degradation, but, overall, their effect is catabolic (i.e., net degradation), which results in decreased muscle mass and weight loss.

Hyperthyroidism and increase food intake

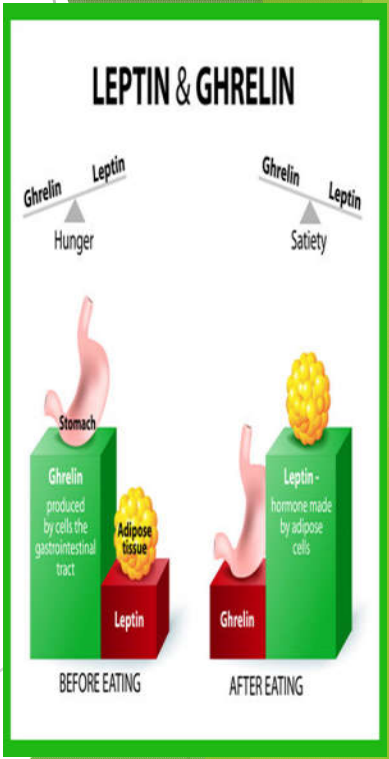
Hyperthyroidism is associated with weight loss despite increased appetite. Increase T3and T4 levels are associated with increased food intake ,possibly as a compensatory response to increased energy expenditure due to uncoupling of oxidative phosphorylation resulting in increased thermogenesis. And its direct effect on hypothalamus.

The mechanisms responsible for the stimulation of food intake by thyroid hormone

Food intake is regulated by complex mechanism involving hypothalamic neuropeptides which respond to peripheral satiety signals like leptin and ghrelin.

Leptin is a fundamental signal for satiety to the brain and also increases thermogenesis thereby playing a major role in energy homeostasis. In animal models of T3 induced thyrotoxicosis, it has been found that decreased plasma leptin level and decreased sensitivity of satiety centre to leptin could contribute to hyperphagia.

Ghrelin is a novel peptide secreted from the fundus of the stomach. It enhances hunger and appetite and transduces signals to hypothalamic regulatory nuclei that modulate energy balance in normal physiology. Despite increase in appetite in patients with hyperthyroidism, serum total ghrelin level has been shown to be normal or low. In majority of the earlier studies, serum total ghrelin was measured rather than acylated ghrelin which is the biologically active form .



At the time of diagnosis of hyperthyroidism, there is a substantial weight loss despite increase in hunger and food intake in majority of the patients. Weight loss in patients with hyperthyroidism is attributable to exaggerated thermogenesis mediated by uncoupling of oxidative phosphorylation by thyroid hormones.

- **Nevertheless, on average the more severe the hyperthyroidism, the greater the weight loss observed. Weight loss is also observed in other conditions where thyroid hormones are elevated, such as in the toxic phase of thyroiditis or if the dose of thyroid hormone pills is too high for a patient. Since hyperthyroidism also increases appetite, some patients may not lose weight, and some may actually gain weight, depending on how much they increase their caloric intake.**

CAN THYROID HORMONE BE USED TO HELP ME LOSE WEIGHT?

- Thyroid hormones have been used as a weight loss tool in the past.

- Studies have shown that excess thyroid hormone treatment can help produce more weight loss than can be achieved by dieting alone, but includes the risk of major negative consequences from the use of thyroid hormone to help with weight loss, such as the loss of muscle protein, loss of bone, and/or heart problems.
- Furthermore, once the excess thyroid hormone is stopped, any weight loss is usually regained.

Diabetes Mellitus

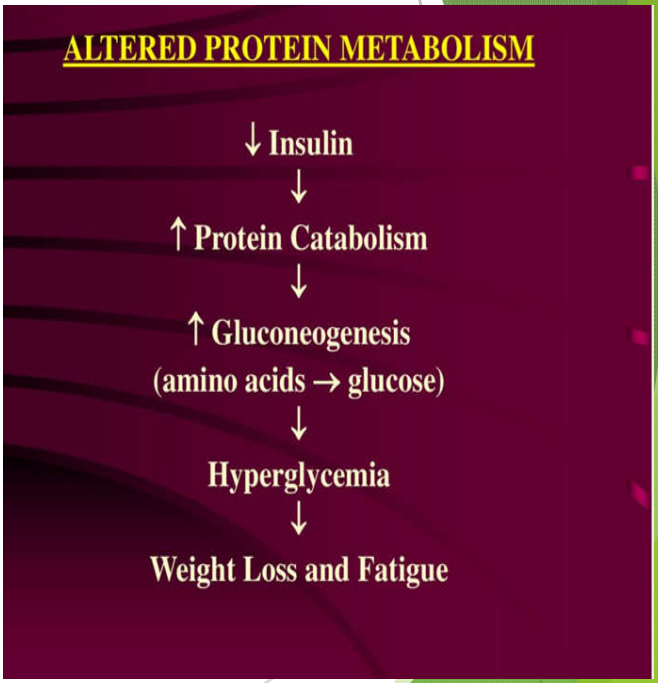
- Chronic disorder caused by increased blood glucose levels due to insulin resistance or inulin insufficiency.

- **There are two types of DM:**

- Type 1 D.M is associated with type 4 hypersensitivity reaction which involves T-cell mediated destruction of pancreatic beta cells ,which produces insulin. This will lead to insufficient amounts of insulin. It is a childhood disorder that peaks at 4-6 and 10-14 years of age. The patient must take a lifelong insulin replacement therapy.

Type 2 D.M (most common) is associated with insulin resistance leading to hyperglycemia which increases the pancreatic production of insulin. Finally, the pancreas will fail and the insulin levels will become low. The risk factors of Type 2 D.M, which is common in adults, are obesity and a family history of diabetes.
- The classic symptoms of hyperglycemia (including polyuria, polydipsia, nocturia, blurred vision, dehydration, frothy smelling of breath in DKA and weight loss).

