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A Practical Approach to Loss of Appetite

Dwijen Das, Tirthankar Roy

ABSTRACT

Appetite is the desire to eat food, sometimes due to hunger. Decreased desire to eat is termed as anorexia. A brief period of anorexia usually accompanies almost all acute illnesses. Long lasting anorexia usually occurs only in people with serious and chronic underlying disorder. Hypothalamus plays a central role for maintaining the appetite along with different neuropeptides. Loss of appetite in acute illness is a sort of acute phase response causes of which may vary from benign viral or bacterial infection or drug induced to very serious lethal conditions like chronic liver or kidney disease, carcinoma stomach and colon.

Detailed clinical history and physical examination usually suffice to pinpoint the cause but in certain situationsa more aggressive approach with a battery of investigations may be needed to diagnosethe exact cause of anorexia. Detailed and extensive investigations in anorexia of shorter duration is usually unnecessary. Change in the pattern of meals served and change of eating environment can change appetite in certain cases. Therapy may be required according to the underlying disease causing anorexia.

INTRODUCTION

Our survival depends on the ability to procure food for immediate metabolic needs and to store excess energy in the form of fat to meet metabolic demands during fasting. Eating behaviour is stimulated by hunger, craving and hedonic sensations and controlled by homeostatic processes. Appetite is the desire to eat food, sometimes due to hunger. Appealing foods can stimulate appetite even when hunger is absent. Appetite exists in all higher life-forms, and serves to regulate adequate energy intake to maintain metabolic needs. It is regulated by close interplay between the digestive tract, adipose tissue and the brain.

Decreased desire to eat is termed as anorexia, while polyphagia (or hyperphagia) is increased eating. Dysregulation of appetite contributes to anorexia nervosa, bulimia nervosa, cachexia, overeating and binge eating.

Loss of appetite implies that hunger is absent- a person with anorexia has no desire to eat. A brief period of anorexia usually accompanies almost all acute illnesses. Anorexia during disease can be beneficial or deleterious depending on the timing and duration. Temporary anorexia during acute disease may be beneficial, since restriction of intake of micro- and macronutrients will inhibit bacterial overgrowth.[1] Long lasting anorexia usually occurs only in people with serious and chronic underlying disorder. Disorders that affect the part of brain where appetite is regulated can cause anorexia as well. In addition, the anorexia-cachexia syndrome is multifactorial and may involve chronic pain, depression or anxiety, hypogeusia and hyposmia, chronic nausea, early satiety, malfunction of the GIT and metabolic alterations.[1,2] Unexplained chronic anorexia is a signal to the doctor that something is wrong. A thorough evaluation of the person's symptoms and a complete physical examination often suggest a cause and help the physician decide which tests are needed.

PATHOPHYSIOLOGY

Feeding and Satiety

Body weight depends on the balance between intake and utilization of the calories. Weight loss is usually the result of reduced energy intake, not increased energy expenditure. Reduced energy intake arises from dieting, loss of appetite, malabsorption or malnutrition.[3] Food intake is regulated not only on a meal to meal basis but also in a way that generally maintains a given set point, for example if animals are starved and then permitted to eat freely, their spontaneous food intake increases until they regain the lost weight. Similarly, during recovery from illness, food intake is increased in a catch up fashion until lost weight is regained.[3]

Role of the Hypothalamus[3]

Appetite and metabolism are regulated by an intricate network of neural and hormonal factors. Regulation of appetite depends primarily on the interaction of two areas: a lateral hypothalamus "feeding center" in the nucleus of the medial forebrain bundle at its junction with the pallido-hypothalamic fibres, and the ventromedial hypothalamus "satiety centre" in the ventromedial nucleus. Stimulation of the feeding centre evokes eating behaviour in conscious individuals, and its destruction causes severe, fatal anorexia in otherwise healthy individuals. Stimulation of satiety centre causes cessation of eating, whereas lesion in this region causes hyperphagia and, if the food supply is abundant, the syndrome of hypothalamic obesity. Destruction of feeding centre with lesion of the satiety centre causes anorexia, which indicates that, the satiety centre functions by inhibiting the feeding centre. Hence, it appears that the feeding centre is chronically active and that its activity is transiently inhibited by activity in the satiety centre after ingestion of the food.

