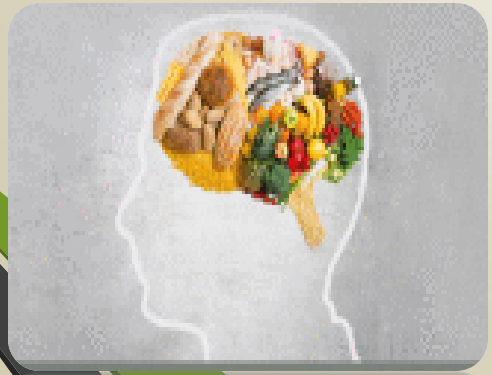

بسم الله الرحمن الرحیم

Nutrition and Neurologic Disorders



Modestly Presented by:
Maryam Bahreynian
PhD in Nutrition Sciences

Nutrition in Neurologic Disorders

- Depression
- Multiple Sclerosis (MS)
- Alzheimer Disease
- Stroke
- Epilepsy
- Anxiety
- Attention-Deficit/Hyperactivity Disorder (ADHD)

Depression

Depression

- Depression is a common disorder affecting about 6.7% or 16 million Americans.
- It is associated with severe symptoms, leading to social role impairment, making it the cause of disability worldwide.
- In addition, about one-third of people do not respond adequately to available treatments.
- Depression affects more women than men.
- The prevalence of depression also varies by ethnicity.

Contributing factors to depression

Multiple factors contribute to depression, including

- genetics,
- nutrition (decrease in fish oils and omega-3 fatty acids),
- environmental stressors,
- hormonal disruption (testosterone deficiency in men),
- and alterations in neurotransmitter function (the monoamine deficiency theory).

- People with certain genetic predispositions may be more susceptible to depression following chronic stress.

- A higher BMI was also linked to depression.

Diagnostic Criteria for Depression

BOX 42.10 Diagnostic Criteria for Major Depression

- Depressed mood or a loss of interest or pleasure in daily activities for more than 2 weeks.
- Mood representing a change from the person's baseline.
- Impaired function: social, occupational, educational.
- Specific symptoms, at least five of these nine, present nearly every day:
  1. Depressed mood or irritable most of the day, nearly every day, as indicated by subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful)
  2. Decreased interest or pleasure in most activities, most of each day
  3. Significant weight change (5%) or change in appetite
  4. Change in sleep: insomnia or hypersomnia
  5. Change in activity: psychomotor agitation or retardation
  6. Fatigue or loss of energy
  7. Guilt/worthlessness: feelings of worthlessness or excessive or inappropriate guilt
  8. Concentration: diminished ability to think or concentrate, or more indecisiveness
  9. Suicidality: thoughts of death or suicide, or has suicide plan

(Modified from American Psychiatric Association (APA): *Diagnostic and Statistical Manual of Mental Disorders*, ed 5, Arlington, VA, 2013, American Psychiatric Association.)

Do you know the 5 most common signs of depression?

The 5 D's of Depression

Pathophysiology

- The monoamine deficiency theory of depression suggests **deficiency of the monoamines** serotonin, dopamine, and norepinephrine.
- Altered monoamine receptor function in the CNS is the main pathophysiologic factor in depression.
- This theory has provided a target for pharmacological treatment.

- Epidemiologic research showed associations between lower seafood consumption and increased depression worldwide.

- Several clinical studies using EPA and DHA omega-3 **supplements** for depression have been conducted, and results **are mixed** but generally **positive**.

Medical Nutritional Therapy

- Is depression the disease that leads one to eat less healthfully, or does an unhealthy diet potentiate the disease?
- A Mediterranean diet-like eating pattern has been examined in relation to depression.
- Studies have shown that diets rich in
  - Fruits and vegetables,
  - olive oil,
  - fish,
  - whole grains,
  - low-fat dairy,
  - antioxidants
  - and low in animal foods

may protect against development of depressive symptoms later in life.

Medical Nutritional Therapy (Cont.)

- Curcumin is a treatment for depression due to its anti-inflammatory effects.
- Effectiveness of common curcumin is decreased because of poor absorption; supplements that provide curcumin with **piperine** enhance bioavailability.
- Low serum zinc levels is common in depressed individuals versus healthy controls.
- Mechanisms of zinc in reducing depression include:
- (1) decreasing dopamine reuptake (by binding to the dopamine receptor),
- (2) promoting excitatory neurotransmitter function.

Multiple Sclerosis (MS)

Multiple Sclerosis (MS)

- MS is a chronic inflammatory disorder of the CNS.
- One of the most common causes of disability among young and middle-aged adults,
- More prevalent in women than men.
- MS affects approximately 2.5 million worldwide.
- In the US, the National MS Society estimates that nearly 403 per 100,000 people are affected.

(National Multiple Sclerosis Society, 2017).

Multiple Sclerosis (MS) (Cont.)

- MS symptoms can start between 10 and 80 years, but onset is usually between 20 and 40 years, with a mean of 32 years.
- Although MS is more frequently seen in European Americans than African Americans, the latter group appears to accumulate disability more quickly.
- The prevalence of MS varies by **geographic location** and generally increases when travel from the equator in either hemisphere.
- It remains unclear whether this altered incidence, represents an environmental influence or genetic difference.

- MS affects the CNS and is characterized by destruction of myelin sheath, which protects axons, that transmit nerve impulses.

- Multiple areas of **optic nerves**, **spinal cord**, and **brain** undergo sclerosis, whereby myelin is replaced with sclera or scar tissue.

- No single test can ascertain whether a patient has MS; however, diagnostic criteria (revised McDonald criteria) were used by clinicians.

- In the worst scenario, MS can cause a person unable to write, speak, or walk. Fortunately, the majority of patients are only mildly affected.

Pathophysiology

- The precise cause of MS remains undetermined.
- A familial predisposition to MS has been noted in a minority of cases.
- Epidemiologic studies have linked the incidence of MS to geographic location and sunshine exposure.
- Studies showed that people born in an area with a high risk of MS who then **migrate** to an area with a lower risk **before the age of 15**, assume the risk of their new area.
- Such data suggest that exposure to some environmental agent **before puberty** may predispose a person to develop MS.

Pathophysiology (Cont.)

- Higher sunlight exposure, and therefore vitamin D production, reduces the risk of MS.

- Poor levels of vitamin D have been linked to increased risk, suggesting a protective effect for vitamin D.

- It is reasonable and safe to consider **vitamin D supplementation** to achieve optimal levels in MS patients, though the **mechanism is not understood**.

- ✓ The evidence is also growing that **smoking** plays an important role in **MS**.

- ✓ Smoking is associated with **more severe** and **rapid disease progression**.

- ✓ Fortunately, the evidence also suggests that **stopping smoking**, (whether before or after the onset of MS), is associated with a **slower progression of disability** (National MS Society, 2015).

Obesity and MS

Obesity in childhood and adolescence, especially among **females**, has been shown to increase risk of developing **MS** later in life.

There is some data of **early adulthood** obesity and **increased risk** as well, and obesity in the already diagnosed may exacerbate inflammation.

- Different viruses and bacteria are being studied for their role in developing MS.
- Previous infection with Epstein-Barr virus (EBV) might increase the risk of developing MS.
- Human herpes virus 6 (HHV-6) is being studied related to triggering relapses. This is an area of active research.
- The theories that have been **disproven** include
  - living with a dog or other small pet,
  - having allergies,
  - exposure to heavy metals,
  - experiencing physical trauma,
  - and exposure to aspartame (National MS Society, 2018b).