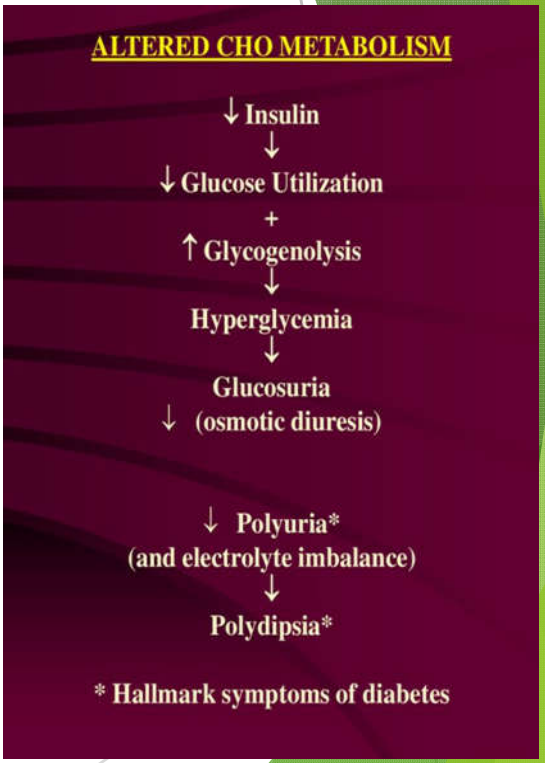
DM and weight loss



DM and weight loss

- Uncontrolled diabetes mellitus can cause weight loss with increased appetite, particularly with new-onset type 1 diabetes mellitus. Although patients with poorly controlled or undiagnosed type 2 diabetes can occasionally present with weight loss, weight gain is much more common.

Undiagnosed or untreated type 1 diabetes can cause weight loss. Glucose builds up in the bloodstream if insulin isn't available to move it into the body's cells. When glucose levels become high, the kidneys work to get rid of unused sugar through urine. This causes weight loss due to dehydration and loss of calories from the sugar that wasn't used as energy.



Kids who develop type 1 diabetes often lose weight even though they have a normal or increased appetite. If blood sugars are very high, patients with diabetes tend to urinate a lot, and this results in dehydration as a possible cause of weight loss. Also, muscle breakdown can occur if sugars are too high, causing an unhealthy weight loss.

- However, some patients with type 2 diabetes can occasionally present with diabetic neuropathic cachexia, an unusual and poorly understood syndrome characterized by profound weight loss (as much as 60 percent of body weight) and often severe neuropathic pain of the anterior thighs.

When to call your doctor?

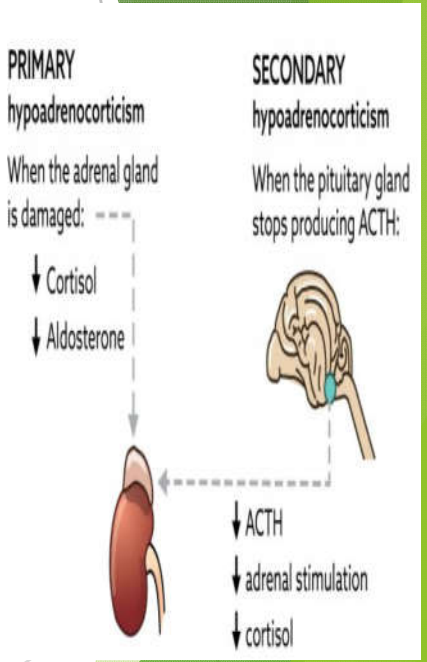
- If you have unintentionally lost more than 5% of your normal body weight, or more than 10 lbs (4.5 kg) in 6 – 12 months or less, you should consult your doctor.
- They will be able to determine what's causing the weight loss (e.g. undiagnosed diabetes) and the best way to treat the problem.
- Look for evidence of weight loss and dehydration. Unintentional weight loss is suggestive of insulin deficiency.

Addison’s disease and weight loss

Adrenal insufficiency can be primary or secondary:

- **Primary adrenal insufficiency: (Addison's disease). It occurs when the adrenal glands are damaged. They don’t make enough of the hormones cortisol and aldosterone. It may occur at any age.**
- **Secondary adrenal insufficiency: This starts when the pituitary gland doesn’t make enough of the hormone ACTH (adrenocorticotropin). As a result the adrenal glands don’t make enough cortisol.**

Cortisol's most important job is to help the body respond to stress. Also:
helps maintain blood pressure and heart function
helps slow the immune system's inflammation response
helps balance the effects of insulin in breaking down sugar for energy.

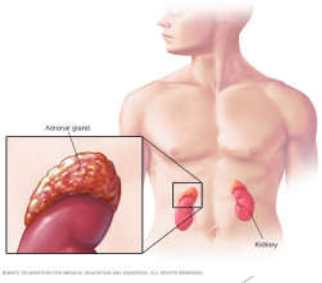


- helps regulate the metabolism of proteins, carbohydrates, and fats.
- helps maintain proper arousal and sense of well-being.

Symptoms may include:

- Weakness ,Fluid loss (dehydration),Lack of appetite ,Upset stomach (nausea), Vomiting, Diarrhea all of these symptoms may contribute to weight loss.

A patient having Addison's disease loses weight due to anorexia and vomiting. Usually despite intaking more food than usual.

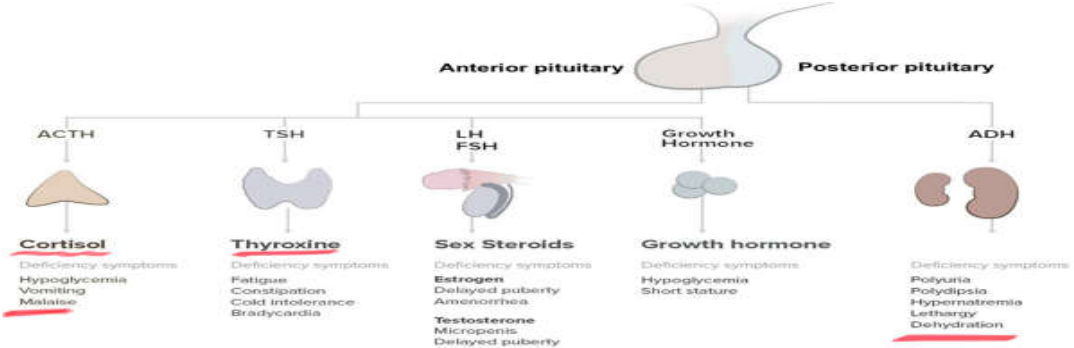


Hypopituitarism and weight loss:

- Symptoms can include:

. Low adrenocorticotropic hormone (ACTH) levels can lead to decreased production of cortisol by the adrenal glands. This can cause tiredness, weakness, dizziness or light-headedness, blackouts (usually as a result of low blood pressure), low blood sugar levels, low sodium levels, weight loss, loss of appetite, nausea, vomiting and diarrhoea.

It may lead to low (TSH) levels leading to decrease production of thyroid hormones by thyroid gland. This can cause tiredness and weight gain.



Pheochromocytoma and weight loss

- **Pheochromocytoma:** is a relatively rare tumor of the adrenal glands,blood and urine analysis can confirm the diagnosis of pheochromocytoma by detecting elevated level of catecholamines in the plasma. Headache, sweating, and a fast heartbeat are typical symptoms, usually in association with markedly high blood pressure.