Neuropeptides such as corticotrophin releasing hormone

(CRH), α- melanocyte stimulating hormone (α-MSH), cocaine and amphetamine related transcript (CART) induce anorexia by acting centrally on satiety centres.[4]

One important polypeptide is Neuropeptide Y, which exerts its action through Y5 receptor in the hypothalamus resulting in increased food intake. Other polypeptides that increase food intake include Orexin-A and Orexin-B. They are synthesized in the neurons located in the lateral hypothalamus. They are also of interest because mutation in the receptor causes narcolepsy.[3,4] A potentially important observation is that accumulation of malonyl-CoA in the tissue inhibits food intake. This substance is produced from Acetyl-CoA and is converted to fatty acids by fatty acid synthase.

Afferent Mechanisms[3,5]

Four main hypotheses about afferent mechanisms involved in the control of food intake are:

i. Lipostatic hypothesis: Adipose tissue produces a humoral signal that is proportionate to the amount of fat and acts on the hypothalamus to decrease food intake and increase energy output.

ii. Gut peptide hypothesis: Postulates that food in the GIT causes the release of one or more polypeptides that act on the hypothalamus to inhibit food intake.

iii. Glucostatichypothesis: Increase glucose utilization in the hypothalamus and produces a sensation of satiety.

iv. Thermostatic hypothesis: Fall in body temperature below a given set point stimulates appetite and a rise above the set point inhibits appetite.

Leptin

It is produced by adipose tissue, and it plays a central role in the long term maintenance of weight homeostasis by acting on the hypothalamus to decrease food intake and increase energy expenditure.[4] Leptin suppresses expression of hypothalamic neuropeptide Y and increases the expression of α-MSH, which decreases appetite. Thus, leptin activates a series of downstream neural pathways that alter food seeking behaviour and metabolism. Leptin deficiency, which occurs in conjunction with the loss of adipose tissue, stimulates appetite.[5] A physiologically active form of marijuana (cannabinoids) that are found in the body increases appetite by an action on their CB1 receptors. The cannabinoid receptor type 1, often abbreviated as CB1, is a G protein-coupled cannabinoid receptor located primarily in the central and peripheral nervous sytem. It is activated by the endocannabinoid neurotransmitter anadamide and 2-arachidonoglycerol (2-AG). The anorexiant action of leptin is antagonised by CB1 blockade. Leptin activates the enzyme phosphotidylinisitol-3-hydroxykinase in hypothalamic cells, and inhibition of this enzyme blocks the effect of leptin.

The gastrointestinal peptides ghrelin, glucagon, somatostatin and cholecystokinin signal satiety and thus decrease food intake. Hypoglycemia suppresses insulin, reducing glucose utilization and inhibiting the satiety centre. A variety of cytokines, including TNFα, IFNγ and Leukaemia inhibitory factor (LIF), can induce cachexia. In addition to causing anorexia, these factors may stimulate fever, depress myocardial function, modulate immune and inflammatory responses and induce a variety of specificmetabolic alterations.[6]

Anorexia ininfection is a part of the Acute Phase Response (APR) to it. The APR can be triggered by lipopolysaccharides, a peptidoglycan from bacterial cell walls, bacterial DNA and glycoproteins, which can trigger production of a variety of pro-inflammatory cytokines. Cytokines causes increased production of leptin from fat stores. They can also signal the central nervous system directly by specialized transport mechanisms through the blood brain barrier.

Mechanism of weight loss includes decreased food intake, malabsorption, loss of calories and increased energy requirements. Hence loss of appetite (resulting in decreased food intake) is directly related to weight loss. Food intake may be influenced by a wide variety of visual, olfactory and gustatory stimuli as well as genetic, psychological and social factors.[5,6]

ETIOLOGY OF ANOREXIA[4]

- Cancer :

- Some types of cancer–including ovarian, pancreatic and stomach cancers–may cause a loss of appetite, usually by affecting a person's metabolism.
- Advanced cancer
- Some cancers may cause the spleen to become larger. When a spleen grows in size, it can push on the stomach, creating a feeling of fullness.
- Ascites, may create a feeling of fullness even after eating a small amount of food.
- Medications, including chemotherapy, immunotherapy, and drugs called sedatives that cause feelings of calmness or sleepiness.
- Radiation treatment or surgery to any part of the gastrointestinal organs, such as the stomach or intestines.