Four disease courses have been identified by the National MS Society:

1. **Clinically isolated syndrome** (CIS): an isolated episode lasting at least 24hours that looks like MS but does not yet meet full criteria of diagnosis. People may or may not go on to develop MS.

2. **Relapsing-remitting MS** (RRMS): the most common type of MS (about 85% of new cases), RRMS is characterized by intermittent neurologic symptoms during attacks (relapses) followed by periods of remission during which the disease does not appear to progress (remissions).

3. **Secondary progressive MS** (SPMS): most people with RRMS eventually develop SPMS, in which disability progresses over time.

4. **Primary progressive MS** (PPMS): accounts for about 15% of people with MS, in which neurologic function declines from the onset of symptoms.

انواع بیماری MS

۱ سندرم جداشده بالینی (CIS)

این دوره با اولین علائم بیماری ام اس همراه بوده و ممکن است فرد به MS مبتلا نشود.

۲ ام اس عودکننده-فروکش کننده (RRMS)

این نوع شایع‌ترین شکل مولتیپل اسکلروزیس است. بیماری در فرد مبتلا برای مدتی فروکش کرده و سپس با علائم جدید یا بدتر عود می‌کند.

۳ ام اس پیشرونده اولیه (PPMS)

در این نوع از بیماری افراد دارای علائم هستند که به تدریج و بدون هیچ دوره عود یا بهبودی پیشرفت می‌کند.

۴ MS پیشرونده ثانویه (SPMS)

افراد مبتلا به RRMS با پیشرفت بیماری به این نوع مولتیپل اسکلروزیس مبتلا می‌شوند که در نهایت بدتر شدن علائم منجر به آسیب شدید عصبی خواهد شد.

Medical Nutrition Therapy

- In two epidemiologic studies of about 9000 total MS patients, **healthier eating habits** were associated with l**ower** levels of **disability** and better quality of life.

- There are **mixed data** on high-fat (ketogenic) versus low-fat diets, longer terms studies seem to favor a diet lower in saturated fat.

- A pilot trial of 60 RRMS patients suggests **ketogenic and fasting-mimicking diet** (FMD) of **3 days a week,** had **higher quality of life** compared with controls.

RRMS: Relapsing-remitting MS

Medical Nutrition Therapy (Cont.)

In the 1950s, a small group of 144 MS patients were followed for more than 3 decades, and those who complied with a **low-saturated-fat diet** (<20 g/day) experienced significantly **less disability** and had lower mortality rates.

However, this study lacked randomization or controls for potential confounders, so it is more directional.

Medical Nutrition Therapy (Cont.)

- A prospective 2-year study (more than 200 pediatric MS patients) found that **SFA tripled** the risk of relapse **for every 10% increase** in energy intake from saturated fat.

- A very small study (10 subjects) found that a **Paleolithic diet in combination with dietary supplements**, **exercise** program, and **meditation** significantly **improved fatigue** in PPMS patients.

PPMS: Primary progressive MS

Medical Nutrition Therapy (Cont.)

- Specific dietary components that may reduce the risk of MS include **fish**, marine sources of **omega-3** fatty acids, **vitamin D**, **fruits and vegetables**, and **whole grains**.

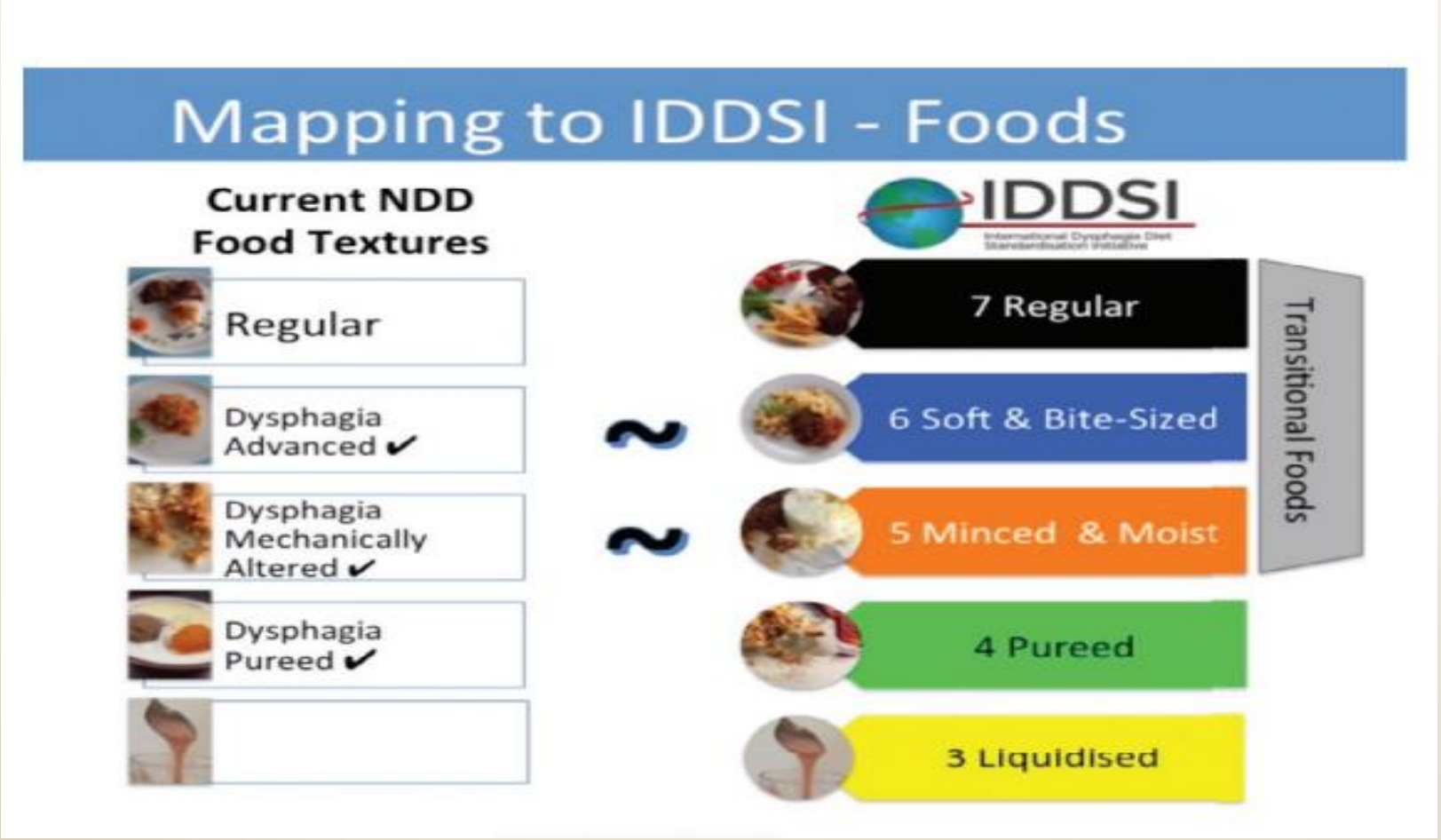
- **Preclinical studies** suggest a **high-salt diet** may **worsen disease** progression,

- but **human studies** have found **both positive and neutral associations**, making sodium and MS a topic for more research.

- Data on Mediterranean diet and MS are few, and suggests it is worth studying.