- The hyperadrenergic state among patients with pheochromocytoma would theoretically cause weight loss with increased appetite, but only 5 percent of patients with pheochromocytomas report weight loss.

Gastrointestinal causes of weight loss:

Inflammatory bowel disease and weight loss:
IBD refers to the two chronic inflammatory disorders of the digestive tract, namely Crohn's disease and Ulcerative colitis. While Crohn's disease can cause inflammation in any part of the gastrointestinal tract, from the mouth to the anus, ulcerative colitis affects only the large intestine.

IBD can reduce the body's ability to digest food properly, resulting in malnutrition and unexplained weight loss. IBD also disrupts the hunger and satiety hormones, leading to decreased appetite.

Can IBS cause loss of appetite and weight loss?

It cannot directly affect a person's weight but the symptoms may cause patients to avoid certain foods, which may lead to weight loss.

What are some reasons for poor appetite?

Appetite loss is reported in about 1 in 5 people with Crohn's disease and in about 1 in 10 people with ulcerative colitis. Unsurprisingly, problems with appetite in people with IBD are worse during flares.
For most people, appetite improves during remission. One small study compared hunger between people with active Crohn's disease, inactive Crohn's disease, and no Crohn's disease. The people with active Crohn's disease reported feeling less hungry than the other 2 groups at baseline and after drinking 500 mL (~2 cups) of water.

There are many reasons for loss of appetite in IBD. Some people may develop food aversions because they associate eating with pain.

After a while, you may try to avoid eating in order to avoid pain or unpleasant symptoms.

Depression is common among people with IBD and can lead to a loss of appetite.

Inflammation and hormone changes probably have a role in poor appetite. IBD changes the levels of hormones such as leptin and ghrelin. These hormones have a role in making you feel hungry or full. They also seem to be out of balance in people with active IBD.

An increase in inflammatory signals, such as tumor necrosis factor-α (TNF-α) and interleukins, has been linked with poor nutritional status.

- An older study showed that people with Crohn's disease who had lost weight reported lower levels of hunger and less pleasure from eating than people who had not lost weight. The people who lost weight reported that they had eliminated an average of 16 of 52 food items. This restriction resulted in a low-calorie intake. Interestingly, in this study, many of the foods had been eliminated at the advice of treating physicians.

How common is weight loss in people with IBD?

- Weight loss is very common in people with IBD. One study found that as many as 80% of people who are hospitalized for Crohn's disease lose weight. Outside the hospital, about 20% to 40% of patients also have weight loss. Weight loss is frequently seen in children with IBD, and weight loss is present at the time of diagnosis in 90% of children with IBD.

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- There are many possible ways to evaluate weight loss. For adults, a common way is to evaluate the percentage of weight loss over a certain period of time .

Calculation:

- [(Usual body weight - actual body weight) / Usual body weight] x 100% = Percentage of weight loss

Significant weight loss:	Severe weight loss:
5% over 1 month	>5% over 1 month
7.5% over 3 months	>7.5% over 3 months
10% over 6 months	>10% over 6 months

Chronic Pancreatitis and Weight Loss:

- **Chronic pancreatitis:** is inflammation of the pancreas that gets worse over time and leads to permanent damage.

- Patients with chronic pancreatitis may suffer from maldigestion and malnutrition. Longstanding inflammation and fibrosis in the gland can destroy exocrine tissue, leading to inadequate delivery of digestive enzymes to the duodenum.

- Maldigestion is associated with inadequate bicarbonate delivery to the duodenum.

  - **Symptoms of Chronic Pancreatitis include:** abdominal pain, nausea, vomiting, postprandial satiety, gastric dysmotility and mechanical gastric outlet obstruction, steatorrhea and **weight loss.**

- **Peptic Ulcer and Weight Loss:**

Peptic ulcers: are open sores in the stomach, upper intestine or esophagus caused by bacterial infections or medications, not by stress or spicy foods. Symptoms include: abdominal pain which is worse at night or when your stomach is empty, vomiting blood or dark or bloody stools.

Peptic ulcer leading to difficulty of swallowing food..

- **food that is eaten comes back up.**
- **feeling unwell after eating.**
- **loss of appetite.**
- **These conditions explain weight loss in patients with Peptic Ulcer.**

Malnutrition and weight loss

Malnutrition is a serious condition that happens when your diet does not contain the right amount of nutrients.It means "poor nutrition" and can refer to:

- undernutrition – not getting enough nutrients.
- overnutrition – getting more nutrients than needed.

Common signs of malnutrition include:

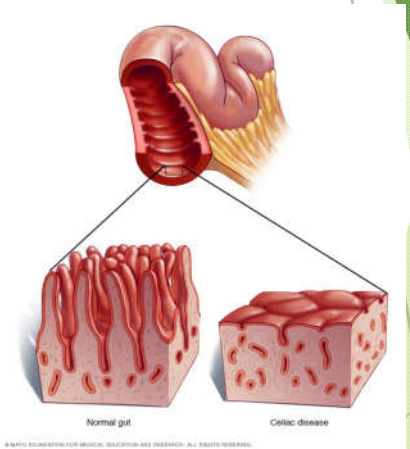
- unintentional weight loss – losing 5% to 10% or more of weight over 3 to 6 months is one of the main signs of malnutrition.
- a low body weight – people with a body mass index (BMI) under 18.5 are at risk of being malnourished .

Celiac disease and weight loss

Celiac disease, sometimes called gluten-sensitive enteropathy, is an immune reaction to eating gluten, a protein found in wheat, barley and rye.

If you have celiac disease, eating gluten triggers an immune response in your small intestine. Over time, this reaction damages your small intestine's lining and prevents it from absorbing some nutrients (malabsorption). The intestinal damage often causes diarrhea, fatigue, weight loss, bloating and anemia, and can lead to serious complications.

In children, malabsorption can affect growth and development leading to weight loss.

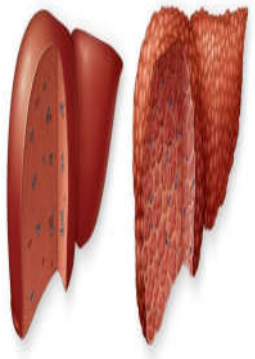


A previous study of liver transplant patients and its relationship to wight loss

Malnutrition is widely described in patients waiting for liver transplantation (LTx). OBJECTIVES: The aim of this study was to assess weight loss and its risk factors during liver disease and up to the first appointment after transplantation. Patients who underwent LTx were retrospectively assessed for weight loss during liver disease while on the waiting list for LTx. The usual weight of the patients before disease and their weight on the first outpatient appointment after transplant were considered. Demographic, socioeconomic, lifestyle and clinical variables were collected to assess risk factors. We retrospectively evaluated 163 patients undergoing LTx between 1997 and 2008.

