Diabetes Mellitus and Alzheimer’s Disease: Pathophysiology, Oral Disease, and Exercise Physiology

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Learning Objectives

• Develop and disseminate information addressing health problems of geriatric patients, with specific focus on diabetes mellitus (DM) and Alzheimer’s Disease (AD)

• Utilize a interprofessional approach to geriatric disease treatment and prevention with an open exchange of information and skill building from faculty and participants.

• Provide interprofessional training for faculty and providers who care for geriatric patients with a focus on team/patient bidirectional communication, prevention of co-morbidities and cultural sensitivity.

• Introduce and develop interprofessional team building skills using standardized patient teaching and simulation training.
Physiological Overview of Diabetes

- Diabetes defined
- Types of diabetes
- What is Glycosolated Hemoglobin A1C? (HgA1C, A1C)
- Treatment
- Chronic complications
- Aging and diabetes
Diabetes Mellitus Defined

• “Clinical diabetes mellitus is a syndrome of disordered metabolism with inappropriate hyperglycemia due either to absolute deficiency of insulin secretion or reduction in the biologic effectiveness of insulin or both”

Greenspan & Gardner, 2011
Type 1 Diabetes Mellitus

• Severe form associated with ketosis if untreated
• Catabolic disorder which circulating insulin is virtually absent, plasma glucagon is elevated and pancreatic \( \beta \) cells fail to respond
• Patients must have insulin to treat this disease
Type 2 Diabetes Mellitus

- Relative insulin deficiency, not absolute insulin deficiency
- Accounts for 80-90% of DM in the USA
- Insulin not needed to survive, though over time secretory capacity to produce insulin by the pancreatic β cells often diminishes over time
- Etiology is complex mix of genetics, tissue insensitivity and lifestyle factors
Subgroups of Type 2 Diabetes

• Obese
  – Insensitivity to endogenous insulin correlated with abdominal fat, distended adipocytes, over nourished liver and muscle cells develop resistance to insulin; hyperplasia of pancreatic β cells and increased insulin; with progression of disease, secondary failure of the pancreatic β cell production with exposure to prolonged fasting hyperglycemia
Subgroups of Type 2 Diabetes - continued

• Metabolic Syndrome (Syndrome X)
  – Syndrome with key elements: hyperglycemia often associated with hyperinsulinemia, dyslipidemia, hypertension and visceral obesity

• Non-Obese
  – Deficient insulin release by the pancreatic $\beta$ cells seems to be the major defect but there is also a combination of insulin resistance; ethnicity and genetics play a factor in development
What Is Hemoglobin A1c?

• Hemoglobin formed by exposure to plasma glucose over time
• Used as a marker for average blood glucose levels over the previous 3 months
• The normal range of HbA1c is 4-5.9%
• Runs >/= 8.0% in poorly controlled DM
• Maintained at < 6.0% to 7.0% in well controlled DM
HgA1C Interpreted

- HgA1C is usually checked every three months by the treating provider
- This is the ability to monitor long-term serum glucose regulation
- The HgA1C level is proportional to average blood glucose concentration over the previous 4 weeks to 3 months
- Calculating the A1C: HgA1C x 35.6 – 77.3 = Average daily glucose
- Example: HgA1C = 11.4%
  - 11.4 x 35.6 = 405.84 – 77.3 = 328
  - 6.5 x 35.6 = 231.4 – 77.3 = 154
  - 5.3 x 35.6 = 188.68 – 77.3 = 111
Treatment of Diabetes Mellitus

- Diet
- Exercise
- Weight loss
- Pharmacotherapy
  - Oral agents
  - Injectables
Chronic Complications of DM

- Neurologic
- Oral
- Vascular
- Ophthalmologic
- Renal
- Cardiovascular
- Skin
- Bone and Joint
- GI/GU
Aging and Diabetes Mellitus