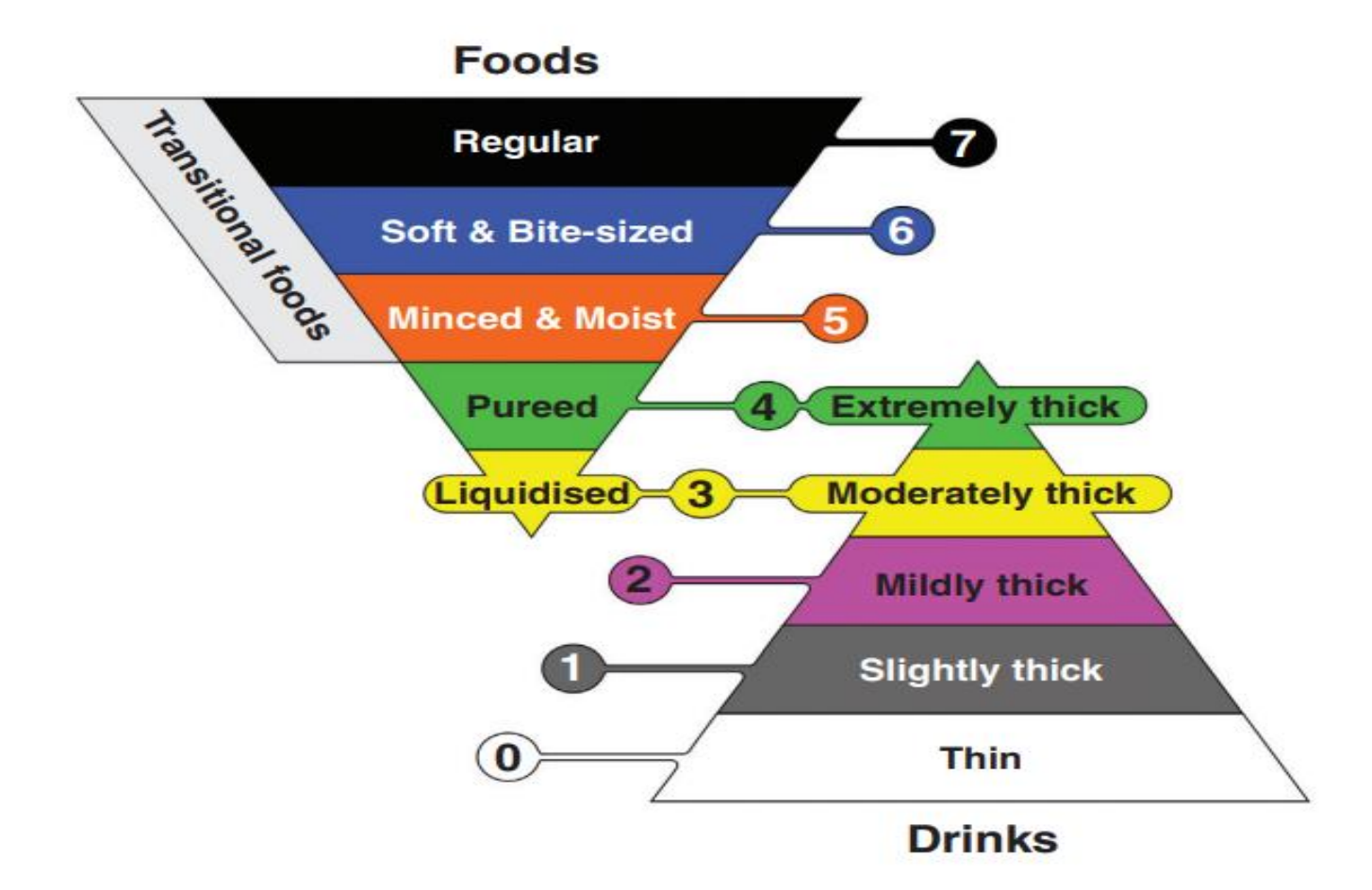
- As the disease progresses, **neurologic deficits** and **dysphagia** may occur.
- Thus, diet consistency may have to be modified along the IDDSI continuum of regular (level 7) to pureed (level 4) foods, even progressing to thickened liquids (levels 2 or 3) **to prevent aspiration**.
- Impaired vision make meal preparation difficult.
- In this situation, reliance on **meal delivery services**, **prepackaged**, **single serving** often permits independent preparation of meals.
- Given the chronic nature of this debilitating disease, patients may require **enteral nutrition support**.

IDDS: International Dysphasia Diet Standardisation Initiative



Levels of National Dysphagia Diet (NDD)

Levels of National Dysphagia Diet (NDD)



Medical Nutrition Therapy (Cont.)

- Neurogenic bladder is common, causing urinary incontinence, urgency, and frequency.
- To minimize these problems:
  - distributing fluids evenly throughout the waking hours
  - limiting them before bed is helpful.
- Some patients severely limit fluid intake to decrease urination frequency, which increases the risk of UTIs.
- Neurogenic bowel can cause either constipation or diarrhea, and incidence of fecal impaction is increased in MS.
- A diet that is **high in fiber** with **additional prunes** and **adequate fluid** can moderate both problems.

Supplemental Vitamins, Minerals, and Herbs Used in MS

Vit/Min/Herb	Relation to MS	Risks	Food Sources
Vitamin D	Higher blood levels associated with lower risk of developing MS	High doses may increase risk of kidney stones in some people	Fish, fortified dairy breakfast cereals. Also produced in the skin in response to sunlight.
vitamins A, C, E	Prevent damage caused by free radicals	Safety of supplement in MS not clearly established; food sources are safest, and supplements can be tested in moderation under care.	A wide variety of fruits and vegetables. Vit A: eggs, fish, carrots, sweet potato, spinach, mangos, broccoli, salmon, pistachios. Vit C: citrus, tomatoes, broccoli, kiwi, bell peppers, strawberries, cauliflower, peas, brussels sprouts, cantaloupe, spinach. Vit E: almonds, hazelnuts, peanut butter, spinach, broccoli, sunflower seeds, sunflower oil, peanuts, corn oil, soybean oil

Vit/Min/Herb	Relation to MS	Risks	Food Sources	Role of RDN
B6	**No clear link**, but patients take for help with energy	High doses can cause numbness, tingling or pain at **doses as low as 50 mg/d**	B6: chickpeas, yellowfin tuna, salmon, chicken breast, fortified cereals, turkey,banana, bulgur, cottage cheese, winter squash,rice, nuts, onions, spinach, tofu, watermelon.	**DRI level from food and dietary supplements.** Do not exceed the UL
B12	**People with MS have low B12 more than general population**;	NA	Eggs, meat, poultry, shellfish, dairy products	**Supplement if necessary, especially if serum B12 is low** or methylmalonic acid **(MMA) level is elevated**

Vit/Min/Herb	Relation to MS	Risks	Food Sources	Role of RDN
Selenium	**Selenium levels are lower in people with MS**	Theoretically may increase the immune response	Seafood, beans, whole grains, low-fat meats, dairy	**Get selenium from foods; if using supplements, avoid exceeding the UL**
Calcium	Old hypothesis with very little evidence supporting it that MS was linked to high intake of milk in childhood with sudden drop off in teen years. **Could help generally with bone health** and this population tends to be at risk for osteoporosis	Use with caution in post menopausal women who are also at risk for CVD	Dairy, eggs, green leafy vegetables, calcium-made tofu	**Encourage food sources at the DRI level** or supplementation if dietary adequacy is not achieved

Vit/Min/Herb	Relation to MS	Risks	Food Sources
Zinc	Data is equivocal; **may activate immune system; may worsen an animal model of MS**	**High dose can cause copper deficiency leading to copper deficiency myelopathy**, which causes symptoms that **mimic MS**	Oysters, beef, fortified cereal, beans, chicken, yogurt, cashews, chickpeas, oatmeal, milk, almonds, kidney beans, peas
Ginkgo Biloba	**One small study shows it may help improve MS fatigue**; inhibits platelet activating factor to decrease activity of certain immune cells, theoretically could help MS; two human studies: **one suggested benefit**, **the larger showed no benefit** to prevent relapses or cognitive dysfunction	**May inhibit blood clotting** so avoid on bleeding disorder or surgery; **may interact with medications**	Tea and Capsules are most common

Vit/Min/Herb	Relation to MS	Risks	Food Sources	Role of RDN
Asian ginseng	One small MS study reports improvement in fatigue; **inconsistent results** in general population studies	**May stimulate immune system**	Tea and Capsules are most common	**Too little evidence to gauge effectiveness**
Cranberry	**May help prevent UTI,** a common issue in MS	**May interact with warfarin/ Coumadin**	Cranberry juice, sauce, fresh	**Monitor blood glucose with diabetes, check for drug nutrient interactions**

Alzheimer Disease (AD)

Dementia and Alzheimer Disease (AD)

- Cognitive impairment is **the stage** between the cognitive decline due to normal aging and the more serious decline of dementia.