RESULTS: Patients lost in average 7.7 to 12.4 kg while ill. Among these indications, patients with alcoholic cirrhosis had lost significantly more weight, and those with hepatitis C virus and autoimmune hepatitis had lost significantly less weight.

CONCLUSIONS: Patients experienced weight loss during liver disease independent of age, sex, schooling and income; however, the etiology of liver disease was related to weight loss.



Summary:

Digestive conditions often cause weight loss directly because they decrease the amount of calories and nutrients the body is able to absorb, or give the patient symptoms that make them not want to eat.

Conditions that behave this way include:

- **Chronic diarrhea and other infections that last a long time, such as parasites.**
- **Chronic pancreatitis**

- Removal of part of the small intestine
- Crohn's disease
- Celiac disease
- Cirrhosis
- Ulcerative colitis
- Peptic ulcers
- Gastroparesis
- Constipation
- Mass tumor in the digestive tract, and
- Cancer of the esophagus, stomach, colon, liver, pancreas, or bile ducts.

Malignancy and Weight loss

Done by : Ghassan Al-falogi

Malignancy and weight loss

Malignancies (particularly gastrointestinal, pancreatic, lung, lymphoma, renal, and prostate cancers) often cause weight loss.

In a prospective cohort study from Spain, 2677 adults were systematically evaluated for unintentional weight loss and 883 were diagnosed within the first six months of evaluation.

Among patients with unintentional weight loss, malignancy was associated with older age, male sex and active smoking.

For many people, weight loss is the first visible sign of cancer. 80 percent of people with pancreatic cancer, esophageal cancer, or stomach cancer have lost a significant amount of weight by the time they're diagnosed.

Malignancy and Weight loss

Cancer patients may have pain, abdominal distention, nausea, vomiting, dysphagia, early satiety due to hepatosplenic enlargement or malignant obstruction.

Cancer treatment can also leads to weight loss.
Radiation and chemotherapy commonly cause a decrease in appetite. Weight loss can also be attributable to radiation and chemotherapy side effects that discourage eating, such as: mouth sores, nausea, vomiting and fatigue

Our immune response to cancer produces pro-inflammatory cytokines and alters your body's metabolism. This disrupts the hormones that regulate your appetite. It also promotes the breakdown of fat and muscle . Also, a growing tumor uses a significant amount of your body's energy, which increases your resting energy expenditure (REE) leading to weight loss

Malignancy and Weight loss

Malignancy and Weight loss

Cachexia is derived from the Greek word kakos, meaning “bad”, and hexus, meaning “condition”.

Cachexia “wasting syndrome” is a chronic hypercatabolic state defined as accelerated loss of skeletal muscle in the context of a chronic inflammatory response, can occur in the setting of advanced Cancer as well as in Chronic infection, AIDS, Heart failure, Rheumatoid arthritis, Celiac disease, Crohns disease and COPD.

Across malignancies, cachexia is highly prevalent, impacting approximately one-half of patients with advanced cancer. While loss of appetite with weight loss is common among cancer patients, the profound weight loss suffered by patients with cachexia cannot be entirely attributed to poor caloric intake. Insufficient oral intake is superimposed upon complex metabolic aberrations that lead to an increase in basal energy expenditure and culminate in a loss of lean body mass from skeletal muscle wasting. In contrast to simple starvation, which is characterized by a caloric deficiency that can be reversed with appropriate feeding, the weight loss of cachexia cannot be adequately treated with aggressive feeding.

Malignancy and Weight loss

Malignancy and Weight loss

What causes cachexia?

Cachexia is associated with increased production of TNFa (called cachectin) which activates the ubiquitin proteasome proteolytic system which is associated with destruction of cellular proteins.

Neuropeptide Y is a neurotransmitter that activates certain centers in the hypothalamus and causes you to feel hungry. In cachexia there is high levels of leptin which is a hormone released from the adipose tissue and disrupting the neuropeptide Y effects. SO, the person losses the appetite

Neurologic diseases and Weight loss

Parkinson's disease

Stroke

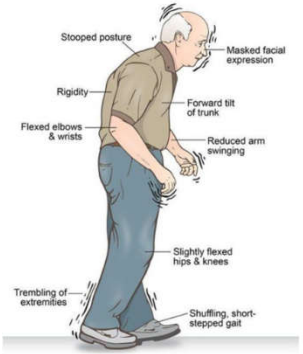
Dementia

amyotrophic lateral sclerosis

Neurologic diseases and Weight loss

Parkinson's disease is a neurodegenerative disorder in which there destruction of neurons producing dopamine in the substantia nigra which is part of the basal ganglia. The basal ganglia controls the body movements through its connections with the motor cortex.

PD is associated with Pill-Rolling tremor(Resting tremor),Rigidity, bradykinesia or hyperkinesia.



T Tremor: shaking, usually starting on one side

R Rigidity: stiffness of the limbs, neck, or trunk

A Akinesia: loss or impairment in power of voluntary movement

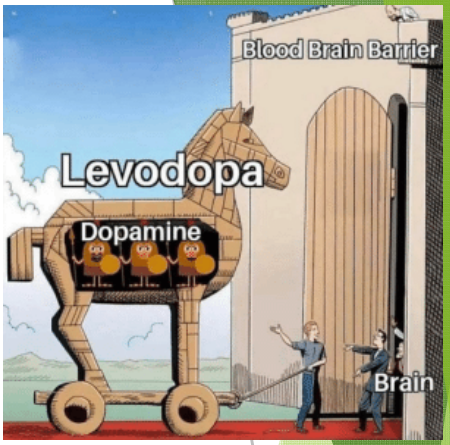
P Posture and balance

Neurologic diseases and Weight loss

PD can cause weight loss :

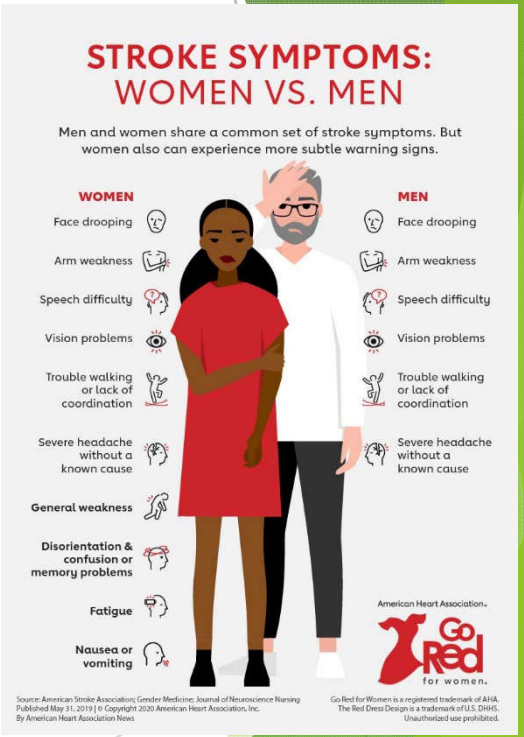
1- Increased energy expenditure due to Dyskinesia which is extra movements (can be a side effect of carbidopa/levodopa0) or Tremor as well as muscle rigidity, if persistent, they can be causes of excessive energy consumption and subsequent weight loss.