- Endocrine and metabolic

1. Hypothyroidism
2. Diabetes mellitus
3. Adrenal insufficiency
4. Pheochromocytoma

- Gastrointestinal disorders

1. Acid peptic disorder
2. Malabsorption
3. Obstruction
4. Pernicious anemia

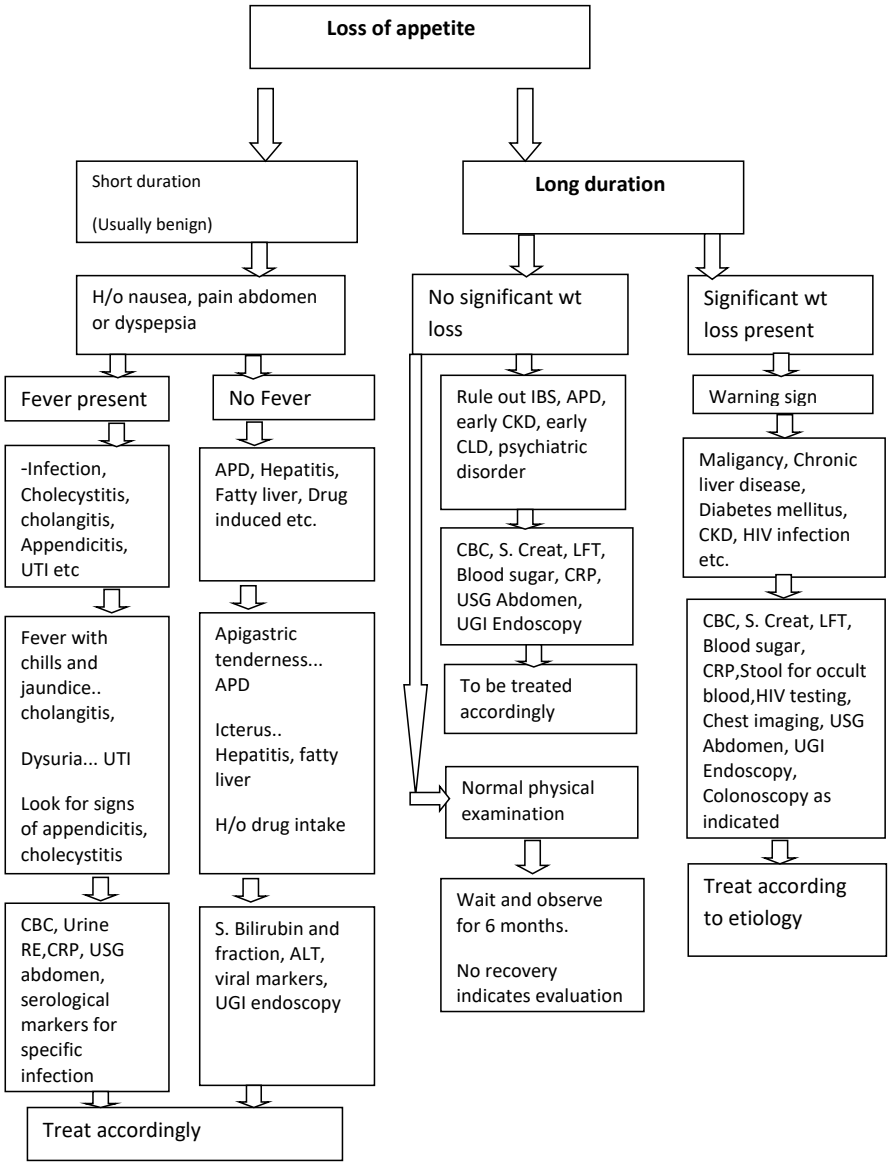

Fig. 1: Algorithmic approach to loss of appetite

5. Pancreatic disorders
- Hepatic disorders

1. Chronic liver disease
2. Viral hepatitis
3. Biliary disorders
4. Acute fatty liver of pregnancy

- Cardiac disorders

1. Chronic ischemia
2. Congestive heart failure

- Respiratory disorders

1. Chronic obstructive pulmonary disease

- Renal insufficiency
- Rheumatologic disease
- Infections

1. HIV
2. Tuberculosis
3. Parasitic infection
4. Subacute bacterial endocarditis

- Medications

1. Amphetamine
2. Dexmethylphenidate
3. Selective serotonin reuptake inhibitors
4. Topiramate
5. Stimulants such as caffeine, nicotine and cocaine
6. Abrupt cessation of appetite increasing drugs like corticosteroids and cannabis.
7. Opiates, NSAIDS.