- It can involve problems with memory, language, thinking, and judgment that are greater than normal age-related changes.

Alzheimer Disease (AD)

- AD affects an estimated 5.8 million Americans (Alzheimer's Association, 2019).
- AD is the 6th leading cause of death in the US and prevalence is increasing at a faster rate than other chronic diseases.
- For example, whereas deaths from CVD decreased by 8.9% between 2000 and 2017, deaths from AD increased by 145%.
- **Early-onset AD**, occurs at ages 30-60 years.
- AD appears to be more prevalent in Western countries.

Percentage change in causes of death (all ages) 2000 to 2017

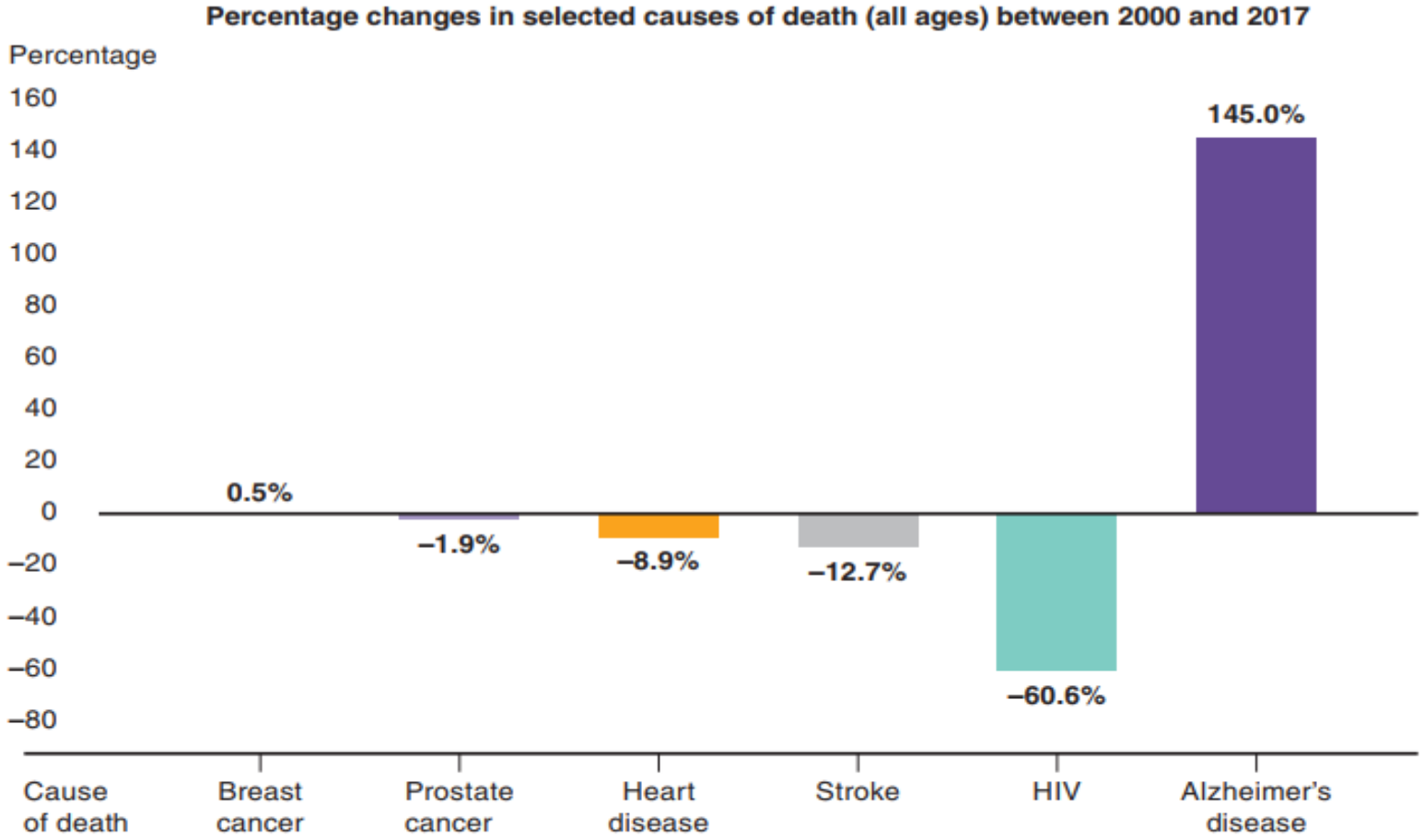


Fig. 42.2 Percentage change in causes of death (all ages) 2000 to 2017. (Adapted from Alzheimer's Association, Factors and Figures Report.)

Estimated lifetime risk for Alzheimer by age and gender, from the Framingham Study

Fig. 42.3 Estimated lifetime risk for Alzheimer by age and sex, from the Framingham Study. (Adapted from Seshadri S, Wolf PA, Beiser A, et al: Lifetime risk of dementia and Alzheimer's disease: the impact of mortality on risk estimates in the Framingham Study, *Neurology* 49(6):1498, 1997. Available from https://n.neurology.org/content/49/6/1498.)

Factors contribute to AD

- Like other chronic diseases, AD develops as a result of multiple factors.

- The most proven risk factor for AD is **advanced age**.

- Other **non-modifiable risk factors** that are associated with higher risk include:
  - positive family history of AD,
  - the presence of the APO-E4 allele
  - female gender, and
  - Down syndrome.

Factors contribute to AD (Cont.)

Modifiable risk factors include:

- cardiovascular disease risk factors (hypertension)
- diabetes
- obesity during midlife
- smoking
- high amounts of alcohol use
- traumatic brain injury
- and low educational level.

Recent research also links the **oxidative stress of air pollution** to **AD risk**.

- Currently, AD is incurable.

- Changes in the brain associated with AD **begin 20 years before symptoms appear**, providing opportunity for **life-style modification** to prevent AD.

- Factors that may be protective against AD include:
  - physical activity,
  - And social engagement.

Pathophysiology

- AD is characterized by microscopic changes in the brain that include **deposition of amyloid plaques**.

- For evaluating dementia, the American Academy of Neurology recommends structural **neuroimaging**, which may include
  - computed tomography (**CT**)
  - magnetic resonance imaging (**MRI**)
  - **screening for depression**
  - **vitamin B12 deficiency**
  - and **hypothyroidism**.

Medical Nutritional Therapy

- A healthier diet during middle-age years (adequate amounts of **B** vitamins, **antioxidants**, **PUFAs**, and **phytonutrients** was associated with **better cognitive function** later in life.

- The **MIND Diet** or **M**editerranean-DASH **I**ntervention for **N**eurodegenerative **D**elay was found to substantially slow cognitive decline with aging.

