AGEING AND LONGEVITY MEDICAL WEBINARS

HANDBOOK

FLORES-GENUINO GENUINO ARQUIZA VISTA

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HANDBOOK

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NOTICE

Medicine is an evolving science. The information in this book has been reviewed for comprehensiveness, accuracy, and currency to the best of our efforts. However, human errors and omissions, updated guidelines and changes in scientific knowledge, may occur. Prudent judgment and due diligence should be exercised by healthcare professionals in applying the information from this book to their individual patients. The authors, editors, and publisher are not responsible for any untoward results of diagnosis or treatment from actual patient encounters. A critical and holistic approach, including careful history and physical examination and considerations of all variables, should be undertaken to ensure patient safety.

Errata to this ebook, if any, will be posted at FB.com/AgeingWebinars.

This webinar handbook is dedicated to the memory of
two esteemed and beloved sisters of the Mu Sigma Phi Sorority

Marilyn D. David-Ruaro†

Salvacion V. Rodriguez-Gatchalian†

FOREWORD

The holding of the *2019 Ageing and Longevity Medical Webinars* as part of the 85th year anniversary celebration of the Mu Sigma Phi Sorority of the UP College of Medicine has made this milestone event more enlightening and educational.

Webinars aim to bridge knowledge gaps. They celebrate the education, experience, and expertise of the UPCM-PGH alumni as primary speakers in the web-based lecture series. The webinar series on *Ageing and Longevity* is very timely, with WHO projections that, by 2020, the number of people aged 60 years and older will outnumber children younger than 5 years old. And in 2050, 80% of older people will be living in low- and middle-income countries. The Philippines is about to experience an increase in its ageing population or those aged 60 years and above. This age group currently accounts for 8.2% of the population, which means that the Philippines is "beginning to age."

The documentation of the webinar series through this e-book will be extremely useful as it serves as a companion handbook to the *2019 Ageing and Longevity Webinar* series. It provides a comprehensive overview of the main issues affecting population ageing as well as approaches to management and interventions. The knowledge and information provided by the webinars and e-handbook will assist policymakers and government leaders in planning for additional services as a result of expected growth in the number of older persons.

It is gratifying to note that the Mu Sigma Phi Sorority has designated the University of the Philippines (UP) Manila National Institutes of Health (NIH) Institute on Aging as its main beneficiary for many activities throughout the year. Fundraising events will retrofit the Philippine General Hospital (PGH) Geriatric Clinic to create a more age-friendly environment; equip other geriatric centers with educational materials and finance the training of its health workers; support *Wellness Initiative and Support for the Elderly (WISE) Health Caravan* to promote overall wellness and health literacy; and provide free immunization through *ImMUnity for the Elderly*. And the latest contribution – the *Ageing and Longevity Webinars* and its companion e-book – will educate not only the health workers but also the general public.

I commend the Mu Sigma Phi Sorority for the various activities that you hosted in support of the elderly. With the increasing number of the elderly in our population, we have to face the challenges of this demographic shift. You came ahead of the others – planning for a future to which others have not given much attention. More power to the spirit of sisterhood, scholarship, excellence, and leadership in educational innovations!

Carmencita D. Padilla, MD, MAHPS
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PREFACE

The digital landscape has truly revolutionized the healthcare field, with virtual opportunities for continuing medical education that have changed the way we gather information and learn. Amidst this global pandemic, online platforms such as webinars are proving to be vital tools in disseminating information and connecting healthcare professionals.

We believe that we successfully navigated this information highway through the highly successful webinar series on Ageing ang Longevity in 2019. Our Friday lunch hour webinars perpetually lacked time to accommodate all questions as participants eagerly typed in their queries. Soon, they were clamoring for a copy of these webinar lectures. Presto! the idea of a companion handbook was born!

We envision this handbook as an easily accessible, high-yield quick reference for general practitioners, other healthcare professionals, and students. It contains a distillation of the precious pearls of information delivered by medical experts in their webinar lectures. Whether reviewing for the medical or specialty board exams or just brushing up on the latest evidence for specific patient concerns, this handbook will be your perfect companion to the archived webinar recordings on the YouTube channel of Ageing Webinars.

Twenty three chapters, carefully and thoughtfully curated, cover the geriatric patient–from the ageing neurons to the ageing nephrons. With a touch of holistic and preventive medicine, we tackle the controversies of vaccination, self-care for the ageing healthcare professionals, and even spirituality in ageing.

It is our hope that this companion webinar handbook will contribute to better health care of the vulnerable ageing population. In partnership with our beneficiary, the Institute on Aging of the University of the Philippines Manila-National Institutes of Health, we dream that our Filipino and global population may overcome this pandemic and achieve healthy ageing.

This ambitious endeavor would not have been possible without the persistence of the authors, peer reviewers, editorial and webinar assistants, sponsors, and all those who helped in one way or another. For this, we are truly grateful.

