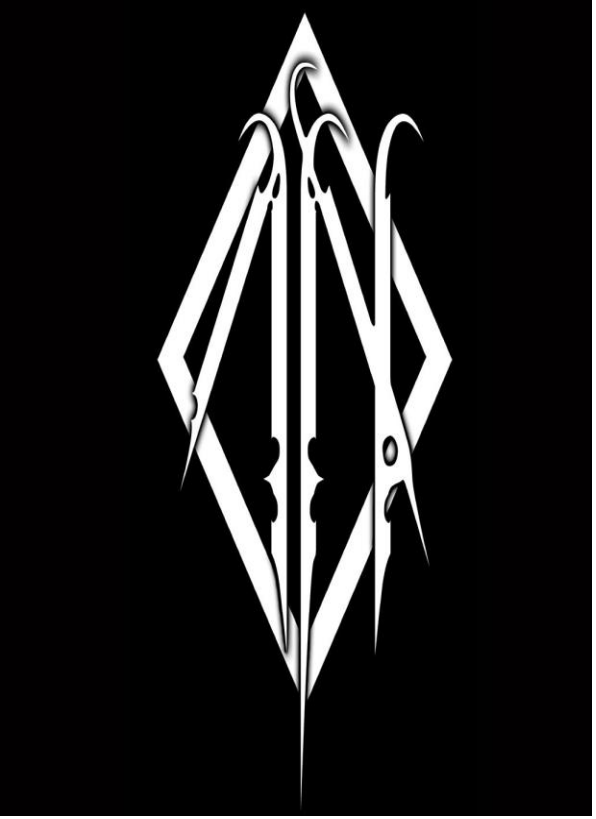

Impacts of amenorrhea on fertility and pregnancy outcomes in patients with anorexia nervosa

A literature Review Study

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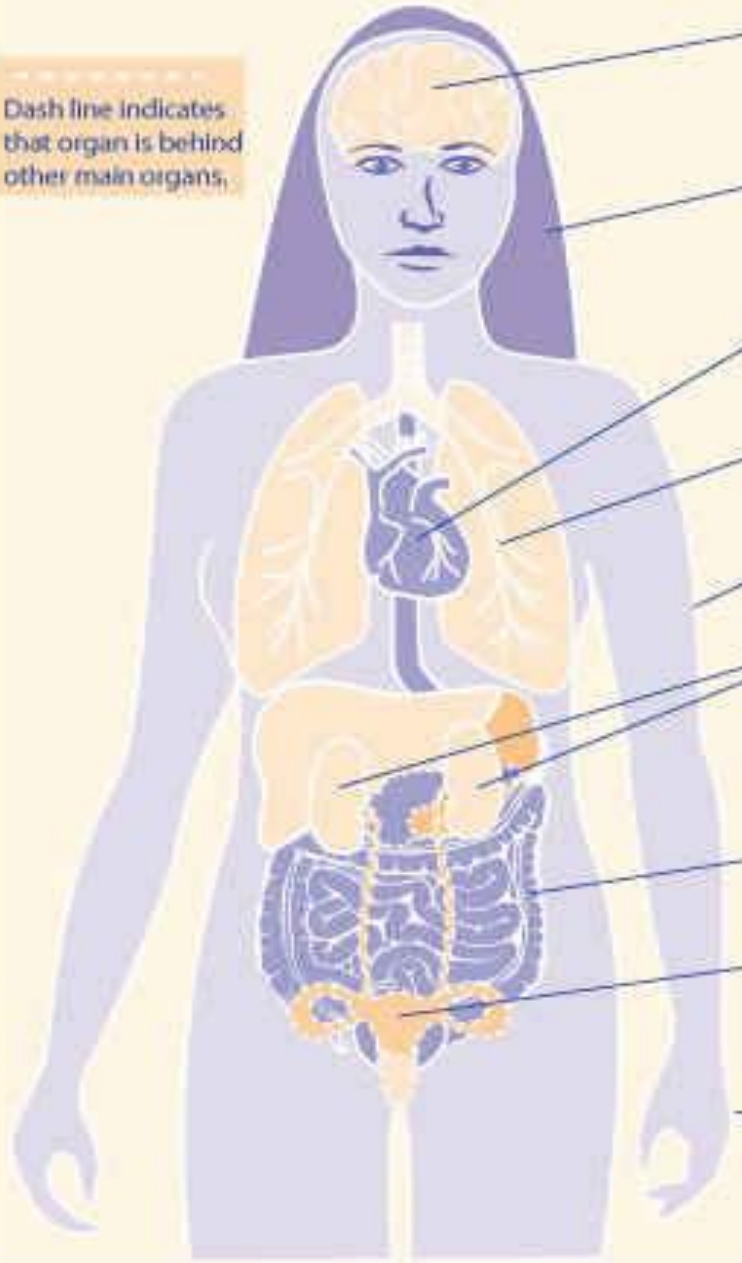
Eating disorders

