Anorexia Nervosa

History of Presenting Illness
(diagnostic criteria from DSM IV)
- History of weight loss (or in children, lack of weight gain)
- Weight loss is Self-induced through avoidance
- Intrusive dread of fatness
- Amenorrhea (or in men, loss of sexual interest)
- Excessive exercise
- Use of appetite suppressants
- History of eating disorders in family
- **BUT NOT BINGE/PURGE:**
  - NO RECURRENT EPISODES OF OVEREATING
  - NO “CRAVING” i.e. no compulsion to eat and then follow it with compensatory behaviour eg. vomiting

Differential Diagnoses (DDx)
- Eating disorder (!)
- Stress-related autophagy
- Drugs
- Cancer
- Pregnancy
- Intestinal parasite
- Psychosocial ramifications of puberty
- Malabsorption disease (eg, coeliac)
- Hyperthyroidism
- Depression

Findings on History
- No necessary previous illness, but may have previous GIT disorder
- History of eating disorder in family
- Gradual decline of school/work performance, missing days etc.

Findings on Examination (Ex)
- Pale, thin, gaunt, sunken face/eyes (BMI below 17.5)
- Sullen/depressed
- Dark circles under eyes (~dehydration, hypovolumia)
- Chapped lips
- Flaking skin
- Brittle hair
- Halitosis (due to ketone bodies in blood stream)

Tests and Investigations
**Blood Count:** looking for metabolic abnormalities consistent with malnutrition
- Low haemoglobin (N = 1.15-1.6 g/L) due to iron deficiency
- Low WBC (N = 4 to 11x10^3 per mm^3) due to malnutrition
- Low plasma glucose (N= 4 to 10 mmol/L; below 2.8 = coma) (or 7 - 11 mg/L)

**Postural Hypotension:** marked difference between standing and sitting/lying blood pressure; normal difference  = 12

**Urinalysis** to eliminate pregnancy: **Expected Negative**

**Stool Sample** to eliminate intestinal infection/infestation **Expected Negative**

ASK: do you think you are thin?
Anorexics will amaze you with the poverty of their insight into their own condition.

ASK THE FAMILY: how are the other kids?
Often there are several eating disorders in the same family- perhaps stemming from the same risk factor

OBESITY/THINNESS most strongly correlated with MOTHERS WEIGHT

Look for signs of
- ANAEMIA
- DEHYDRATION
- MALNUTRITION
- KETOACIDOSIS

put together by Alex Yartsev: Sorry if i used your images or data and forgot to reference you. Tell me who you are.
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By GP:
- referral to psychiatrist (specialist in eating disorders)
- does the pt require resuscitation, rehydration, nutrient replacement therapy?

By Specialist: DEFINITIVE TREATMENT:
- Nutritional Rehabilitation:
  - Dietician will work with pt. to devise a feeding regime to gain minimum healthy weight
  - 1st take detailed nutritional history and ask about weight-loss behaviours
  - INFORM about dangers of over/under eating, excess exercise, starvation metabolism
  - Then when target weight is reached, a maintenance diet is prescribed

HOSPITALISATION may be needed if pt. is emaciated, or there is low compliance, or a family crisis supervenes.
- Psychotherapy: somatic focus must be combined with cognitive behavioural therapy and supportive psychotherapy. Aim is to:
  - understand the personal significance of weight loss;
  - help deal with weight gain;
  - to have her accept and become attuned to her body;
  - to improve her self esteem;
  - to assist her to reintegrate home, school and peer group.

Treatment must continue for a long period of time even after weight and eating patterns have normalised. Compulsory treatment may be necessary.

Epidemiology
Mainly Women (10:1) – TYPE A PERSONALITY is a risk factor
Prevalent in cultures where food is plentiful
(worldwide prevalence = 0.5%; in America 2.3% in females)
Mortality ~ 10% chance every 10 years
OCDs in >20% of sufferers
Anxiety disorders in 65%
Depression in 68%

Prognosis
The relapse rate is high (50% in the first year and 90% overall),
the death rate is 1% per year with 20% dead by 20 years,
the illness lasts around 5 years on average
Biochemistry of weight loss

Energy intake of the body is balanced by its energy output ("energy balance equation"): thus, increasing output or decreasing input will unbalance the equation and force autophagy (where the body uses stores of energy to satisfy its basic metabolic needs)

Energy intake = food intake in kilojoules or calories
Energy output =
- resting metabolic rate (RMR),
- energy cost of arousal,
- the energy cost of work and activity,
- thermogenesis (heat production)
- shivering,
- non-shivering
- diet-induced thermogenesis. On eating, there is a specific stimulation of the sympathetic nervous system which leads to thermogenesis. Carbohydrate and protein eaten in excess may also stimulate thermogenesis. Fat does not elicit thermogenesis.