- Three **parameters of cognition** (delayed recall, learning ability, and memory) were significantly associated with **Hb-A1c** levels in the range of 4.3-6.5%, showing the effect of even **moderate blood glucose levels**.

- **High fructose intake** and a **deficiency of omega-3** fatty acids affect **cognitive abilities**

Key nutrients that involve in **AD** and brain health include:

- ✓ B-vitamins **folate, B12**, and **B6** ;
- ✓ **choline**;
- ✓ **iron**;
- ✓ **potassium**;
- ✓ **vitamins A, E**, and **D**;
- ✓ **omega-3** fatty acids, **saturated fat**;
- ✓ **cholesterol**
- ✓ **Polyphenols, caffeine/coffee, and curcumin**

- Folate is an important nutrient for prevention and treatment of AD.
- Participants who had intakes at or above the **400mcg RDA** for **folate,** had a **55% reduction** in risk of **AD**.
- **Adding folate** at **1mg/day** in AD, resulted in improved function.
- Overall, **multivitamins** resulted in **improved immediate recall memory**.

- **High folate** levels in the presence of **low vitamin B12** status worsens the enzymatic functions of vitamin B12, which can lead to **hyper-homocysteinemia** and **elevated MMA**, and **both are associated with cognitive impairment**.

- Inadequate levels of vitamin B12 can affect the risk for cognitive decline, AD, and dementia.

- This problem is exacerbated by the fact that approximately **10-15% of elderly** individuals are **B12 deficient** (<200 pmol/L) with **reduced ability to absorb vitamin B12**.

- Vitamin E Deficiency leads to poor transmission of nerve impulses.
- Adequate vitamin E may help slow progression of AD, but only when needs are met **through the diet, not supplements**.
- Most vitamin E supplements are synthetic α tocopherols, which may **increase risk of vitamin E deficiency**.
- High levels of α tocopherol (more than 100 IU/day) can induce a relative **deficiency of the other tocopherols**.
- Therefore, supplementation with synthetic vitamin E, **especially at doses more than 100** IU **is not recommended**.

- Iron accumulation in the brain is another hallmark of AD.
- Iron also released **in the breakdown and repair process of myelin sheaths**. In this sense, the more myelin sheath breakdown, the greater the accumulation of iron.
- Brain regions most affected by AD, have **higher levels of ferritin**.
- Excessive levels of iron in the brain can **promote free radical damage**, **lipid peroxidation**, and **cellular death**.

- The effect of dietary iron within recommended ranges and risk of AD **is not clear**.
- In some regions where consumption of **dietary red meat**, (the richest source of heme iron), is **less**, **lower incidence of AD** is reported.
- Recommendations stand to **limit consumption of excessive iron in the diet**.
- If taking a multivitamin, choose one **without iron**.

- Whereas high intakes of saturated fat and cholesterol are associated with higher risk of CVD, the **links to AD are not clear**, which may be **due to the individual's APOE genotype**.

- In a meta-analysis of 12 observational studies, it was shown that **in 4** of the 12 **studies**, **saturated fat increased AD risk** while **one study** showed **an inverse relationship**.

Medical Nutrition Therapy for Alzheimer Disease

- A **Mediterranean-style diet** may **slow cognitive decline**.
- A multivitamin supplement containing at least **400 mcg of folate**, **1000 IU of vitamin D**, and **500 mcg of B12**.
- If the **serum vitamin B12 level is under 300** pg/mL or **serum homocysteine or methyl-malonic acid are elevated**, a trial of **vitamin B12 injections** is reasonable.

- Low levels of the omega-3 EFA DHA are present in those with dementia.

- Increasing omega-3 (diet or supplement) is **helpful** in those with **mild cognitive defects than** in those with **severe AD**.

- AD is 70% less common in India than in the US, and this is due to a diet **high in turmeric**, the source of the bioactive compound curcumin, which is the spice that makes Indian curries yellow.

- **Curcumin may combat the buildup of beta-amyloid plaques** involved in AD.

- A shortcoming of supplementing curcumin is that it is poorly absorbed.

- **Piperine**, (major active component of black pepper), can **increase the bioavailability of curcumin.**

- Combining **curcumin and vitamin D** was also associated with increased amyloid clearance by macrophages.

- In the **MIND diet**, greater intakes of dark leafy greens, berries, nuts and seeds (MUFA and PUFAs) have been shown to be protective in AD and are emphasized whereas **red meats, cheeses, and fried foods are limited**.

Stroke

Stroke

- Stroke occurs either when the brain’s blood supply is suddenly interrupted.
- Stroke is responsible for about one in every 20 deaths.
- Stroke is a leading cause of serious disability in the US.

Factors contributing to stroke

- Advanced age is the most significant risk factor for stroke.

Modifiable risk factors:

- hypertension (major contributor)
- smoking (major contributor).
- poor diet,
- obesity,
- coronary heart disease,
- diabetes,
- physical inactivity,
- excessive alcohol intake.

- About 80% of strokes are preventable.
- People with a **history of stroke** are also at increased risk of **severe COVID-19** progression.

Nutrition Guidance to Reduce Stroke Risk

Recommended	
Mediterranean type diet	**Anti-inflammatory**, **antioxidant**, **antithrombotic** lower morbidity and mortality from stroke
DASH diet	Largely plant-based plus dairy products with low salt intake Associated with **reduced risk of stroke**
Plant-based diets	**Large amounts of vegetable sources** than animal sources
Fruits and vegetables	**5–9 servings a day** Ensures adequate intake of dietary fibers, minerals (**potassium, magnesium**), vitamins (**folic acid**) **Reduction of BP** Association with **reduced risk of stroke**
Nuts	**20–30 g/day** for heart health and **reduced risk of stroke** **Improves markers of oxidation, inflammation, and endothelial function**

Nutrition Guidance to Reduce Stroke Risk

Recommended	
Whole-grain cereals	Adequate intake for heart health **Improvement of BP, body weight, insulin resistance, lipid profile, and subclinical inflammation** **limited evidence for a reduced risk of stroke at higher intakes**
Legumes	Support heart health **No association between legumes intake and stroke risk**
Olive oil	Use extra virgin olive oil as main fat **Reduced risk of stroke** with higher intakes of extra virgin olive oil
Chocolate	**Moderate intake of dark chocolate is associated with reduced risk of stroke** **Increased HDL, decreased LDL oxidation, improved endothelial function, and reduced BP**

Nutrition Guidance to Reduce Stroke Risk

Recommended	
Fish	Fish twice a week for heart health **PUFA, vitamins D and B, potassium, calcium, and magnesium contained in fish may have favorable vascular effects** **Reduced risk of stroke** with higher fish consumption
Milk and dairy products	**Regular intake of low-fat milk and dairy** products recommended **High content of calcium, magnesium, potassium, and bioactive peptides** **Lower risk of stroke** observed with regular moderate consumption of low-fat milk and dairy products
Coffee	**Moderate regular intake** recommended **Associated with lower risk of stroke** Contains **polyphenols, chlorogenic acid, caffeine, and lignans**

Nutrition Guidance to Reduce Stroke Risk

Recommended	
Tea	**Moderate intake** recommended, especially **green tea** Favorable health effects of **antioxidants, catechins** Higher tea consumption is associated with **reduced risk of strokes**
Alcohol	Moderate intake of 1 drink/day for women; 2 drinks/day for men may reduce risk Moderate consumption is associated with improved lipid profile, reduction in platelet aggregation, beneficial effects on inflammation, and antithrombotic effects **Alcohol abuse associated with increased risk of stroke**

