Nutritional Considerations and Mood Disorders

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Statistics

- Depression is a common mental disorder with a complex etiology.
- Depressive disorders affect 121 million people worldwide and are the third leading cause of burden of disease in high-income countries.
- Depression can be diagnosed reliably in primary care, but not all treatments are effective. According to a World Health Organization report, 36–50% of serious cases in developed countries and 76–85% of serious cases in less-developed countries do not receive treatment.

Lancet 2006 and JAMA 2004
Statistics

• Major depressive disorder is very common, with a lifetime prevalence of 17% and a rate almost twice as high in women as in men. 

• 19% - 34% of depressed patients still do not respond to acute antidepressant treatment.

• 29–46% may fail to achieve and sustain a full remission. 

• 15% - 50% will have a recurrence of depression despite continuous antidepressant treatment. 
  Psychiatr Ann 1994

• By the year 2030, the World Health Organization estimates that unipolar depressive disorders will rank second in the leading causes of disability-adjusted life years. 
  World Health Organization, 2005
Life Expectancy

- Individuals with major mental disorders have life expectancies 25-30 years shorter than those of the general population.
  - Coronary heart disease
  - Diabetes mellitus
  - Cerebrovascular disease

- Antipsychotic medicines can contribute to weight gain and associated metabolic disorders.  
  
  Endocrine News – 9/2010
Folate and Depression

• Low blood folate and cobalamin (vitamin B-12) concentrations have been found in patients with major depression in a number of studies. J Affect Disord 1990, Psychiatr Prax 1995 and Acta Psychiatr Scand 1989

• Low blood folate concentrations have been associated with a poor response to antidepressant treatment. Psychiatry Res 1994 and Am J Psychiatry 1997

• There has been an inverse correlation between blood folate concentrations and the severity of depression. Psychiatry Res 1994 and J Affect Disord 1990

• Between 10% and 30% of depressed patients may have low folate concentrations, and these patients appear to respond less well to antidepressants. Nutrition 2000
Vitamin B12 deficiency also has been linked to psychiatric disorders:

- Impaired memory
- Irritability
- Depression
- Dementia
- Psychosis (rare)

Wintrobe's Clinical hematology. 10th ed. Baltimore: Williams & Wilkins, 1999

Studies indicate that older patients tend to present with neuropsychiatric disease in the absence of hematologic findings.

Measurements of metabolites such as methylmalonic acid and homocysteine have been shown to be more sensitive in the diagnosis of vitamin B12 deficiency than measurement of serum B12 levels alone.
Study

- In a large study of 406 patients with known vitamin B12 deficiency,
  - 98.4 percent had elevated serum methylmalonic acid levels.
  - 95.9 percent had elevated serum homocysteine levels (defined as three standard deviations above the mean).
  - Only one patient out of 406 had normal levels of both metabolites, resulting in a sensitivity of 99.8 percent when methylmalonic acid and homocysteine levels are used for diagnosis.
  - 28 percent of the patients in this study had normal hematocrit levels, and 17 percent had normal mean corpuscular volumes.

Am J Med. 1994
Pyridoxine and Neurotransmitters

• Dopamine
• Norepinephrine
• Serotonin
• Tyramine
• Tryptamine
• Taurine
• Histamine
• Gamma aminobutyric acid (GABA)
Homocysteine and Depression

- High serum concentrations of homocysteine may be associated with depression in middle-aged men.

AJCN – 12/2004
**SAMe**

- **Low SAMe concentrations have been observed in the cerebrospinal fluid of depressed persons.**
  J Neurol Neurosurg Psychiatry 1990

- **There is a positive correlation between an increase in plasma SAMe concentrations and an improvement in depressive symptoms.**
  Acta Neurol Scand Suppl 1994

- **The activity of the enzyme methionine adenosyltransferase, which is involved in the manufacture of SAMe, has been shown to be low in depressed schizophrenic patients but high in manic patients.**
S-adenosyl-L-methionine (SAMe)