2-Decreased food intake because some people with difficulty swallowing associated with PD will typically slow down their eating and reduce their consumption in an attempt to eat without coughing or choking. Also, Depression, a common non-motor symptom of PD, and Nausea, a side effect of PD medications, have a significant impact on appetite.



Neurologic diseases and Weight loss

- Dementia is not a specific disease but is rather a general term for the impaired ability to remember, think, or make decisions that interferes with doing everyday activities. Alzheimer's disease is the most common type of dementia. Though dementia mostly affects older adults, it is not a part of normal aging.
- Patients with dementia can experience BW loss from reduced energy intake owing to their decreased mental status, which causes them to simply forget or refuse to eat.
- Stroke is associated with Dysphagia, so patients try to slow down their eating and reduce their consumption in an attempt to eat without coughing or choking



Weight loss in advanced chronic diseases

Done By : Amro Bani Hani

First : HF and cardiac cachexia

- Cardiac cachexia defined as documented non-edematous weight loss of >6% of the previous normal weight observed over a period of **>** 6 months
- Cachexia is a well-known problem in patients with end-stage chronic HF, and it is a risk factor of death for the patients at this stage of the disease. It is estimated to affect between 5% -15% of HF patients, especially those with HF with reduced ejection fraction (HFrEF).
- The annual mortality due to cardiac cachexia is 20–40%. Although the cardiac cachexia problem is well known and well documented, it is still difficult to develop a specific therapy for its prevention and treatment due to the multifactorial myocardial injury.

First : HF and cardiac cachexia

- **Pathophysiology of cardiac cachexia in CHF :** Although the mechanism of cardiac cachexia is not entirely understood, it is probably multifactorial and associated with elevation of the resting metabolic rates , anorexia, immunologic, metabolic, and neuro-hormonal changes :
- It is common in CHF patients to come with hypo-albuminemia (mainly due to increased volume of distribution). It seems that hypo-albuminemia provokes changes in the activity of inflammatory cytokines. It causes increased secretion of TNF-alpha, IL-1 and IL-6, and all of them further activation of catabolic processes.
- **The multifactorial mechanism of cardiac cachexia include:**

I. Increased energy requirements : Patients with CHF have increased resting energy requirements through a variety of mechanisms which are inflammation, sympathetic activation, increased work of breathing, and tachycardia.

First : HF and cardiac cachexia

II. Decreased nutrient absorption:

- In CHF, there can be reduced perfusion to the gastrointestinal system which may contribute to decreased absorption of nutrients
- Elevation of pro-inflammatory cytokines(TNF-alpha, IL-1,IL-6) due to chronic HF causes chronic generalized inflammation, including the alimentary tract. This inflammation results in the thickening of intestinal walls and increased bacterial growth .
- These changes have a negative influence on the absorption of nutrients from intestines which result in mainly proteins malnutrition and, consequently, muscle wasting, because muscle wasting causes elevation of serum amino acids to provide substrates for gluconeogenesis which increased energy expenditure.
- In addition patients with CHF have congestive hepatomegaly and abdominal fullness (congested intestinal veins) which causes also impairment of intestinal absorption as well as nausea and vomiting.

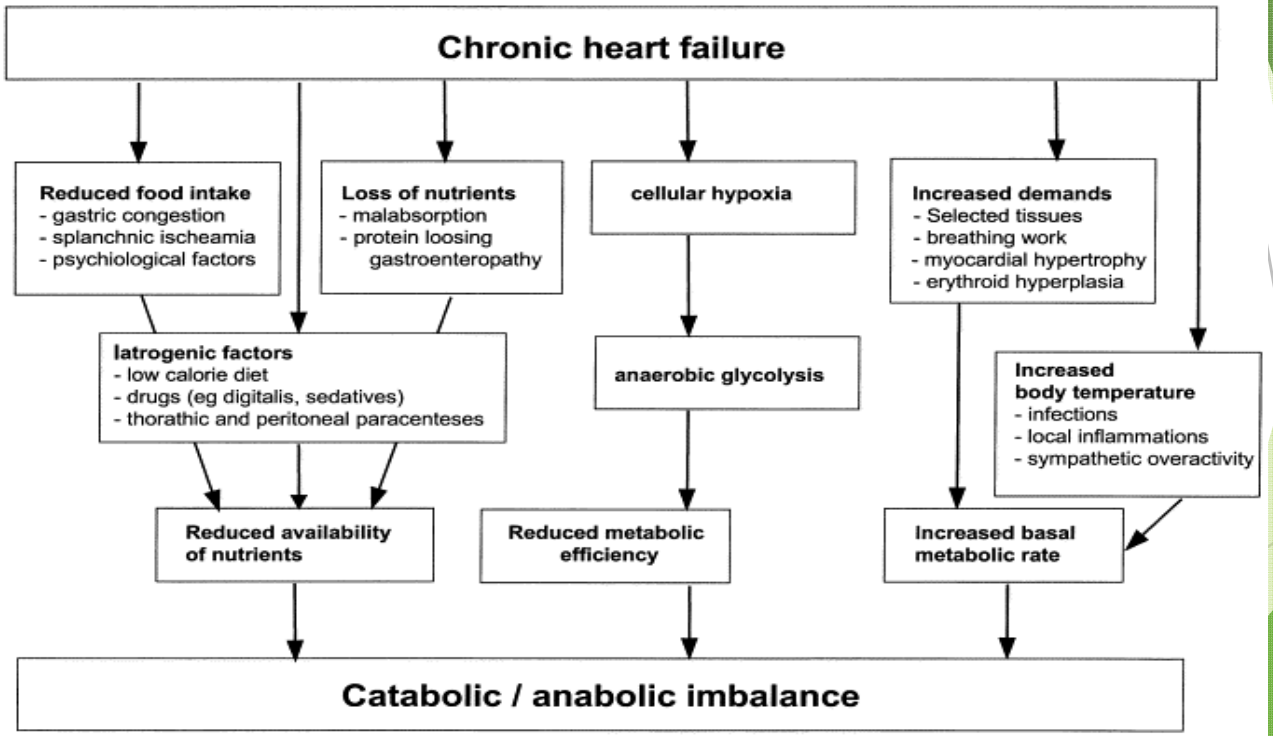
First : HF and cardiac cachexia

III.Metabolic alterations: there are multiple metabolic alterations involved in the pathophysiology of cardiac cachexia. However, at the core is increased flux of protein, that is, decreased protein synthesis, increased protein catabolism, or both, resulting in a net loss of lean tissue. Although there are multiple proteolytic pathways in tissues, the most important one in cachexia appears to be the ubiquitin–proteasome pathway. This pathway is activated by NF-kB, which is, in turn, stimulated by inflammatory cytokines and reactive oxygen species which tend to be elevated in CHF patients .