- Prevalence of DM approximately 26.9% of 10.9 million patients >65 years (National Diabetes Information Clearinghouse, 2011)
- Many with diabetes mellitus are obese and have other contributing characteristics such as age, gender, ethnicity, and BMI
- DM contributes to functional limitations
- Inflammatory markers: C-reactive protein (CRP) contribute to functional limitations in geriatric patients
Diabetes Statistics: Las Vegas

- 207,700 = total DM diagnosed and undiagnosed in Las Vegas in 2010
- Annual deaths = 1,840
- Total annual costs in 2010 = $2.6 Billion
- Future predictions:
  - 2015 = 282,700 pts with DM (cost = $3.5B)
  - 2025 = 451,800 pts with DM (cost = $5.5B)

http://www.altfutures.org/diabetes2025/
2010 Nevada Statistics: Seniors

• Senior population in Las Vegas = 329,600
• 164,800 pre-diabetes
• 88,600 with diabetes
• Total annual cost = $866 million
  – Medical costs = $609 million
  – Nonmedical costs = $257 million
DM and the Geriatric Patient

• Increased risk factors:
  – Increased BMI
  – Increased waist circumference
  – Hypertension
  – Age, gender, ethnicity

• Multidisciplinary assessment:
  – Physiological: medical, dental, nursing
  – Functional
  – Psychological
Alzheimer's Disease (AD)

- Defined: “Alzheimer’s disease is a neurodegenerative disease of the brain characterized by a clinical dementia with prominent memory impairment and specific microscopic pathology including senile plaques and neurofibrillary tangles”
Prevalence

• 5.3 million American’s of all ages have Alzheimer’s disease in 2015

• 5.1 million people are age 65 and older, with 200,000 under age 65

• 2/3 of American’s with Alzheimer’s disease are women

• By 2025, it is estimated that 7.1 million American’s age 65 and older will have AD
Projected Increases in AD

- The projected increases in AD rise sharply in 2030 as the baby boomer generation achieves age 65.
- The biggest increases in AD happened during ages 65-85 with a 2.5% incidence at age 65-70 years old and peaking at 50% in those over age 85.
- Average AD patient lives approximately 10 years from diagnosis to death (range 4-12 years)
Alzheimer’s Disease Pathology

• There are two main pathology features: senile plaques and neurofibrillary tangles.

• **Senile plaques** contain a specific type of amyloid, often referred to a β-amyloid or as “Aβ”. (This amyloid does not have anything to do with systemic amyloid or amyloidoses)

• Researchers believe these Aβ may cause the plaque damage in AD
AD Pathology - continued

• Neurofibrillary tangles
• Tangles are composed of hyperphosphorylated form of microtubule-associated protein Tau
• Tau is like the support beams or rivets in this microtubule system
• Tangles are like skeins of yarn; amount said to correlate with severity of AD

AD Diagnostic Criteria

• DSM-IV and National Institutes of Neurological & Communicative Disorders (NINCDS-ADRDA)

• Key Elements are:
  – Dementia
  – Progressive decline in: memory and at least one other major area of cognition (language, executive function)
  – No disturbance of consciousness, such as delirium or acute confusional state
  – Decline in function cannot be explained by another medical or brain disease
# Common Signs, Symptoms, and Stages

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Treatment

• Cholinesterase inhibitors
  – This class of drugs improve memory and other aspects of cognition, improved function, and reduce behavioral and neuropsychiatric sx.
  – They should be established as soon as a diagnosis is established, and continued until the goal of treatment is only hospice. Ultimately the goal is the pt to die care, dignity and comfort.
Interprofessional Team Care

- The AD team should include medical and non-medical members:
  - Medical providers: physician, dentist, nurse practitioner, physician assistant
  - Nutritionist, physical therapist, geropsychiatrists, occupational therapist
  - Home health case managers
  - Elder-law attorneys, support services (transportation, home care aid)
  - Care giver support!
Oral Disease T2D and Alzheimer’s Disease

• Why is oral health important?
• Common oral manifestations
  – Dental caries
  – Periodontal disease
• Oral Mucosa changes
• Salivary glands
Common Behavioral Oral-systemic Disease Risk Factors

- Diet
- Smoking
- Stress/Control
- Alcohol
- Hygiene
- Physical inactivity
Why is Oral Health Important?