Natural medications for psychiatric disorders: considering the alternatives. Philadelphia: Lippincott Williams & Wilkins, 2002:44.
Tryptophan and Tyrosine

Natural medications for psychiatric disorders: considering the alternatives. Philadelphia: Lippincott Williams & Wilkins, 2002:44.
Adverse Effects of SAMe

- Mild insomnia, lack of appetite, constipation, nausea, dry mouth, sweating, dizziness, and nervousness. CNS Drugs 1996

- Increased anxiety, mania, or hypomania have been reported in patients with bipolar depression. CNS Drugs 1996, Br J Psychiatry 1987 and Lancet 1983

- Patients with a history of bipolar disorder should be advised not to take SAMe unless they are also taking a mood stabilizer.
SAMe Dosage

- Recommended doses range from 400 to 1600 mg/d, although some persons may require doses > 3000 mg/d to alleviate depression.

AJCN-11/2002
Maternal Depression

- Maternal depression is very common globally, the prevalence of which ranges from 15% in the United States to 35% in low-income South African mothers.

- The average prevalence of maternal postpartum depression within 6–8 wk after childbirth is 13% in the general population.
  Int Rev Psychiatry 1996
Clinical Studies

- Clinical studies and experimental work using animal models have both revealed a link between zinc status and neuropsychological disorders such as depression and anxiety.

- Zinc deficiency has been shown to induce depression-like and anxiety-like behaviors, supplementation has been used as a treatment for major depression.

- Zinc administration has shown to improve the efficacy of antidepressant drugs in depressed patients and may have a particular role to play in treatment-resistant patients.

Curr Opin Clin Nutr Metab Care. 2010 Aug
Molecular Mechanisms of Zinc

- Regulation of neurotransmitter systems
- Antioxidant
- Neurotrophic factors
- Neuronal precursor cells

Curr Opin Clin Nutr Metab Care. 2010 Aug
Zinc and Depression

- Patients with depression have lower plasma or serum zinc concentrations than do nondepressed patients, and some studies suggest that low serum zinc may be a marker of treatment resistance in depression.

Vitamin D

• Patients who live at higher latitudes and are at risk of vitamin D deficiency are also more prone to developing schizophrenia, and vitamin D deficiency has been associated with depression.

Schizophr Res 2002 and J Nutr Health Aging 1999
Magnesium Deficiency

- Cognitive disorders, psychiatric disorders, and mental depression are occasional features of cachexia and may be associated with hypomagnesemia.

- Levine et al showed that patients with acute depressive disorders had elevations in the ratio of calcium to magnesium in both serum and cerebrospinal fluid.

- Hypomagnesemic patients have reported confusion, disorientation, agitation, hallucinations, and depression.

- Magnesium has been effective in alleviating depressive and manic symptoms in rapidly cycling bipolar disorders.

Am J Clin Nutr 1999 and Neuropsychobiology 1999
Choline

- Choline is an essential nutrient found in animal products such as liver, egg, and meat, but also in some vegetable products, including wheat germ and soy beans. J Nutr 2003

- Despite the presence of a pathway for endogenous synthesis of choline, a choline-deficient diet impairs growth, memory, and hepatic, renal, and pancreatic functions in mammals.

- Choline plays an important role in the central nervous system, both for the synthesis of membrane phosphatidylcholine and for acetylcholine. Modern Nutrition in Health and Disease. 10th ed. 2006
Stress

- Stress, an anxiety component, induces an increase in adrenal catecholamines, which increases the demand for methylation reactions required in norepinephrine and adrenaline synthesis. Lancet 1982

- Synthesis of biogenic amines may increase the demand for one-carbon units for methionine synthesis, derived from choline, as well as folate-dependent pathways.
Choline and Anxiety

- In a large population–based study (5918) of the Hordaland Health Study, including both sexes and 2 age groups of 46–49 and 70–74 y, choline concentrations were negatively associated with anxiety symptoms but not with depression symptoms.
Long-chain PUFAs and the Human Brain

- The n–3 and n–6 PUFAs comprise 14% and 17% of the total FAs in the human brain and are predominantly DHA and arachidonic acid (AA; 20:4n–6), respectively.