IV.Angiotensin II plays a key role in cardiac cachexia. It promotes proteolysis in the muscular tissue by increased secretion of IL-6 as well as decreases the activation of muscular satellite cells, thus disturbing regeneration of injured muscular fibers.

The fluid retention associated with chronic heart failure often masks the extensive loss of lean body mass.

First: HF and cardiac cachexia



Secondly: COPD and pulmonary cachexia

- **COPD** is lung disease which primarily characterized by the presence of airflow limitation resulting from airways inflammation and remodeling, often associated with parenchymal destruction and the development of emphysema.

- The prevalence of cachexia is variously presented as 20–40% in COPD patients. It is a determinant of mortality in COPD, independent of airflow obstruction.

- A recent unbiased statistical approach suggests that not all COPD patients but only the emphysematous phenotype is prone to cachexia.

Secondly: COPD and pulmonary cachexia

Pathophysiology of pulmonary cachexia in COPD : The potential mechanism has been variously suggested to result from the following:

I.Energy imbalance: It was postulated that due to airways obstruction, the work of breathing was increased **(**increased respiratory muscle work**)**,and hyper-metabolism has been noted in COPD patient.

In certain study found that resting energy expenditure was to be 10% higher in COPD patients than in normal subjects of a similar age, height and weight. The oxygen cost of exercise has also been found to be higher than in normal subjects.

So, without a corresponding increase in caloric intake, patients would inexorably lose weight because obstruction was irreversible.

Secondly: COPD and pulmonary cachexia

It is noted that there is some fibre-type shift in skeletal muscle in COPD away from type I and towards type II. It is known that type II muscle uses more oxygen per unit work output than type I, thus, there is an extra metabolic load due to oxygen-inefficient muscle usage.

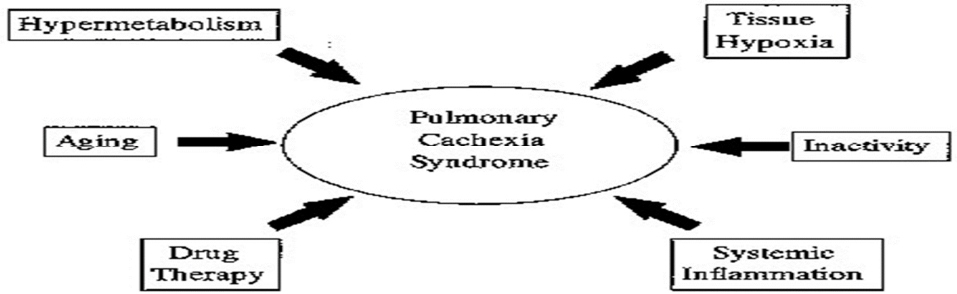
Another factor is that cachexia itself leads to anorexia, and this must create a vicious circle, such that the more weight lost, the less food is taken in.

II.Arterial hypoxemia : It has been suggested that the hypoxaemia of COPD is a causative factor in cachexia. Hypoxaemia may increase the generation of ROS and TNF-a, which may in turn give rise to inflammatory changes leading to cachexia.

Secondly: COPD and pulmonary cachexia

III. Systemic inflammation : TNF-a is noted to be high in COPD patient .It is a molecule that has among its effects the up-regulation of the transcription factor NF-kB (which activate ubiquitin–proteasome pathway), which in turn up-regulates the protein breakdown machinery in cells, providing a molecular mechanism for muscle loss.

IV. Disuse atrophy of the muscles : Patients with severe COPD are very inactive. Thus, extreme inactivity may play a role in cachexia.



Thirdly: cachexia in chronic kidney disease

- The definition of CKD is based on the presence of kidney damage or decreased kidney function indicated by a glomerular filtration rate <60 for three months or more, irrespective of the cause.
- In patients with chronic kidney disease (CKD) managed with or without dialysis, the prevalence of cachexia has been reported to range from 30-60%.

- **The pathophysiology of cachexia in CKD:**

- The pathogenesis of cachexia in renal patients is multifactorial, but anorexia and reduced food intake, as well as profound changes in macronutrient metabolism are the driving forces, leading to a practically not reversible catabolic status.

- one of the most important player in the pathogenesis of cachexia in renal patients is the reduction of appetite, that is, anorexia**.** **Anorexia** in CKD patients is multifactorial. It could be caused as a symptom of Uremic toxicity (uremia is commonly high in CKD patients).

- Also anorexia can be caused by inflammation. In a large study involving a cohort of 331 patients undergoing maintenance hemodialysis, the presence of impaired appetite (reported by 38% of the patients studied). Interestingly, anorexia was associated with increased circulating levels of surrogate markers of inflammation, that is, Tumor Necrosis Factor-α and C-reactive protein. These data points to inflammation as the major trigger of the molecular cascade of events eventually leading to anorexia.

- inflammation may also trigger the progressive wasting of skeletal muscles by inflammation-mediated activation of specific proteases. In uremic patients, the first step in muscle protein loss is the activation of caspase-3 which cleaves the complex structure of muscle. Then, the ubiquitin-proteasome system is activated, which rapidly degrades proteins released by caspase-3 cleavage of muscle proteins.

- As with heart failure, fluid retention in advanced kidney disease often masks the true loss in lean body mass.

Drugs-related weight loss

1. Drugs causes anorexia (medications suppressing appetite):

A-Anticonvulsants (e.g., Topiramate)

B-Appetite Suppressants (e.g., Phentermine)

C-Bupropion

D-Metformin (Glucophage)

E-Opioid Analgesics

F-Stimulant Medications (e.g., amphetamine)

G-Theophylline

2. Drugs causes altered taste or smell:

A-Allopurinol

B-ACE Inhibitors

C-Calcium Channel Blockers

D-Levodopa

E-Propranolol

F-Spironolactone (Aldactone)

Drugs-related weight loss (cont…)

3.Drugs causes dysphagia :

A) Bisphosphonates. B) Doxycycline. C) Iron Supplementation. D) NSAIDs.

E) Potassium Supplementation.