- Teeth are designed to last over the course of life!
  - Loss due to disease
    - Dental caries - 85% > 65 y/o
    - Periodontal Disease - 98% > 65 y/o
    - Disease does not remain localized

- There is a strong link between oral disease and chronic diseases.
  - Systemic disease
    - T-2-D
    - Heart disease,
    - Cognitive decline

- “Oral health is essential to general health and well-being”

The U.S. Surgeon General
Healthy Periodontium
# Classifications of Periodontal Disease

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<tr>
<th>Stages</th>
<th>Cause</th>
<th>Time interval</th>
<th>Brief histological depiction</th>
<th>Concise clinical description</th>
<th>Management options</th>
</tr>
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<td>Gingivitis</td>
<td><em>Systemic factors</em>: Medication induced xerostomia, gingival enlargement, immune status, mouth breathing, <em>Local factors</em>: biofilm, plaque(gram-positive cocci and filaments), calculus deposits</td>
<td>4-7 days-Initial lesion, &gt; 14 days-chronic lesion Local host response</td>
<td>Chronic inflammatory cells, not associated with junctional epithelium periodontal ligament and connective tissue (CT) breakdown</td>
<td>Erythema, tissue edema, bleeding on probing/manipulation</td>
<td>Reversible after meticulous oral hygiene, removal soft/hard deposits. Salivary substitutes: Oral balance Moi-Stir MouthKote XeroLube Sialogogues: Evxac(Cevimeline) be aware Adverse side effects Caphosol artificial Saliva</td>
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<td>Advanced lesion transition to periodontitis</td>
<td><em>Systemic factors</em>: Medications, xerostomia, physical/cognitive impairment, chronic illness, social habits, financial constraints, oral health literacy <em>Local factors</em>: biofilm (gram-negative bacteria and spirochetes) expands into the subgingival space, calculus deposits, occlusion, tooth morphology/proximal contact, defective restorations, chronic advanced endodontic lesions</td>
<td>Local host response, &gt;14 days Distant host dependent response</td>
<td>Response to biofilm noxious substances cause chronic inflammatory elevated levels of monocytes; lymphocytes induce fibrotic response that has both local (CT breakdown and alveolar bone resorption) and systemic inflammatory manifestations.</td>
<td>Inflammation has extended to clinical loss of adjacent attachment, pocket depth 4-5 mm in moderate disease, advanced disease pocket depth &gt;5mm, evidence of alveolar bone loss. Evidence of furcation involvement, tooth mobility is associated with chronic inflammation.</td>
<td>Meticulous oral hygiene, with removal of supra/sub gingival soft/hard deposits, Non alcohol based Chlorhexidine gluconate 0.12% oral rinse(Peridex) Fluoride (Duraphat) varnish (Post periodontal surgery) Essential Oils (Listerine) Tricosan (Colgate Plax)</td>
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Periodontal and gingival tissues
Elderly have a higher plaque (thin sticky film of bacteria that adheres to the surface of teeth) score

• Gingivitis
• Periodontitis

[Insert clinical images of gingivitis and periodontitis]
Periodontal Disease (PD)

- Diet accumulation of biofilm on the retentive surfaces of dentition affect majority elderly
- **Oral disease and T2D are chronic inflammatory diseases with bidirectional relationship**
  - There is increasing evidence that patients with T2D and poor glycemic control have an increased risk of PD
  - PD contributes to increased insulin resistance leading to increased risk/progression of T2D
Impact of Diabetes on Periodontal Bone Loss

Diagram:
- Bacteria + Diabetes → Inflammation
  - ↑ Osteoclasts
  - ↓ Osteoblasts
  - ↑ Bone Resorption
  - ↓ Bone Formation
- Decreased Coupling and Net Periodontal Bone Loss
Periodontal Disease