- Saturated FAs account for nearly one-third of all FAs; monounsaturated FAs and other PUFAs account for the remainder.

- Both DHA and AA accumulate rapidly in neural tissues during the brain growth spurt that occurs during gestation and the first year of life.
Omega-3 Fatty Acids

- Higher n-3 PUFA concentrations lead to higher membrane fluidity, which in turn increases serotonin transport. Am J Clin Nutr 1995 and Am J Physiol 1992

- Both inflammation and atherosclerosis have been associated with depression and could link fatty acids and depression.
  
  Biol Psychiatry 1998
  J Affect Disord 1996
n-3 vs n-6 Fatty Acids

- DHA and EPA can be synthesized from the parent n–3 FA alpha-linolenic acid (ALA) in the liver through a series of elongation and desaturation steps.

- There is been recent concerns that the efficiency of this process may be low (8%) because both n–6 and n–3 FAs share and compete for the same enzymes that are used for desaturation and elongation.

- n-6 FAs such as linoleic acid are widely present in vegetable oils, seeds, nuts, margarine, grains, eggs, and some meats, whereas n–3 polyunsaturated FAs (PUFAs) are found primarily in canola and soybean oil, flaxseed, walnuts, eggs, some meats, and cold water fish.
  
  Am J Clin Nutr 2006

- Intakes of n–6 FAs have increased, resulting in a high ratio of n–6:n–3 FA intakes in the diet that may be associated with an increased risk of mental health disorders.
  
  Biol Psychiatry 2005 and Am J Clin Nutr 2000
Fatty Acid Composition

• There is a large body of evidence showing that fatty acid composition influences the biophysical properties of neuronal membranes. Prog Clin Biol Res 1988

Fatty acids effects:
  o Receptor function
  o Neurotransmitter reuptake
  o Signal transmission

• In animal models of depression, diet has been shown to influence membrane properties, eg, n-3 PUFA–enriched food augments serotonin receptor sensitivity. Am J Clin Nutr 1995
DHA and Depressive Disorders

DHA status

DHA concentration in neural tissue

Membrane fluidity and structure

Inflammatory response

Serotonin, norepinephrine and dopamine metabolism and signaling

Cytokine production (i.e., interferon-γ, tumor necrosis factor-α and interleukin-10)

Major depressive disorders
Case Study #1

20 year old female
Initial visit: January 2, 2008
Chief Complaint: Migraine headaches and chronic sinusitis
  o History: PMS, three to four sinus infections per year, migraines for the past four to five years, depression and anxiety.
  o Surgery: Fractured fifth digit of right hand.
  o Examination: Cheilosis, dry skin. Neurological and orthopedic examination were WNL.

Medications: Yaz (OCA) and OTC analgesics and anti-inflammatories
SpectraCell: Vitamin B12, Pantothenate and Vitamin D. Spectrox - 57.5%
  ➢ Marginal Values: Riboflavin, folate, choline, serine, CoQ10 and vitamin E
Case Study #2

50 year-old Female
CC: Allergies and Fatigue
PMHx: Hypercholesterolemia, Eczema, Depression, HTN and PMS.
SpectraCell results (3/29/2010)

**Deficient:** Vitamin B12, Vitamin D, Calcium, Zinc, Selenium and Glutathione. Fructose intolerance
Spectrox: 52%
71 Year-old Female  
CC: Rheumatoid arthritis and digestive disorders  
PM Hx: HTN, Depression, Fatigue, Gastric ulcer  
Medications: Prednisone, Arava, Methotrexate, Toprol XL, Benicar/Hct, Prozac and Nexium.  
SpectraCell results (3/19/2010):  

*Deficient:* Vitamin B6, Folate, Serine, Carnitine, Glutathione, Vitamin E and Vitamin K2.  
Spectrox: 51.0%
Commonly asked questions

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   **YES**

2. Is the presentation being recorded?
   **YES**

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