- Are predominantly diseases of females, who comprise between 90% and 95% of patients diagnosed with anorexia nervosa or bulimia nervosa (Yanovski 2000).

- Anorexia nervosa has the highest standardised mortality rate of any psychiatric disorder and all eating disorders cause significant short and long term psychological and physical morbidity.

(see themselves as
fat even when emaciated

Anorexia affects your whole body



Brain and Nerves
can't think right, fear of gaining weight, sad, moody, irritable, bad memory, fainting, changes in brain chemistry

Hair
hair thins and gets brittle

Heart
low blood pressure, slow heart rate, fluttering of the heart (palpitations), heart failure

Blood
anemia and other blood problems

Muscles, Joints, and Bones
weak muscles, swollen joints, bone loss, fractures, osteoporosis

Kidneys
kidney stones, kidney failure

Body Fluids
low potassium, magnesium, and sodium

Intestines
constipation, bloating

Hormones
periods stop, problems growing, trouble getting pregnant. If pregnant, higher risk for miscarriage, having a C-section, baby with low birthweight, and post partum depression.

Skin
bruise easily, dry skin, growth of fine hair all over body, get cold easily, yellow skin, nails get brittle

Epidemiology and Pathophysiology of Anorexia Nervosa

- They are being reported with increasing frequency in developing societies (Riggs 1999)
- Evidence supporting a genetic component to eating disorders who have a sibling with anorexia nervosa having a 10-20 times higher risk of developing the disease (Riggs 1999)
- The lifetime incidence of anorexia nervosa is reported to be between 0.5% and 3.7%. (Yager 2000)

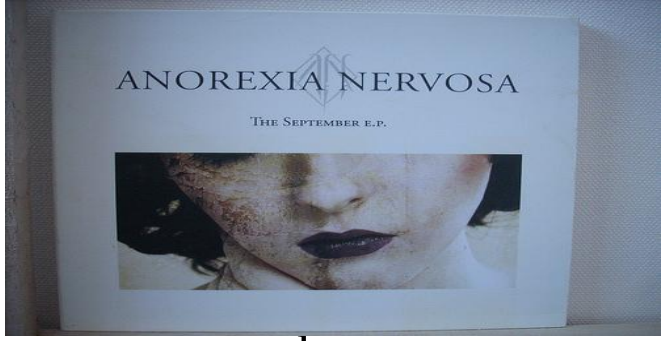
Specific Symptoms of Anorexia Nervosa

- Amenorrhea is one of the key diagnostic criteria for anorexia nervosa (Rollins et al 1978) and can result because of an abnormality in the hypothalamic-pituitary-ovarian axis, causes by **Nutritional deficiency** and **Low body weight**.

- Secondary Amenorrhea is the absence of menstrual bleeding in a woman who had been menstruating but later stops menstruating for 3 or more months

- Disturbances in central dopaminergic and opioid activity have been described in anorexia nervosa and both these substances are known to modulate gonadotropin-releasing hormone (GnRH)-mediated luteinizing hormone (LH) release (Golden et al 2006)

Anorexia Nervosa



- Neuroendocrine disturbances result in delayed puberty, amenorrhea, anovulation, low estrogen states, increased growth hormone, decreased antidiuretic hormone, hypercarotenemia, and hypothermia (Stoving etal 1999).

- Women who are underweight, because of unwise dieting experience disruption of their reproductive ability (Green et al. 1988).

- Weight loss is in the range of 30% below (ideal weight) results in amenorrhoea. Ideal body weight equals 45 kg (100 lbs) for 150 cm (5 ft) and then 2.3 kg (5 lbs) for each additional 2.5 cm (inch) in females.