- Is a sequelae of diseases
- Accounts for 30-35% of tooth loss
- >Men, ↑ in 30-40’s and older

Risk Factors
  - Diabetes
  - Medications which dry the mouth
    - Hypertension, renal, diuretics
  - Smoking
  - Hormonal changes
Risk Factors

• Specific examples of risk factors for periodontal diseases are age, gender, socioeconomic status, genetics, plaque biofilm, self-care, tobacco, stress, and diabetes

• Not all risk factors are modifiable
Prevention of Periodontal Disease

• Requires daily mechanical plaque control (toothbrushing and interdental cleaning) often supplemented with chemical control measures for plaque biofilm as an additional component (adjunct) of the primary treatment

• Fluoride mouth rinses can be used to aid in preventing root and coronal caries
Common Oral Manifestations

Dental caries

Modifiable risk factors
- diet dependent
- medication
- stress

Older adults
- Higher plaque score
- 4x more likely to have unrestored dental caries than children
Oral Mucosa

- Glossodynia (Burning tongue/painful sensation)
  - Etiology: idiopathic
  - Other causes
    - Trauma/Ill fitting prosthesis
    - Nutritional deficiencies, i.e. Vit B, Fe
    - Onset of T-2-D
    - Differential Dx screen pt for depression

- Clinically manifestation:
  - Beefy red appearance-exfoliating
  - Associated with xerostomia
  - Chronic burning

- Management: lab test to R/O
  - Fungal infection/Candidiasis
  - Nutritional deficiencies
- Poor wound healing
Salivary Glands

• Xerostomia (dry mouth)
• Salivary hypofunction
• Sialadenosis (enlargement of salivary glands)/noninflammatory disorder (parotid)
  – Associated with T-2-D
  – Malnutrition
  – Alcoholism
  – Bulimia

[Insert clinical image of salivary hypofunction]
Alzheimer’s Disease and Oral Disease

• A number of studies have found that those who experienced tooth loss of half or more of their natural dentition before 35 years of age had a 1.7 greater risk for Alzheimer's disease.

• Evidence to support that IL-6, and other cytokines will cross the BBB

• In all these studies it was concluded that oral disease is a risk factor for Alzheimer's
Other Manifestations of AD that Will Effect Oral Disease

- Xerostomia - medication induced
- Fever
- Malaise
- Dysgeusia (altered taste)
- Stomatitis – *Candida*
- Spasms of the muscles of mastication
- Tardive dyskinesia
- Hyposalivation
- Reduce appetite
- Decrease social contact
- Decline in IADL
- Lack of oral hygiene practice - *Irritable/Combative*
- Decline in self-care ADL - *forget to remove prosthesis*
Health is shaped by an interaction of biological, physiological, behavioral, and environmental factors that unfold over the course of life.
Exercise and Diabetes

• What is the best intervention to reduce HgA1c levels & maintain functional capacity (Verdijk et al., 2013)?

• Exercise intensity

• Exercise prescription
  – Adults with and without diabetes

• Challenges of safe exercise
Exercise and Diabetes
What is the Best Intervention?

• Many studies in past 10+ years have shown that Hemoglobin A1c levels are decreased with aerobic ex, resistance ex, or a combination in individuals with Type 2 diabetes

• However, many of these studies were underpowered in terms of comparing the types of exercise
Studies with Adequate Power and Control Groups

• Sigal et al., 2007: greatest benefit with combination but benefit with all exercise in HgA1c levels – exercised 4.5 hrs per week

• Church et al., 2010: significant benefit in HgA1c levels with combination but benefit with all – aerobic ex at 65% of VO2 max – aerobic & resistant groups exercised 2.33 hrs/wk & combo group exercise 2.42 hrs/wk for 9 mos

• Conclusion: combination for HgA1c levels
Exercise Prescription
Adults w/ Type II DM

• Submaximal endurance test (such as 1 mile walk) should be performed by a PT to estimate VO2max to measure baseline for improvement & compare to norms for age (ACSM’s Guidelines for Exercise Testing & Prescription, 9th ed) or the Six Minute Walk Test (American Thoracic Society) to compare distance to norms for the less fit