- Disorders of mouth and teeth
- Age related factors

1. Physiologic changes
2. Decreased taste and smell

- Neurologic

1. Stroke
2. Dementia
3. Parkinsonism
4. Neuromuscular disorders

- Social

1. Isolation
2. Economic hardship

- Psychiatric

1. Depression
2. Anxiety
3. Anorexia Nervosa: There are two types of anorexia nervosa: anorexia nervosa binge/purge type- The individual suffering from this disorder will purge when he or she eats. This is typically a result of the overwhelming feelings of guilt the sufferer experiences in relation to eating; they compensate by vomiting, abusing laxatives or excessively exercising. In restrictive anorexia nervosa- the individual will fiercely limit the quantity of food consumed, characteristically ingesting a minimal amount that is well below their body's caloric needs.
4. Bereavement
5. Alcoholism
6. Smoking (heavy)
7. Bulimia nervosa is type of binge eating behaviour characterized by frequent episodes of binge eating associated with emotional distress and sense of loss of control. Binge eating is eating in a discrete period of time (eg 2 hours) an amount of food that is significantly larger than is typical for most people during the same defined period. This behaviour is associated with a perceived loss of control of eating during this time. Compensatory behaviours used by individuals with bulimia nervosa include self-induced vomiting, laxative abuse, excessive exercise generally experienced as being joyless and/or compulsive, episodes of fasting or strict dieting, diuretic abuse, use of appetite suppressants, failure to use insulin in those with type I diabetes, and/or use of medications intended to speed metabolism (eg. thyroid hormone). DSM-5 diagnostic criteria require episodes of binge eating that occur at least once weekly for 3 months. Dizziness, light headedness, palpitation, dry skin, pharyngeal irritation, abdominal pain with self induced vomiting, dysphagia, bloating, constipation and amenorrhea are some of the symptoms of bulimia nervosa. Physical examination may reveal bilateral parotid enlargement, dental caries, sudden diffuse hair loss, acne, dry skin, nail dystrophy and scarring resulting from cutting, burning and other self induced trauma, bradycardia, tachycardia, hypothermia and hypotension, edema and clinical obesity.

APPROACH TO THE PATIENT (FIGURE 1)

The first step is to access the duration of anorexia from the history, whether it is of acute onset or chronic. Acute onset anorexia is mainly associated with infections, oral disorders, major surgery, etc. Chronic underlying medical disorders, medications, psychiatric disorders are associated with prolonged anorexia.[7] Proper examination of the individual to access signs of wasting, fever, features of bulimia (e.g. loss of teeth, enamel, knuckle ulcerations and calluses). Abdominal examination to access tenderness, distension, free fluid and abdominal lump should be performed. Proper psychiatric and behavioural status should be looked for, and the social and economic status of the patient must be considered. One should look for enlarged lymphnodes, as tuberculosis is a major cause of anorexia in our country and also enlarged neck nodes sometime indicates GI malignancy.[7]

The review of system should focus on signs and symptoms that are associated with disorders that commonly cause anorexia.[8] These include fever, cough, pain, shortness of breath, palpitations and evidence of neurological diseases. Gastrointestinal disturbances, including dysphagia, nausea and vomiting, change in bowel habits should be sought for. Travel history, use of alcohol and cigarettes and all the medications should be reviewed and the patient should be questioned about the previous illness and surgery as well as diseases in the family. Risks for HIV infection should be sought for.[9]

As part of the history it is important to determine the duration and pattern of anorexia, including past fluctuations in weight and whether weight loss is progressive or stabilized.[8] Anorexia in a person whose weight has been stable for many years andwho has presented with history of weight loss that is progressive, are more worrisome and require more immediate follow-up. Other factors to consider, include intention to lose weight, decreased caloric intake, physical activity and age of the patient. New onset anorexia or dyspepsia in elderly may be a warning feature of underlying malignant diseases.

Following questions should be answered in a case of anorexia:

1. Is a disease process causing the symptoms?
2. Is it secondary to other symptoms (e.g., nausea)?
3. Is the patient troubled by the symptoms?
4. Is the family worried about the eating habits?
5. How much weight has been lost?
6. Is the decreased appetite a new symptom?