Nutrition Guidance to Reduce Stroke Risk

Recommended	
Dietary calcium	Adequate dietary intake recommended Possible **beneficial effects of low-fat dairy products on BP** and systemic inflammation, particularly in **overweight individuals**
Magnesium	Adequate dietary intake recommended **Beneficial effects on BP, insulin resistance, and blood lipids**
Potassium	Meet DRI recommendations **Blood pressure–lowering effect** **Inverse association between potassium intake and risk of stroke**
Folates	Adequate dietary intake recommended as it has been **associated with lower risk of stroke**

Nutrition Guidance to Reduce Stroke Risk

Recommended	
Vitamin C	Adequate dietary intake recommended **Prevention of endothelial dysfunction, anti-inflammatory and antihypertensive role** **Both higher dietary and blood levels of vitamin C are associated with reduced risk of stroke**
Vitamin D	**Correct for deficiency**, **Favorable role on BP, insulin sensitivity, endothelial function**, **Low blood levels of vitamin D are associated with increased stroke incidence**
Dietary fiber	Adequate dietary intake of **at least 25 g/day** through plant foods recommended to reduce BP, improve insulin resistance, lipid profile, inflammation, and endothelial function **Dietary fiber intake is associated with reduced risk of stroke**

Nutrition Guidance to Reduce Stroke Risk

Recommended	
Low-glycemic load carbohydrates	A low-glycemic load diet is recommended **A high dietary GL is associated with risk of stroke**
Dietary fats	Intake of MUFA-rich and PUFA-rich foods recommended, **especially to replace saturated fats and refined carbohydrates**
Protein	Adequate dietary intake recommended **No sufficient evidence for association between protein intake and stroke**
Eggs	**No recommendation available as no association with stroke was documented**

Increase risk of stroke

May Increase Risk	
Western diet	A highly processed **Western diet** that is high in meat, saturated fats, and refined carbohydrates and low in whole grains, fruits, vegetables, legumes, nuts, seeds, and fiber is associated with multiple **chronic diseases** including **stroke**
Meat and processed meat	**Limit meat to 1–2 times per week**; **limit processed meat as much as possible** Likely linked to the unfavorable effects of **SFA, lipid peroxidation, and high salt of processed meat on BP** High intake of meat and processed meat is associated with **higher risk of stroke**
Sodium	**Reduce to 2 g/day or below (5 g of salt)** **Strong relationship between higher salt intake and risk of elevated BP and stroke**
Sweetened beverages	**Limit due to unfavorable effect on LDL, VLDL, blood glucose, and insulin** **Associated with increased risk of stroke**

Medical Nutrition Therapy

- Lifestyle and behavior changes including diet are key components to primary prevention of stroke.
- Mediterranean diet **supplemented** with nuts or extra virgin olive oil reduced stroke.
- Foods that improved inflammatory markers include **nuts, low-fat dairy, whole grains, and antioxidant-rich fruits and vegetables**.
- In particular, a diet **high in omega-3** fatty acids has benefits against stroke.
- Current dietary recommendations: seafood **twice per week** help meet omega-3 intake goals.
- **Keep in mind** that **omega-3 fatty acid supplements** have **not shown the same benefit** and are contraindicated for anyone taking **warfarin or aspirin**.

- **Dysphagia**, commonly accompanies stroke and contributes to complications (malnutrition, pulmonary infections, disability, increased length of hospital stay).

- In some instances, **enteral nutrition** via a tube feeding is required to maintain nutritional health until oral nutrition can be resumed.

- Malnutrition should be prevented.

Epilepsy

Epilepsy

- Epilepsy is a chronic condition characterized by recurring seizures.
- Seizures are caused by abnormal electrical activity of a group of neurons.
- 1.2% of the total U.S. population has active epilepsy.
- Seizures before age 2 are usually caused by fever, developmental defects, birth injuries, or a metabolic disease.
- An electro-encephalogram can help understand seizure activity.

Medical Nutrition Therapy

- The classic ketogenic diet, since the 1920s, is a well-established non-pharmacologic treatment for epilepsy.
- A 2018 statement advocates for implementing **a ketogenic diet** to manage epilepsy **even before medications**.
- While the exact mechanisms are not clearly understood, therapeutic benefits may be due to neuron protection against reactive oxygen species.
- Two mouse models suggest that **gut microbiota is altered** by ketogenic diet, **correlates to seizure protection**.

Medical Nutrition Therapy (Cont.)

- Originally designed using ratios of 4:1 or 3:1 (grams of fat to non-fat) to achieve strong and consistent ketosis,
- Less restrictive versions are now available that can also be effective.
- The **modified ketogenic** diet uses lower ratios (e.g., 1:1 and 2:1), and **modified Atkins** are also beneficial.

Medical Nutrition Therapy (Cont.)

- Short-term **side effects** include fatigue, headaches, nausea, constipation, hypoglycemia, especially in the first few weeks on the diet.
- The dietary fat ratio can be decreased to improve tolerability.
- Ensuring adequate **fiber and fluid** can help manage gastrointestinal distress and improve compliance with the ketogenic diet.
- Although the diet is restrictive and requires continued effort, **ketogenic diets are effective in reducing seizure** frequency **by 50%** or more **in about half of patients** who are otherwise **resistant to drugs.**

Medical Nutrition Therapy (Cont.)

- **Improvement in seizure** control can take **up to 3 months after diet** has been implemented.
- Antiepileptic drugs **are not stopped** but may be reduced after the diet therapy is effective.
- The majority of the diet is composed of **fresh meats, eggs, cheese, fish, heavy whipping cream, butter, oils, nuts, and seeds**.
- **Vegetables and fruits are added in small amounts** within the current diet prescription.
- A **carbohydrate-free multiple vitamin and mineral supplement** is necessary.

Medical Nutrition Therapy (Cont.)

- However, additional vitamins and minerals are often necessary, including **calcium, vitamin D, and selenium**.
- All prescription and over-the-counter medications (e.g., pain relievers, cold remedies, mouthwash, toothpaste, and lotions) **must be checked for sugar content** to minimize carbohydrate.
- **It is important that the diet be strictly followed**; the smallest amount of extra carbohydrate can cause a breakthrough seizure.
- Weight and height should be monitored because a **rapid rate of weight gain can decrease ketosis and reduce effectiveness**.

Anxiety

Anxiety

- Anxiety disorders are the most common mental illness in the US.
- The prevalence of anxiety in developed countries is 13.6-28.8% and are **higher in developed nations** than in developing ones.
- The underlying etiology of anxiety is not well understood.
- Different forms of anxiety include
  - generalized anxiety disorder (GAD), اختلال اضطراب فراگیر
  - panic disorder, اختلال هراس
  - obsessive compulsive disorder (OCD), اختلال وسواس فکری عملی
  - post-traumatic stress disorder (PTSD), اختلال استرس پس از سانحه
  - and social anxiety disorder. اختلال اضطراب اجتماعی

Pathophysiology

- Difficult life circumstances that provoke stress can exacerbate underlying anxiety disorders.

- These can include relationship stress, job stress, sadness, and physiologic stressors, such as sleep disorders, menopause, thyroid disease, and food allergies.

- Hormonal imbalances, including high or low thyroid, low progesterone, and high or low testosterone levels, can also trigger anxiety.

Medical Nutritional Therapy

- **Blood sugar imbalance** or **being hungry** can trigger anxiety.
- Eating smaller, balanced meals and routine mealtimes is recommended.
- **Nutritional deficiencies** may be present, especially of vitamin **D**, **B** vitamins, and **magnesium**.
- **Magnesium deficiency** can cause anxiety, and anxiety also can cause increased magnesium losses.
- A multivitamin with **100 mg magnesium** and **B vitamins** was shown to **decrease anxiety**.