- ***Weight loss also occurs with several drugs of abuse:***

- **alcohol** :. When someone drink their body is more focused on breaking down alcohol rather than burning fat. Many alcohol-dependent patients consume most of their calories from alcohol and thus have several nutritional deficiencies in addition to weight loss. However, weight loss in patients with alcoholic cirrhosis may be masked by secondary ascites and fluid retention.
- **Cocaine** : There is a widespread assumption that cocaine use suppresses one's appetite and thereby contributes to weight loss.
- **Opiates** directly inhibit the appetite center, decrease gastrointestinal motility and may have side effects like nausea and vomiting so that leads to weight loss
- **Smoking** can lead to weight loss by increasing metabolic rate , decreasing metabolic efficiency or decreasing caloric absorption (depress appetite) and so this leads to weight loss.

Causes of involuntary weight loss

- HIV and other infections
- Psychiatric
- History and Physical examination

Done by : Bassam otoom

HIV and other infections

Weight loss in patients with HIV infection is usually episodic, occurring with secondary infections or gastrointestinal diseases, and leads to a reduction in energy intake.

Patients with HIV disease may have symptoms such as nausea vomiting and lack of appetite that may result in loosing weight

If HIV is not treated, the virus will cause progressive weakening of the immune system, a process which occurs at different rates in different people. Once significant damage to the immune system has occurred, which typically takes at least several years, people with HIV can develop infections that are not usually seen in people with normal immunity. These “opportunistic infections” can cause serious disease in patients with advanced HIV some of these opportunistic infections is yeast infection that is caused by candida albicans that will lead to candidiasis in mouth (that will lead to cream colored and slightly raised patches in the mouth , soreness , and easily bleeding) another one is candidiasis in esophagus that leads to dysphagia and loss of appetite.

HIV and other infections

Many chronic infections lead to involuntary weight loss As an example, many patients with active tuberculosis experience weight loss as a result of nausea , abdominal pain and lack of appetite. Some patients who take a medication for TB as isoniazid drug may experience side effect such as feeling tired or nauseous and loosing his appetite that may be a cause of weight loss. Another example is in patients with chronic hepatitis C may be associated with a reduction in steatosis , abnormal liver enzymes , liver Cirrhosis or scaring of the liver over time and that will lead to symptoms like skin problems (like lichen planus , porphyria cutanea and cutaneous necrotizing vasculitis) , nausea , vomiting and loss of appetite that will lead to weight loss

Lichen planus

Porphyria cutanea

Other infections

Beside HIV, HEP C & TB
Cytomegalovirus mononucleosis as a cause of prolonged fever and prominent weight loss in immunocompetent adults.
Patients with CMV experience symptoms like fever , night sweats , sore throat , swollen glands , and loss of appetite that will cause weight loss.

It was concluded that CMV mononucleosis should be considered in the differential diagnosis in patients with prolonged fever and weight loss if lymphocytosis is present.

Parasites: Tapeworms will cause you to lose weight because you have this huge worm in your intestines eating your food. Another example is in patients with giardiasis infection they will have symptoms of diarrhea, abdominal cramping , bloating gas , nausea , fatigue and loss of appetite that will cause weight loss

University of Manchester researchers have said that: “Weight loss following infection with intestinal worms is the body's way of Fighting off the parasites”
There was a study on mice , the conclusion of the study :

They found that immune cells called T-cells responded to the worm

infection by driving up levels of cholecystokinin the latter increase has a knock-on effect of driving down another hunger hormone, leptin, which influences what type of immune response the body needs to produce.

This then triggers the type of immune response needed to expel the worms from the gut

When they artificially added leptin back into the infected mice, the immune system mounted the wrong response and the intestinal worms remained in the gut for longer

Psychiatric disorders

Psychiatric illness can be a common cause of involuntary weight loss, occurring in 10 to 44 percent of community-dwelling participants. psychiatric disorders particularly depression, account for 31 to 58 percent of cases of involuntary weight loss in nursing home patients.
People with serious mental illnesses such as schizophrenia, bipolar disorder and major depression can lead to loosing appetite and therefore weight loss

The role of depression in weight loss is difficult to determine due to the frequency of overlapping causes, such as social isolation to the patient with weight loss , physical disabilities, dementia, dysphagia, medication/drug use, and multiple chronic diseases .

Anorexia nervosa

Is an eating disorder characterized by an abnormally low body weight, an intense fear of gaining weight and a distorted perception of weight. People with anorexia place a high value on controlling their weight and shape, using extreme efforts that tend to significantly interfere with their lives.

Physical symptoms :
Extreme weight, Thin appearance , Abnormal blood counts , Fatigue , Insomnia , Dizziness or fainting , Bluish discoloration of the fingers , Hair falls out , Absence of menstruation , Constipation and abdominal pain , Dry or yellowish skin , Intolerance of cold , Irregular heart rhythms , Low blood pressure , Dehydration , Swelling of arms or legs

People with anorexia nervosa is exercising excessively

Bulimia nervosa

Is an eating disorder in which People are eating large amounts of food with a loss of control over the eating and then trying to get rid of the extra calories in an unhealthy way.

To get rid of calories and prevent weight gain, people with bulimia may use different methods. For example, you may regularly self-induce vomiting or misuse laxatives, weight-loss supplements, diuretics or enemas after bingeing. Or you may use other ways to rid yourself of calories and prevent weight gain, such as fasting, strict dieting or excessive exercise.

Symptoms : Dental problems , sore throat , swollen glands in your neck and face , Heartburn indigestion bloating , Irregular periods, Weakness, exhaustion, bloodshot eyes , Calluses on your hands from making yourself vomit , Gaining and losing weight often. Dizziness or fainting , Feeling cold all the time , Sleep problems , Dry skin, and dry and brittle nails ….Your weight in bulimia nervosa is usually in the normal range, but you may be overweight.

	Anorexia nervosa	Bulimia nervosa
Weight	• Significantly underweight	• Normal weight or overweight
Eating habit	• Eat little food/few calories	• Eat large amount of food, then purges by vomiting and/or using laxatives.
Body image	• Too concern on weight & appearance. • Dangerously thin but has false image that the body is still fat	• Too concern on weight & appearance.
Medical symptoms	• Weakness, fatigue • Nutritional deficiencies • Low blood pressure • Heart problem • Kidney problem • Hair loss • Lanugo (fine hair all over body) • End of menstruation	• Weakness, fatigue • Dehydration • Mouth and throat problems such as sore throat, sores in mouth, ulcers, dental problems etc.

History

The history of a patient with weight loss includes documenting the weight loss, assessing the pattern of weight loss, evaluating for eating disorders and possible occult intentional weight loss, and evaluating the consequences of the weight loss (such as malnutrition).