Biochemistry of starvation:

1st order of business: BRAIN NEEDS GLUCOSE; primary source is glycogen in the liver
OTHER ORGANS THAT CANT DO WITHOUT GLUCOSE: Testes, Kidney Medulla, Erythrocytes

Blood glucose falls by 2/3rds = COMA eg. in diabetes (all glucose gets bound in cells)

- STEP 1: GLYCOLYSIS: GLYCOGEN is catabolised to release a small amount of glucose for the brain
  LASTS 1 DAY-
  GLUCONEOGENESIS occurs: production of glucose out of raw materials eg glycerol
- STEP 2: LIPOLYSIS occurs: free fatty acids released into bloodstream,
  - to be used in β-oxidation: turn into AcetylCoA molecules, then get used in Krebs Cycle
  - KETONE BODIES are produced from AcetylCoA, which the brain can use instead of glucose
- FAT LASTS 2-3 MONTHS: longer in fat people
- STEP 3: LAST RESORT:
  PROTEOLYSIS in MUSCLES occurs to release amino acids for the Kreb Cycle
  (get deaminated and turned into carbon chain skeletons, then slotted in wherever they fit along the cycle; ammonia is released as result) IF BRAIN IS STARVED permanent loss of frontal lobe matter occurs (!!)

Glucose Homeostasis:

GLUCAGON converts ATP into Cyclic AMP; INSULIN re-converts it into AMP (deactivating it)
Cyclic AMP activates the protein kinases which activate glycogenolysis and deactivate glycogen synthesis
**BMI** = weight divided by height squared

Healthy range: 18.5 to 25; 30+ is obese, less than 18.5 is underweight, less than 16.5 is emaciated

**Biochemistry of Krebs Cycle:**

**Fuel Use in Cells**

- **GLUCOSE**
  - Glucose-6-Phosphate
    - **Glycogen**
      - Glycogen-lysis
    - Glycogen-genesis
  - Glycolysis
  - GLYCOGEN
  - lactic acid with lactate dehydrogenase
  - ANAEROBIC with Lactate Dehydrogenase
  - AMINO ACIDS
  - PYRUVATE
    - **KETONE BODIES**
      - eg. acetoacetate, hydroxybutyrate
    - Lipolysis
    - Fatty Acids
    - β-oxidation of fatty acids into C₂ chunks
    - TRIGLYCERIDES
      - Lipolysis
      - Lipogenesis
    - FREE FATTY ACIDS
    - Acetyl CoA = C₂

**Krebs Cycle**

- **PRODUCTS:**
  - Coenzyme A (reused)
  - H₂O (reused)
  - CO₂ (exhaled)

**USEFUL PRODUCTS:**
- Electron and H⁺ carriers
  - eg. NAD, FAD:
    - transport H⁺ ions and electrons into oxidative phosphorylation reaction

**RAW MATERIALS:**
- ADP, Inorganic Phosphate, Oxygen.

**Ketogenesis**

**Electron Transport Chain:**
A sequence of membrane proteins arranged in order of increasing redox potential; operated by NADH and FADH. Electrons move down the redox gradient and the resulting energy is used to pump H⁺ ions out of the inner mitochondrial membrane. Purpose is to build a negative charge inside the membrane and thus attract H⁺ ions back into the mitochondrion. The membrane is impervious to H⁺ except for proton channels; therefore the protons have no choice but to operate the ATPase enzyme.

**Oxidative Phosphorylation:**
The conversion of ADP and inorganic phosphate into ATP. This is done by Proton-translocating ATPase. This enzyme is activated by the passage of H⁺ ions into the mitochondrion through a proton channel to which the ATPase is linked. 3 H⁺ ions for 1 ATP molecule.
The curved arrows are a shorthand way of showing the reactants and products. For example, in step 3 the NAD$^+$ reacts with isocitrate to produce α-ketoglutarate, CO$_2$, NADH, and H$^+$. The last two then leave the site of the reaction.
Secretion, gland:

- **Saliva (Amylases)**
  - From 3 pairs of salivary glands
- **Lingual Lipase**
  - From surface of tongue
- **Pepsinogen**
  - From “chief cells” in the base of gastric glands in the middle stomach (the “body”)
- **Mucus**
  - To coat the walls of the stomach and protect them from acid/enzyme damage
  - From Goblet cells in the pylorus (distal stomach)
- **Bile**
  - From the liver; stored in gall bladder

Location, action:

- **MOUTH**
  - Mastication by teeth (food becomes a moistened compact bolus)
  - Lubrication by saliva
  - Carbohydrates broken down by amylases
  - Triglycerides broken down by lingual lipase
- **OROPHARYNX**
  - Muscular swallowing action
- **LARYNGOPHARYNX**
  - Muscular swallowing action
- **OESOPHAGUS**
  - Muscular swallowing action
- **STOMACH**
  - Bulk storage of swallowed bolus
  - Mechanical muscular churning of the bolus (peristalsis)
  - Acid secretion (HCl; pH 1.5-2.0) denaturates proteins, deactivates foreign enzymes, breaks down plant cell walls and animal connective tissue, activates pepsin from pepsinogen
  - Pepsin breaks down proteins by attacking peptide bonds
  - Intrinsic Factor facilitates absorption of vitamin B12 in the intestine
  - Overall result is acidic viscous soup-like chyme
- **DUODENUM**
  - About 25 cm of small intestine
  - Mixing of chyme, intestinal juice and digestive secretions of pancreas and liver
  - Intestinal Juice coats the walls of the small intestine and reduce the acidity of the chyme
  - Pancreatic alpha-amylase breaks down starches
  - Proteases break down large protein complexes
  - Peptidases break down proteins into amino acids
  - Nucleases break down nucleic acids
  - Bile emulsifies the lipids in the chyme
  - Pancreatic lipase breaks down complex lipids into fatty acids
- **JEJUNUM**
  - About 250 cm of small intestine
  - Absorption of nutrients
- **ILEUM**
  - About 350 cm of small intestine
  - Some absorption of nutrients
- **PROXIMAL COLON**
  - About 75 cm of total colon, comprising the ascending colon and transverse colon
  - Colonic bacteria generate Vitamin K, Vitamin B5 and Biotin
  - 10% of all GIT absorption occurs in the proximal colon
- **DISTAL COLON**
  - About 75 cm of total colon, comprising the descending colon and sigmoid colon
  - Storage of wastes and reabsorption of water
- **RECTUM**
  - Peristaltic expulsion of wastes

Absorption:

- **Relevant anatomy:**
  - Trace quantities of simple lipids + carbohydrates through the capillaries in the tongue and soft palate
  - Nothing is specifically absorbed except some drugs (eg aspirin) and ethyl alcohol; this is due to the thick mucous coating of the stomach walls
  - Absorption occurs mainly in the JEJUNUM:
    - Peptides
    - Amino acids
    - Fructose
    - Glucose
    - Lipids
    - Water minerals
    - Vitamins
  - The Proximal colon absorbs:
    - Water
    - Vitamin K
    - Biotin
    - Vitamin B5
    - Some bile salts
    - Urobilinogen (product of bacterial metabolism of bilirubin from bile)
    - Toxins (ammonium ions, indole, scatole, and hydrogen sulfide)
Absorption of Nutrients in the Gut: Villous cells ABSORB, Crypt cells SECRETE.

Water:
- can be transported passively (osmosis, which is solute-driven)
- or actively (by water-carrying proteins)

Action of OSMOTIC LAXATIVES:
- eg. mannitol: solute-driven absorption disrupted by insoluble sugar
- therefore great volumes of water don’t get absorbed
- therefore diarrhoea results

**Diagram**:
- **Small Intestine**
  - Na^+ pump
  - Co-transporter: Transports both Na^+ and Cl^- 
  - Na^+ and Cl^- escape through Cl^- channels
  - Na^+ and K^+ ions traffic freely

- **Large Intestine**
  - Na^+ pump
  - 2K+ pump
  - 3Na^+ pump
  - 2K+ and glucose
  - 3Na^+ and glucose

- Duodenum Villi
  - Sodium/Glucose Co-Transporter
  - Glucose
Absorption of:
- Water:
  - driven by solute; lipid bi-layer readily admits water (20% of total)
  - Most water (80%) gets transported by transport proteins AQUAPORINS (passively)
- Gases:
  - Completely passive (by diffusion)

Protein transport is both SATURABLE and INHIBITABLE:
SATURABLE transport: eg. glucose: when there is an end-point for absorption, and then no more.
INHIBITABLE transport can be interrupted by specific blockers
Protein transport usually requires sodium to pump

**Behavioural science:**
**Taking a meaningful nutritional history:**
RECORD: time consuming but accurate log of all consumed foods/drinks; depends on compliance.
Most useful if run over longer periods
24 hr RECALL: quick, provides a snapshot of intake- how good is the patients memory?
Diet History: for long-term accustomed food intake, eg. *on average, what do you eat in an average day*?
- may be useless if the pt has poor memory or the diet is highly variable

**Food Frequency Questionnaire**- accurate but depends on pt motivation, patience, memory and intelligence.

**WHICH METHOD TO CHOOSE?** Depends:
- want accurate measurements or descriptive assessment?
- Short or long-term?
- Can the pt be relied on to provide an accurate assessment?

**Genetics**
Obesity and thinness are most closely related to the normal weight of the biological mother

**Pharmacology**
most commonly non-specific **antidepressants**, either for depressive illness or for obsessive compulsive symptoms which may impede recovery
ALSO perhaps a Sustagen ™ type protein+carbohydrate re-feeding schemata