Medical Nutritional Therapy

- A recent study (445 healthy females) showed that higher intake of fermented foods that contain probiotics such as **yogurt, kefir, pickles** may be **protective against social anxiety symptoms**.
- High consumption of **fruits and vegetables** as well as **exercise** frequency were also negatively correlated with social anxiety.
- **Deficiencies in L-tryptophan, L-phenylalanine, or L-tyrosine are associated with anxiety**.
- Integrative therapies such as **meditation**, **mindfulness**, and **yoga** may also be helpful.

Medical Nutrition Therapy for Management of Anxiety

Assess for **vitamin D, magnesium, and B** vitamin, and **essential fatty acid** status

Eliminating caffeine for 3–4 weeks is recommended

Switching from coffee to green tea can also be helpful as it has less caffeine

Regular meals with protein and low glycemic carbohydrates **to promote stable blood sugar**

Adding a multivitamin, folate, B12, zinc, magnesium, and vitamin D

Integrative Therapies for Anxiety

- GABA: Deficiency of the neurotransmitter gamma-amino-butyric acid (GABA) is associated with anxiety.

- Inositol: Inositol can be helpful in treating anxiety and panic disorders and is very safe.

- Lavender: The smell of lavender is calming, so keeping a vase full of **lavender flowers** (even dried) around or using a **lavender oil spray** can be helpful.

Attention-Deficit/Hyperactivity Disorder (ADHD)

Attention-Deficit/Hyperactivity Disorder (ADHD)

- ADHD is a common neurological disorders of childhood that affect behavior and socialization.
- ADHD also might **affect eating behaviors** and **nutrient intake**, which can manifest as **food aversions**, **hypersensitivity to textures and flavors**, and **inadequate intake**.
- ADHD is beginning in childhood and often extending into adulthood.
- Between 9.5-11% of children in the US diagnosed with ADHD.

Factors contribute to ADHD

- The causes of ADHD are not well understood.

- Genetic factors
- Alcohol, drug, or tobacco use during pregnancy
- Premature delivery or low birth weight
- Environment, exposure at a young age; lead, pesticides
- Brain injury

- Television, sugar **do not cause ADHD**, although they can **exacerbate symptoms**.

Nutrition Assessment

Anthropometric measures:

- Height and weight
- **Medications may cause anorexia** resulting in inadequate energy intake and slowing of growth, especially with long-term use.

Dietary intake:

- A detailed **dietary history** should be obtained.
- Evaluate **the mealtime environment** to identify ways to reduce distractions through changing seating or limiting electronics.

Medical Nutrition Therapy

- Standard treatment includes **behavioral therapy** (47% of children) and/ or **medication** (62% of children).
- Medications tend to reduce appetite and/or weight gain, especially in the first year of use.

- When weight gain is a concern, care providers offer higher fat/sugar foods to encourage intake.

- This may contribute to obesity seen in adolescents and adults with ADHD.

- Encourage weight gain by offering
  - **calorically dense foods before medication**;
  - **small and short frequent meals**;
  - **and limiting visual/auditory distractions at meals** (TV, tablets).

- **Restricted diets** for ADHD were proposed in 1970s, starting with the **Feingold diet**.

- **Feingold diet:** eliminates salicylates and artificial food, and additives.

- **Gamma-linolenic acid** (GLA) and **EPA** appear to be **the most effective** of the EFAs trialed.

- Typical **“Western” diets** are **low in omega-3** fats and have been **linked to ADHD**.

- While research on diet and ADHD remains **inconclusive**, **reducing** intake of **processed foods**, **increasing** intake of **omega-3** fatty acids, and **ensuring appropriate weight gain and growth** should be part of MNT for ADHD.

TABLE 45.5 Proposed Dietary Interventions in Neurobehavioral Disorders

Dietary Interventions	Associated Disorders	Guidance for Use
Additive/food dye–free diet Removal of synthetic food dyes: Blue 1 & 2, Citrus Red 2, Green 3, Red 40, Yellow 5 & 6, sodium benzoate	May reduce hyperactive and attentional issues in ADHD, ASD, and typically developing children with sensitivities (Garcia et al, 2017; Lange et al, 2017; Ly et al, 2017)	Requires instruction in label reading, may increase cost of some food products
Elimination diets Elimination of common allergens, usually milk, egg, wheat, soy, peanuts, tree nuts, fish/shellfish May also exclude other foods limiting diet to a handful of hypoallergenic foods	Food allergies Eosinophilic esophagitis ADHD ASD	Used temporarily for identification of problematic foods Requires detailed logs of intake and behavior to detect patterns Foods introduced systematically Removal of food for prolonged time can lead to rebound allergy response in sensitive children and can lead to food refusal in ASD When foods are reintroduced, identify foods that the whole family can eat to encourage social inclusion Requires instruction in label reading, may increase constipation especially if highly processed grains are used

FODMAPs diet SCD Elimination of classes of carbohydrate to address low levels of digestive enzymes or alterations in microbiome	Gastrointestinal concerns such as Crohn disease, ulcerative colitis, carbohydrate intolerance ASD with gastrointestinal symptoms	Requires detailed education for both consumer and RDN, both diets include staggered restriction/introduction which is helpful for identifying target foods and minimizes risk, specifically with SCD. SCD can lead to nutrient deficits for young children with limited diets. SCD may limit variety of textures which may influence progression of textures in feeding therapy (see Appendix 28)
GF and CF diets Eliminate casein-containing foods (milk from cow, goat, sheep, etc.) and/or gluten-containing foods (wheat, rye, barley)	Celiac disease (GF), commonly used with DS, ASD, and ADHD Cerebral folate deficiency (CF) Food allergies	Identify foods that whole family can eat to encourage social inclusion, requires instruction in label reading, may increase constipation especially if highly processed GF grains are used. Ensure calcium adequacy with CF diet.

ADHD, Attention-deficit/hyperactivity disorder; *ASD*, autism spectrum disorder; *CF*, casein-free; *DS*, Down syndrome; *FODMAPs*, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; *GF*, gluten-free; *RDN*, registered dietitian nutritionist; *SCD*, specific carbohydrate diet.
References: Sathe et al, 2017; Ly et al, 2017; Ptomey and Wittenbrook, 2015; Mastrangelo, 2018; Garcia et al, 2017.

TABLE 45.6 Examples of Effects of Nutrient Supplementation in Neurobehavioral Disabilities

Omega-3 fatty acid supplementation	ASD: Little evidence supports the effectiveness of omega-3 supplementation to improve core or associated ASD symptoms (Sathe et al, 2017) ADHD: Modest support for decreased lability, increased attention, and decreased oppositional behavior with GLA and EPA supplementation (Lange et al, 2017) FAS: Possible benefit prenatally and postnatally (Murawski et al, 2015)

Magnesium	ASD: No evidence to support use (Garcia et al, 2017) ADHD: Evidence inadequate to support use (Lange et al, 2017)
Probiotics	ASD: No evidence to support use for ASD, but moderate evidence to support use in treating gastrointestinal issues such as constipation (Garcia et al, 2017) Other disorders: May help to relieve constipation

ADHD, Attention-deficit/hyperactivity disorder; *ASD*, autism spectrum disorder; *EPA*, eicosapentaenoic acid; *FAS*, fetal alcohol syndrome; *GLA*, gamma-linolenic acid.

یافته های مطالعات اخیر

The relationship between nutrition and depression in the life process: A mini-review

Ekinci G, et al.