We humbly offer this handbook to the Divine Healer who inspires and strengthens us beyond our human limitations.

Your editors,
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Marilyn D. David-Ruaro, MD, MHPED, FPOGS, FPSSTD, FPSUOG† (1951–2020)

by Filomena T. Santiago-San Juan, MD

On January 7, 2020, the field of Obstetrics and Gynecology of the Philippines lost its passionate teacher, while the University of the Philippines Medical Alumni Society lost its loyal alumna.

Dr. David-Ruaro finished her medical degree at the UP College of Medicine in 1976. She advanced her knowledge in teaching when she obtained her masteral degree from the National Teacher Training Center for Health Professions at UP Manila. Subsequently, she chaired the Committee on Medical Education and Training at Manila Doctors Hospital and authored the Manila Doctors Hospital Residency Training Book.

She obtained her residency in Obstetrics and Gynecology at the UP Philippine General Hospital and proceeded to become the first Trophoblastic Disease Subspecialist of the Trophoblastic Disease Section of the hospital. She subsequently became active consultant and head of the Trophoblastic Disease Section in Medical City and Manila Doctors Hospital. She was promoted and became the Chairman of the Department of Obstetrics and Gynecology, Manila Doctors Hospital, authoring the Hospital Clinical Guidelines and Pathways in the Management of different obstetrical and gynecological diseases. She was a founding member and subsequently became the President of the Philippine Society for the Study of Trophoblastic Diseases in 2018-2019.

Dr. David-Ruaro was committed to the ideals of the UP College of Medicine. She was active in the activities that nurtured the UPCM alumni, later becoming the President of the UP Medical Alumni Society, making the society responsive to the needs of the college, fellow alumni and the community.

Her sense of community service was illustrated in her activities as a loyal sister of the Mu Sigma Phi Sorority. She pioneered the Mu Health Caravan in 2009, providing free health education and medical services to the rural communities of the country. She was an excellent resource speaker in the topic of Ageing in Women.

Dr. Marilyn David-Ruaro was an academician who nurtured young residents in obstetrics and gynecology and advanced their knowledge and skills; a leader who worked hard to pursue the visions and missions of the organizations she led. Most of all, she was a well-loved and respected friend, colleague, and sorority sister who would be most remembered for her dedication and passion in delivering community-oriented health education and medical services – a true daughter of the UP College of Medicine.

Tribute to My Superstar: SALVACION R. GATCHALIAN, MD† (1952–2020)

by Dr. Maria Carmen B. Batacan-Nievera

Where to start to write about Ma'am Sally?

Ma'am Sally was one of the best pediatricians and pediatric infectious disease specialists in the Philippines and in Asia, if not the world. She was a great researcher and mentor whose name alone served as a seal of credibility on any scientific publication or presentation. She was much sought out for conferences and was known as a "blockbuster" lecturer in our circles.

She lived life to the fullest! There was nothing mediocre about her – from the way she delivered lectures, to the way she dressed, to the way she spoke with passion, to the way she ate her food (with spicy vinegar). Everyone immediately noticed whenever she entered a room because of her colorful, well-coordinated outfits, and matching jewelry. She lit the place up – and dazzled! She loved to dance, and was very good at it. But there was a lot more to her than that, as she was truly a lady of passion – for life, for disease prevention, for saving lives. We had marathon nights debating about hepatitis B, discussing polio, and so on. She would call for meetings with everyone who was essential for much needed communication materials, projects, activities, etc. A few times, she sought to meet senators to give them a piece of her mind about the ruckus on vaccination that she saw was detrimental to the health of our nation's children.

She was full of surprises! We, her mentees, were quite used to her calling us up to request that we deliver lectures on her behalf. No one dared say 'no,' of course; we loved her too much to refuse. We knew that, were the circumstances reversed, she would have done the same for us.

Above all else, she was so full of love for her husband, children, and siblings. Endless conversations with her made us feel as though we were part of her family. How she gushed about Dr. Ed, the love of her life. How she doted on her children, so loving and well-brought-up.

In the past couple of years, she volunteered to serve in her church as a lector. And surprise of all surprises, she was up in the wee hours of the morning and was ready for church before 6:00 AM. I remarked how this was such a change, but she seemed to be more happy and at peace. I have never seen her more serene and glowing with an inner joy.

If there are rock stars, movie stars, and K-pop stars, Ma'am Sally was the superstar among pediatricians here and abroad… and she was my superstar.

Look out, heaven! You have a lady who will staunchly advocate for the health of the Filipino child and the Philippine nation – she will be relentless, and she will not stop until she knows that the nation's health is in a much better place.