- Amenorrhea is an important risk factor for severe osteoporosis.
- The prevention of osteoporosis is one of the main challenges for primary care physicians.
- It is at adolescence that most of a person's peak bone mass is acquired (Carmichael 1995.
- Adolescent patients with anorexia nervosa are therefore less likely to reach their peak bone density and are at risk of premature osteoporosis and fractures, as well as being at risk of irreversibly stunting their growth (Neinstein 1996, Mehler 1995)

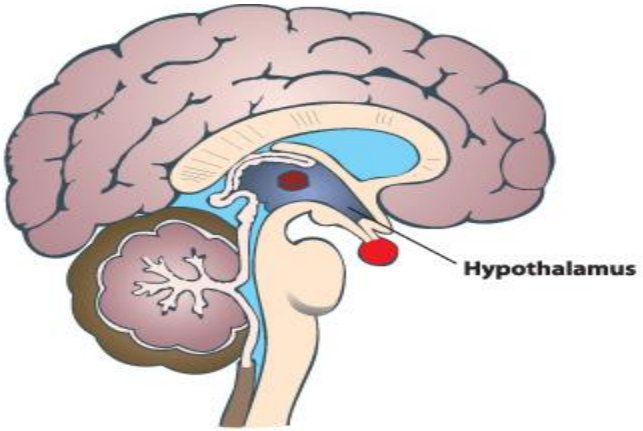
HOW ADIPOSE TISSUE MAY REGULATE FEMALE REPRODUCTION

- *The* amounts of fat are important, since the female must be big enough to reproduce successfully (Frisch, 1977).
- Adipose tissue is a significant extragonadal source of oestrogen (Siiteri, 1981).
- Conversion of androgen to oestrogen takes place in adipose tissue of the breast and abdomen (Nimrod & Ryan, 1975), the omentum (Perel & Killinger, 1979), and the fatty marrow of the long bones (Frisch *et al. 1975).*

- Compared with normal women very thin women have high levels of the 2-hydroxylated form of oestrogen, which is relatively inactive and has little affinity for the oestrogen receptor.

- In contrast, obese women metabolize less oestrogen to the 2-hydroxylated form and have a relatively higher level of the 16-hydroxylated form, which has potent oestrogenic activity (Schneider et al. 1983).