Experimental Gerontology, 2023

- ✓ Food preferences, and nutrient content of the diet were found to be associated with depression.
- ✓ It is known that **probiotic supplementation** can be effective in preventing of depression, and **omega-3** fatty acids are associated with the severity of depression symptoms.
- ✓ **Vitamin D and vitamin B6** are involved in the production of serotonin.

Conclusion

- Low levels of **vitamin B12** are associated with the severity of depression.
- It is known that **folic acid** contributes to the recovery of depression **by increasing the effectiveness of antidepressant** drugs.
- **Selenium, magnesium and zinc** have a protective effect against depression.
- **Copper** is protective against depression by playing a role in the conversion of dopamine to norepinephrine.
- Considering the effects of food on depression, people's **nutritional status**, **diet quality**, **adequate dietary intake** of vitamins and minerals are closely related to people's mental health.

Diet and depression: A systematic review of whole dietary interventions as treatment in patients with depression

Swainson J, et al.

Journal of Affective Disordes 2023.

- ✓ This study found that **Mediterranean diet** might be an appropriate treatment for depression.
- ✓ However, the **mechanism is not clear**, (through anti-inflammatory mechanisms or via weight loss in overweight patients).
- ✓ Future research investigating the impact of dietary interventions on a large-scale is needed.

Mediterranean Diet and Lifestyle in Persons with Mild to Moderate Alzheimer's Disease

Dominguez LJ, et al.

Nutrients 2024

- **AD patients had a low adherence to the Med-Diet** and very **low physical activity**.

- Public health strategies to promote the Mediterranean diet and physical activity for older people should be a priority.

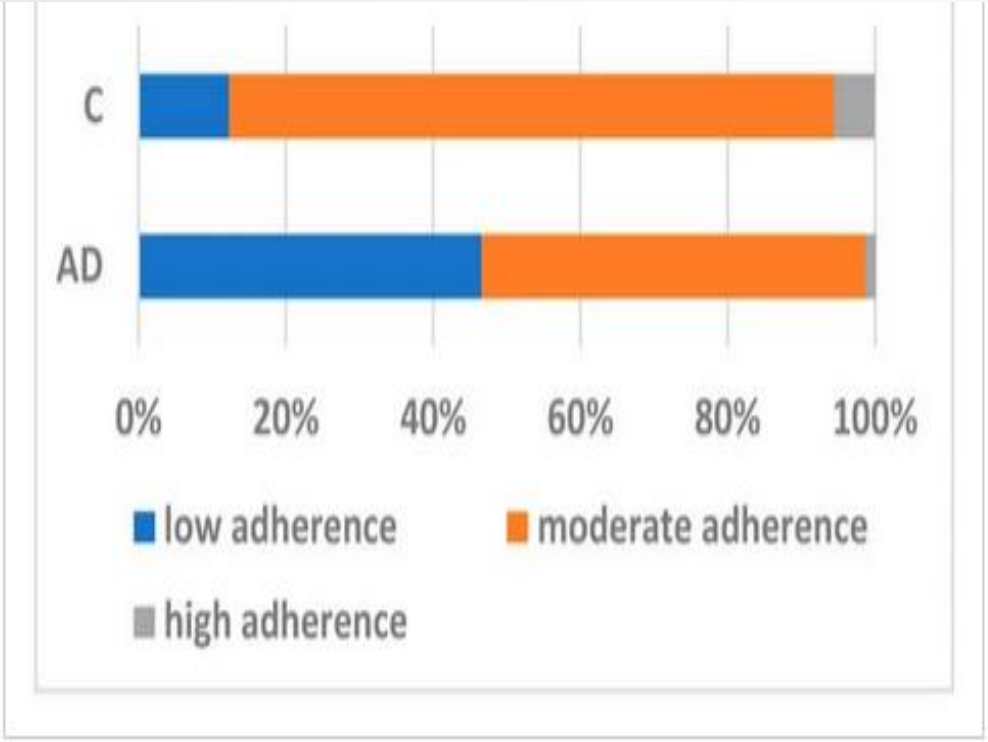
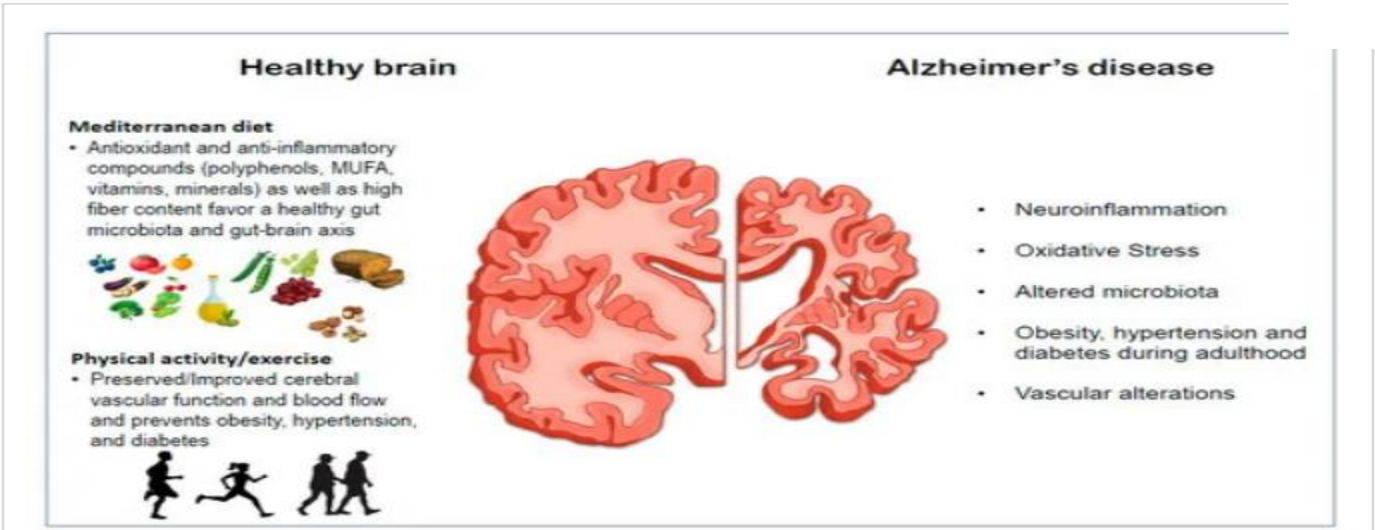


Figure 1. Adherence to Mediterranean diet in cases and controls. AD: Alzheimer's disease; C: controls.

Some mechanisms that explain the neuroprotective effects of the Mediterranean diet and physical activity in the prevention of AD



خواص ضدالتهابی و آنتی اکسیدانی ترکیبات موجود در رژیم مدیترانه ای
MUFA، پلی فنولها، ویتامین ها و مینرال ها، فیبر
رشد میکروبیوم روده
فعالیت بدنی: بهبود عملکرد عروق و جریان خون، پیشگیری از چاقی، دیابت و پرفشاری خون

Association of MIND diet with cognitive decline among Black and White older adults

Agarwal P, et al.

Alzheimers Dement 2024.

- The intake of **MIND** diet may slow cognitive decline in both Black and White older adults.

- This association may vary with other lifestyle and vascular risk factors.

✶ MIND: Mediterranean-Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay

Effect of Mediterranean diet on body mass index and fatigue severity in patients with multiple sclerosis: A systematic review and meta-analysis of clinical trials

Moravejolahkami AR, et al.
Heliyon 2024.

After analyzing 228 entries, we found five Randomized Controlled Trials (RCTs) with a total of 540 participants, who had an average disease duration of 8.5 years.

Adherence to MeD may improve BMI and fatigue severity in MS patients.

Further RCTs are needed to confirm the current results.

از توجه شما سپاسگزارم