Documented weight loss :
Only 50 percent of patients reporting weight loss had true weight loss. Therefore, it is important to obtain previous weight records.

Pattern of weight loss :
It is important to determine the duration and pattern of weight loss, including past fluctuations in weight and whether weight loss is progressive or stable. Recent weight loss in a person whose weight has been stable for many years, and weight loss that is progressive, are more worrisome and require more immediate follow-up.

History

- Evaluation for eating disorders and intentional weight loss: Clinicians should question patients regarding possible intentional weight loss from dieting.

It is also important to elicit associated symptoms, medications, as well as functional and social factors associated with poor food intake.

Associated symptoms:
Malignancy
Malabsorption : symptoms of malabsorption include steatorrhea, muscle loss, watery diarrhea
Psychiatric disorder
Medications
Functional factors : such as dysphagia, poor dentition, or poor cognition/dementia may contribute to weight loss
Social factors : how the patients gets food , travel and sexual history of the patient

Physical examination

assess the overall appearance, skin changes (e.g., melanoma or spider angioma), presence of lymphadenopathy, cardiopulmonary status, hepatosplenomegaly, abdominal mass, breast/prostate abnormalities, rectal examination with stool hemoccult, and any neurologic deficit. In observational studies, abnormal physical findings were common among those with malignancy . As an example, in a prospective cohort study of 101 patients, 12 out of 22 patients (55 percent) diagnosed with cancer as the cause of weight loss had an abnormal physical examination finding

Spider naevi

Abdominal mass

Diagnostic tests,

In patients with documented weight loss of ≥5 percent of usual body weight and positive findings on history or physical examination, further testing should be focused on confirming the suspected diagnosis. A basic diagnostic evaluation should include:

1- Complete blood count (CBC): to evaluate the overall health and to detect diseases such as anemia, infections and leukemia.

2- Electrolytes

3- Glucose and hemoglobin A1c: to exclude Diabetes mellitus.

4- Calcium.

5-Renal function and urinalysis: to exclude kidney diseases

6- Hepatic function: to exclude liver diseases because it causes weight gain so if weight loss occurs it's probably not due to liver abnormality.

7- Thyroid-stimulating hormone: for thyroid function assessment.

8- Stool hem-occult: to evaluate any gastrointestinal bleeding.

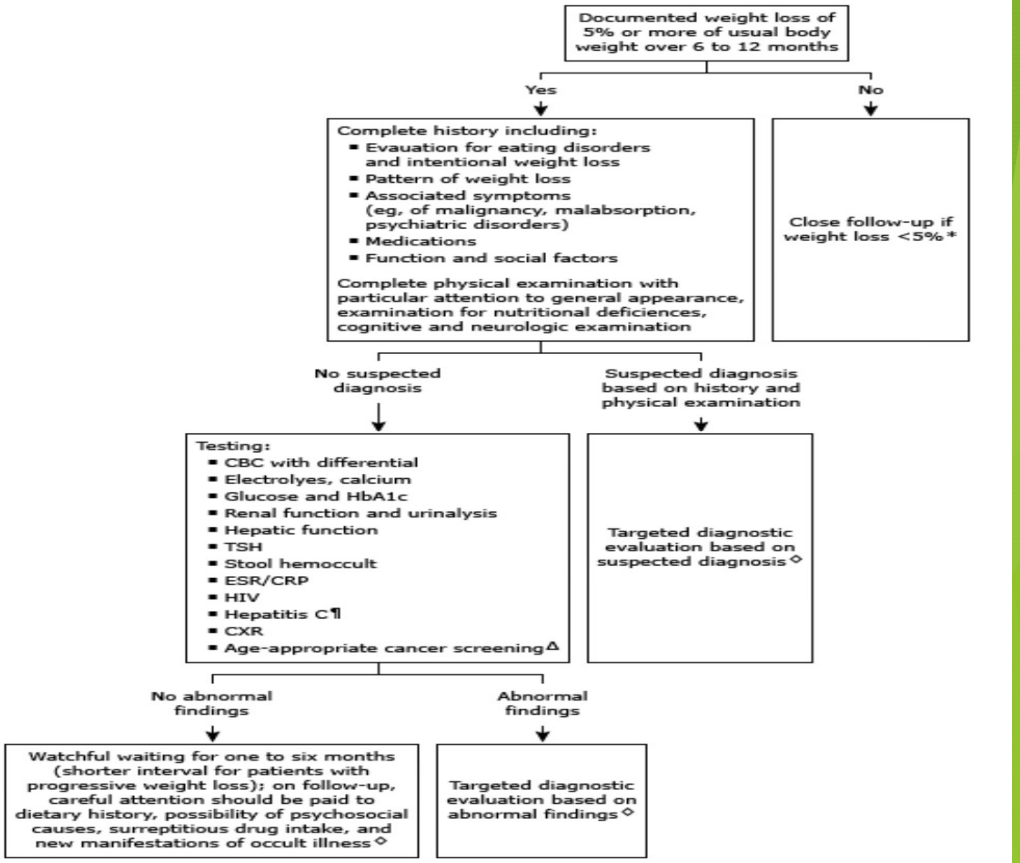
9-Hepatitis c.

10-Human immunodeficiency virus (HIV).

11- Chest radiograph: to exclude TB and Malignancy.

12- Age-appropriate cancer screening.

Management,


Documented weight loss of 5% or more of usual body weight over 6 to 12 months
Yes
No
Complete history including:
Evauation for eating disorders and intentional weight loss
Pattern of weight loss
Associated symptoms (eg, of malignancy, malabsorption, psychiatric disorders)
Medications
Function and social factors
Complete physical examination with particular attention to general appearance, examination for nutritional deficiences, cognitive and neurologic examination
Close follow-up if weight loss <5%*
No suspected diagnosis
Suspected diagnosis based on history and physical examination
Testing:
CBC with differential
Electrolyes, calcium
Glucose and HbA1c
Renal function and urinalysis
Hepatic function
TSH
Stool hemoccult
ESR/CRP
HIV
Hepatitis C¶
CXR
Age-appropriate cancer screening△
Targeted diagnostic evaluation based on suspected diagnosis◇
No abnormal findings
Abnormal findings
Watchful waiting for one to six months (shorter interval for patients with progressive weight loss); on follow-up, careful attention should be paid to dietary history, possibility of psychosocial causes, surreptitious drug intake, and new manifestations of occult illness◇
Targeted diagnostic evaluation based on abnormal findings◇

References :

1-Up To Date
2-Davidson principles and practice of medicine
3-Step Up To medicine
4-Costanzo physiology
5-differint articles

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Thank You!