7. If so, did it start after an upsetting event, such as the death of a family member or friend?

Physical examination

Several prospective studies have verified the importance of a complete physical examination in evaluating anorexia and the unexplained weight loss.[10] It should start with weight determination and documentation of vital signs. The clinician should assess the overall appearance, skin changes (eg. turgors, scar from prior surgery, melanoma or spider angiomata and stigmata of other disorders),oral thrush or dental diseases, thyroid gland enlargement, presence of lymphadenopathy, pallor, icterus, cardiopulmonary status, hepatosplenomegaly, abdominal mass, breast/prostate abnormalities, rectal examination with stool hemoccult, and any neurologic deficit.[9,10] In observational studies, abnormal physical findings were common among those with malignancy.[10]

Diagnostic testing

In patients with positive findings on history or physical examination, further testing should be focused on confirming the suspected diagnosis. When the history and physical examination do not indicate a likely diagnosis, a basic diagnostic evaluation should include:

1. Laboratory testing: Complete blood count with differential, chemistries (electrolytes, glucose, calcium, renal and hepatic function, thyroid stimulating hormone), hemoglobinA1c, urinalysis, stool hemoccult, and erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP).[9]
2. Diagnostic imaging: Chest radiograph.
3. If a GI cause is suspected, endoscopy and colonoscopy with biopsies may be helpful.

We do not recommend CT scanning in the initial workup, although CT scan may be indicated based on history or physical examination. Further studies should be based on results of these initial tests. Despite an appropriate initial evaluation, a clear cause for anorexia is often not found. Watchful waiting for one to six months is preferable to a battery of testing with low diagnostic yield.[10] As organic disease is rarely found in patients with a normal physical examination and initial diagnostic testing, a waiting period of one to six months is unlikely to result in an adverse outcome.[11] On follow-up, careful attention should be paid to dietary history, possibility of psychosocial causes, surreptitious drug intake, and new manifestations of occult illness.

TREATMENT

Home remedies for loss of appetite[12]

1. Indian Gooseberry (amla)
2. Ginger
3. Black Pepper
4. Cardamom (elaichi)
5. Carom Seeds (ajwain)

Keep mealtimes and snacks flexible

Worrying about not eating can further affect the appetite. It is better to include variety in food served and food according to choice of the patient.[12]

Try not to skip meals. Make an effort to eat regularly even if it is only a few bites. Small frequent meals and snacks throughout the day are advised. Some people may have a better appetite in the morning, better to advice a large breakfast in them.[11,13] Try eating a bedtime snack.

If care has been taken for someone with cancer, try not to blame them for not eating. Do not bribe or threaten them to get them to eat.

Make meals appealing and fun[12]

Appetite is very much affected by how food looks and by the eating environment. An appealing food in an atmosphere of fun may do the trick. Recognize that what is appealing one day may not be the same the next day.

Make every calorie count

We should advice to prevent weight loss by increasing the nutritional value of the food served, especially with calories and protein.

Allow to eat whatever and whenever the person wants. Small snacks and meals every 1–2 hours throughout the day is a preferred option. Eat well during times when the appetite returns.[12]

Keep healthy, high-protein, high-calorie snacks available so they are ready to eat when patient's appetite returns. Eat food high in calories and protein when the appetite is poor. These foods include fish, chicken, turkey, eggs, cheese, milk, ice cream, yogurt, beans and lentils. Add butter to vegetables, cooked cereal and rice to add fat and calories.[12] Between meals, sips of drinks with high calories and protein are advisable. Add sugar syrup, honey or jelly to vegetables, meats, cereals, waffles and rolls to add calories.[13]

Increase the protein and calorie content of milk products. Double the protein and calorie content of whole milk by adding powdered dry milk.

Try doing light exercise or walking before meals, in fresh air if possible. Increased activity just before eating and fresh air both stimulate the appetite.

Eating atmosphere should be pleasant and relaxed, preferably with friends and family members whenever possible. Eating with someone else distracts attention from food and can increase the amount consumed.[12]

Physicians may prescribe drugs to stimulate appetite in some cases. These drugs may include megestrol (Megace) or corticosteroids (steroids).[13]

Some people claim that marijuana helps increase their appetite. To date, studies haven't shown for certain, that marijuana can effectively improve appetite.[11]

The management of anorexia depends on the specific underlying cause. Treatment strategies include, but are not limited to, pharmacologic therapy (eg, infections,

endocrinopathies), surgery/radiation (eg, malignancy), behavioral therapy (eg, depression, anorexia nervosa) and/or nutritional support (eg, dementia, dysphagia). The medications most often used in the early 2000s include mirtazapine (Remeron), a tetracyclic antidepressant; cyproheptadine (Periactin), an antihistamine; dronabinol (marinol, THC), an antiemetic; nandrolone, oxymetholone, and oxandrolone, which are anabolic steroids related to the male sex hormone testosterone; and megestrolacetate (Megace), a synthetic derivative of the female sex hormone progesterone. In addition to these prescription drugs, fish oil (eicosapentaenoic acid or EPA) has been recommended as an alternative or complementary treatment forundesired weight loss.

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