HYPOTHALAMIC DYSFUNCTION, GONADOTROPHIN SECRETION AND WEIGHT LOSS

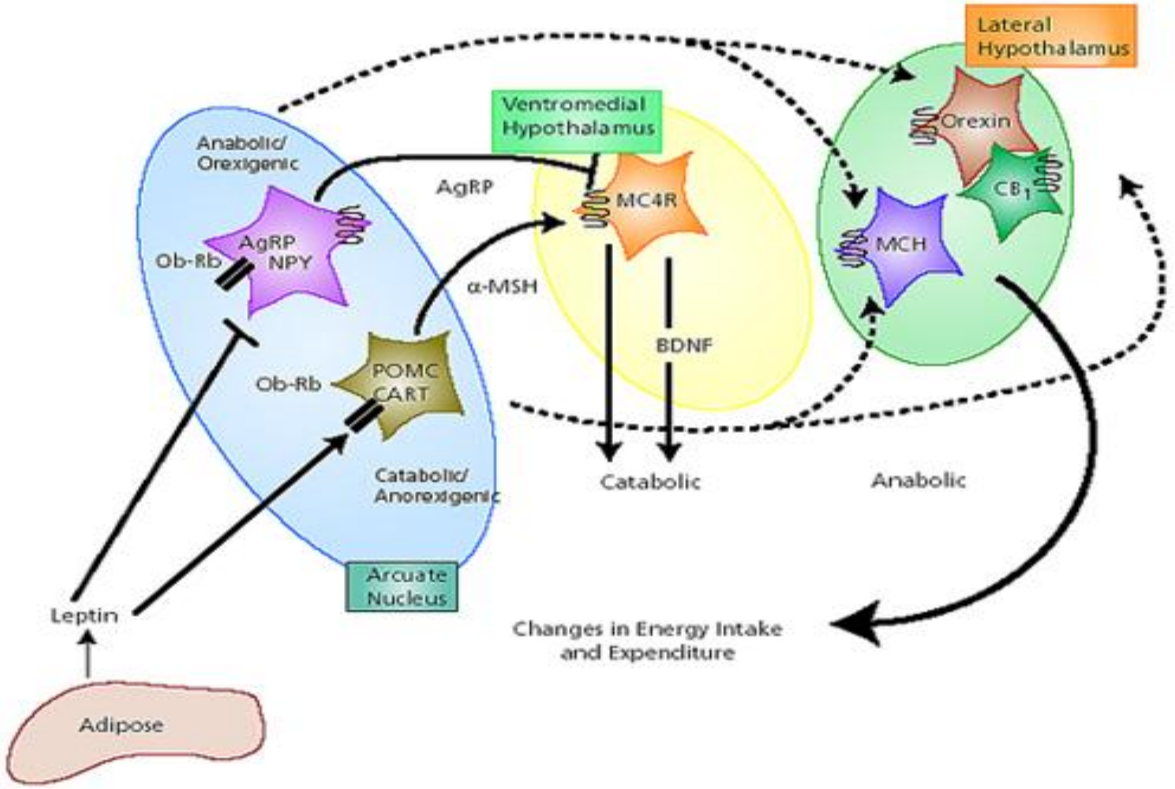


- The amenorrhoea of underweight and excessively lean women is due to hypothalamic dysfunction (Vigersky *ef al. 1977; Nillius 1983).*
- Women with this type of hypothalamic amenorrhoea have changes in the secretion of the gonadotrophins, luteinizing hormone (LH), follicle-stimulating hormone (FSH), and oestrogen:
- (1) LH, FSH, and oestradiol levels are low,
- (2) The secretion of LH and the response to GnRH are reduced in direct correlation with the amount of weight loss (*Vigersky et al. 1977),*

- Supportive that this type of hypothalamic amenorrhoea is the finding of Van der Spuy *et al. (1988) that women in whom ovulation had been* induced had a higher risk of low-birth-weight babies who were small for dates, and this risk was greatest (54%) in those who were underweight.

- These authors conclude that the most suitable treatment for infertility secondary to weight-related amenorrhoea is dietary, rather than induction of ovulation.

Role of leptin in energy-deprivation states: normal human physiology and clinical implications for hypothalamic amenorrhoea and anorexia nervosa



- Leptin is an adipocyte-secreted hormone that plays a key part in energy homoeostasis.
- The main role of this hormone is to signal energy availability in energy-deficient states.

Role of leptin

- Anorexia nervosa is associated with low concentrations of leptin
- Leptin can restore ovulatory menstrual cycles and improve reproductive, thyroid, and Insulin-like growth factor 1 hormones and bone markers in hypothalamic amenorrhoea
- Future studies confirm the initial data, r-metHuLeptin could prove a better treatment for hypothalamic amenorrhoea

Evaluation of patients

- Evaluation of patients with suspected eating disorders includes a thorough history and physical examination as well as baseline screening laboratory tests.

- A high index of suspicion is needed to detect patients with eating disorders because many are in denial about their illness.

Treatment for eating disorders includes

- ***Nutritional rehabilitation,***
- ***Behavioral therapy,***
- ***Antidepressant therapy.***

Estrogen therapy: Still a major question

- Whether or not **estrogen replacement therapy** is an effective therapeutic option for the bone loss associated with anorexia nervosa remains a major question.

- In a randomized prospective study of 48 women followed for a mean of 1.5 years, estrogen/progestin replacement and calcium supplementation did not prevent or reverse bone loss in women with anorexia nervosa (Klibanski 1995).

- In a subanalysis among patients with severe weight loss (those who weighed less than 70% of ideal body weight) estrogen/progestin prevented bone loss but did not increase bone density.

- Primary care providers often prescribe estrogen replacement for young amenorrheic low-weight women.

- Amenorrhea is a known risk factor for osteopenia, and it occurs in persons with anorexia nervosa (AN)
- Studies of the efficacy of hormone therapy or oral contraceptives (OCPs) in increasing the bone mass of women with AN have not consistently shown positive results
- The mechanism by which the osteopenia develops and reverses is thought to be nutritionally mediated.
- The role of nutrition in the recovery of bone has been underestimated. Indeed, therapy consisting of OCPs or estrogen replacement was associated with continued fractures or bone loss.