• Intensity: moderate intensity aerobic exercise defined as 3-6 METS or 150 Kcal/day
Examples of 3 to 6 MET Activities

• 3 MET
  – Walking 2.5 mph level

• 4 MET
  – Biking <10 mph leisure
  – Walking 3.5 mph level, brisk

• 5 MET
  – Stationary bike – 100 Watts (5.5), light effort
  – Low impact aerobics
  – Walking 4 mph level

• 6 MET
  – Biking 10-11.9 mph leisure
Exercise Prescription - continued

- Church et al, 2010 recommend 46 minutes of vigorous aerobic exercise (60-80% of VO2max) 3 days per week for HbA1c decreases in adults with Type II diabetes
- Church et al, 2010: Work up to 47 minutes of resistance exercise 3 days/wk for adults with Type II diabetes (8-10 exercises of large muscle groups; 8-12 repetitions to fatigue for healthy adults ACSM 2007) but dilemma: How to prescribe? Individualized and supervised initially and periodically
- Mode: any exercise that uses large muscle groups to an appropriate level of the patient’s capacity, needs, & interest
- Warm-up and cool-down
Challenges of Safe Exercise

- Recommend that patients see a physical therapist for initial evaluation and instruction in exercise program (2-3 visits plus 1-2 F/U visits over time)
- Many older adults have musculoskeletal problems and other co-morbidities that mean that the exercise prescription would have to be tailored to each individual patient as much as possible
- Precaution: Acute cardiac events significantly associated with episodic physical activity so must progress vigor of activity slowly (Dahabreh and Paulus, 2011)
Aerobic Exercise and AD

• What has aerobic exercise been shown to accomplish for patients with AD?
  – Decrease the risk of developing AD (Budson & Solomon, 2011)
  – Enhance memory (Scarmeas et al., 2009a)
  – Slow memory loss (Budson & Solomon, 2011)
  – Enhance cognitive function (Weuve et al., 2004)
How Are These Benefits Achieved?

• Several studies using rats have shown that aerobic exercise results in new brain cells developing in the hippocampus (Galvan & Bredesen, 2007)
What is the Role of the Hippocampus?

• Part of the limbic system
• Assists in the consolidation of information from short-term memory to long-term memory and also spatial navigation (Wikipedia)
• Hence the early symptoms of loss of memory & disorientation in AD
Physiologic Basis of Other Benefits of Aerobic Exercise for AD

• Can increase brain volume (Colcombe et al., 2006; 2008; Galvan & Bredesen, 2007)
• Can improve cognitive function (Weuve et al., 2004)
How Much Aerobic Exercise?

• The rat studies have shown a direct relationship between the amount of aerobic exercise and the development of new cells in the hippocampus (Galvan & Bredesen, 2007)
• “Some exercise is good, and more exercise is better.” (Budson & Solomon, 2011, p 218)
• Follow the guidelines for diabetes management and the precautions
The Cost of Diabetes in the US

• In 2007, total costs were $174 billion
  – Direct medical costs = $116 billion – after adjusting for population age and sex differences, average medical expenditures among people with diagnosed DM were 2.3 times higher than what expenditures would be without diabetes
  – Indirect costs = $58 billion – disability, work loss, premature mortality
Cost and Payment for Health Care

• Most geriatric patients enrolled in Medicare have significant out of pocket expenses related to outpatient care and dental services
• Outpatient physician providers = 15% cost covered by patient
• Dental care = 76% covered by patient
• Physical therapy outpatient costs = approximately 19%
Retirement Income

- Median income for age 65 and older in 2010 = $25,757 (Social Security Administration)
- The poverty rate for people age 65 and over was 8.7%
- Average spend 12-14% of their income on healthcare or $3,090 - $3,605
Summary: Chronicity of DM

- Neurologic
- Oral
- Vascular
- Ophthalmologic
- Renal
- Cardiovascular
- Skin
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