Hormone replacement therapy

- hormone replacement therapy (HRT) has been used to improve the patient's bone mineral density and initiate menses.
- The evidence supporting the use of HRT in patients with AN is weak; therefore, its use is not generally recommended.
- In addition, because HRT induces monthly menstrual bleeding, the patient may believe that her body is functioning normally when it is not.
- Clinical consensus recommends that menstrual periods should not be artificially induced in anorexic patients (Bachrach et al 199, Grinspoon et al 2002).
- Nutritional stabilization in order to prevent bone loss remains the cornerstone of treatment.

- Conclusions from a review of 119 outcome studies revealed that, on average, less than half of patients recovered (Steinhausen, 2002).

- Calculated from statistics recovers about 50% of the disease-stricken completely, one third of them will be improved over time, while about. 20% remain chronically ill patients.

Obstetric Concerns

- The incidence of eating disorders in pregnancy has been reported to be as high as 1%.
- Some apparent risk factors for developing an eating disorder in pregnancy include age, 30 years, lower socioeconomic status, and previous history of an eating disorder (Turton 1999).
- In a study by Bulik et al., women with a history of anorexia nervosa did not differ from control patients in the rate of pregnancy or mean number of pregnancies (Bulik 1999).
- These patients have a significantly increased incidence of miscarriage and preterm delivery, and a markedly higher perinatal mortality rate (more than six times the expected rate) (Bulik 1999).

Obstetric Concerns

- It is important to note that the increased risk for miscarriage persisted in patients who were in remission from their anorexia.
- Anorexic patients also have up to a 66% chance of developing postpartum depression (Morgan 1999)
- Patients who are actively engaging in anorexic behavior during pregnancy require nutritional counseling and close follow-up to encourage weight gain.

Pregnancy/infertility

- Some data support the notion that women with a past or current eating disorder are more likely to develop hyperemesis, give birth to infants with low birth weight and small head circumference, and small-for-gestational age infants.
- Eating-disorder patients also appear to be at a higher risk for caesarean section and postpartum depression (Sollid 2002, Carter 2003).
- Pre-pregnancy counseling for eating-disorder patients requires the multidisciplinary collaboration between a specialist in high-risk pregnancies and a mental health professional.
- In particular, some mothers who have an active eating disorder or who have had an eating disorder in the past have difficulty with feeding their babies and young children (Agras 1999, Russell 1998, Stein 1994).
- These mothers are obviously in need of significant nutritional counseling and physician involvement to ensure normal development of the child.

Talking therapies

- Talking therapies (eg counselling), develop a healthier attitude towards food and body.
- A nutritionist should help these patients to choose their meals and learn right nutritional habits.

Psychopharmacology

- Medications such as antidepressants, antipsychotics, and mood stabilizers may help some anorexic patients when given as part of a complete treatment program. Examples include: olanzapine (Zyprexa, Zydis), selective serotonin reuptake inhibitors (SSRIs), and antidepressants. These medicines can help treat depression.

- Control trials of tricyclic antidepressants, monoamine oxidase inhibitors and anxiolytics have not found to be useful.

Psychosocial interventions

- Adolescents should be involved in family therapy (Eisler et al 1997), individual therapy that mixes compassionate support with cognitive restructuring and improved interpersonal skills has been found meaningsfull (Dare et al 2001,Lock 2002). Cognitive behavioural therapy (CBT).

- Clinical consensus that is psychotherapy is useful to the patient after their malnutrition has been corrected.

Prognosis

- In one large meta-analysis, 47% of patients fully recovered; 33% improved somewhat; and 20% developed chronic, relapsing anorexia.

- Patients with later age at onset of the disorder, binge-purge behavior, and concurrent mood disorders have a worse prognosis for full recovery (Bowers & Ansher 2008)

Conclusion

- Amenorrhea is a common cause to encourage women to apply for gynecological evaluation.
- Medical providers should help patients and their families to have access to multidisciplinary care with a mental health provider, dietician, dentist and experienced medical provider.
- Primary care physicians have a crucial role to note the severity of this chronic mental illnesses while assessing the patient's physical status.
- Future research aimed at prevention of AN by early identification and education leading to a better understanding of this life-threatening illness

- Thank You