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SECTION 1

HEAD, NECK AND SENSORY ORGANS

Frances Evangeline S. Vista (Editor)

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1 DEMENTIA AND ALZHEIMER'S DISEASE

Grace O. Orteza, MA, MD, FPNA

Delivered as a webinar on January 25, 2019

https://bit.ly/ALMW_Ch1_Dementia

KEY POINTS

- Dementia is a common debilitating disease characterized by impairment of intellectual and mental functions.
- Majority of dementia is due to Alzheimer's disease, which is due to amyloid plaques in the brain.
- A 4-step diagnostic algorithm may be used as a guide; with imaging, gait analysis, olfactory testing, and biomarkers as additional diagnostic tests when indicated.
- Early detection and prevention of dementia by maintaining a healthy lifestyle is key.
- Pharmacologic intervention delays the course of dementia.

LEARNING OBJECTIVES

- To define dementia, Alzheimer's disease, and their relationship to ageing
- To provide an overview of the assessment and diagnostic tools for dementia and Alzheimer's disease
- To outline the management plan for dementia and Alzheimer's disease

I. DEFINITION

A. What is Dementia?

- It is a common, progressively debilitating disease especially in the elderly.
- It is defined as an impairment of intellectual function with compromise in multiple spheres of mental activity.
  - It is **acquired** – differentiates **dementia** from **intellectual disability**
  - It is **persistent** – differentiates **dementia** from **delirium**, which is temporary
  - It affects **multiple spheres of mental function**
- Majority (50–80%) of dementia is due to Alzheimer's disease (AD), with or without cerebrovascular contribution.

B. What is the Burden of Dementia?[1]

- 10% of all individuals 65 years of age and older are affected by dementia.
- One third (35%) of individuals 85 years of age and older are affected by dementia.
- Dementia is the top 5 (based on WHO Global Burden of Disease 2004) and top 9 (based on Institute for Health Metrics and Education [IHME] 2010) leading contributor to Disability Adjusted Life Years (DALY) burden among people aged 60 years and older.

C. What is Alzheimer's disease?[2]

- AD is the most common neurodegenerative disorder caused by deposition of amyloid plaques in the brain.
- The pathology in the brain occurs approximately a decade before the subtlest symptoms occur. This is called the preclinical stage of AD.

II. DIAGNOSIS OF DEMENTIA

A. Diagnostic Criteria

- Mild Cognitive Impairment (MCI) due to AD National Institute on Aging/Alzheimer's Association Mild Cognitive Impairment (NIA-AA MCI) Core Clinical Criteria[3]
  a. Complaint by the patient, family member, and physician noting that patient is forgetful
  b. Objective evidence of impairment (1–1.5 SD below the mean) in one or more cognitive domains, including memory
  c. – difficult to determine clinically
  d. Independence in functional abilities
  e. Not demented
  f. Etiology must be consistent with AD pathophysiology; vascular, traumatic or other medical causes should be ruled out
- All-cause Dementia
  - Not functionally independent; cannot perform activities of daily living without assistance
  - Problems in judgment, language, visual spatial ability, changes in personality and behavior
  - Atypical presentations
  - Onset of AD is insidious and gradual progression
- Probable AD
- Possible AD

B. Diagnostic Algorithm

- Is this mild cognitive impairment, dementia or part of normal ageing?

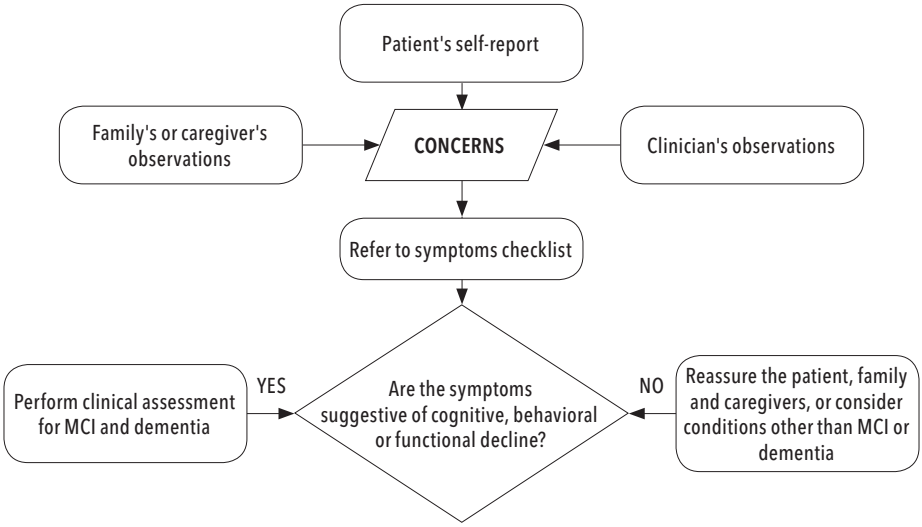

FIGURE 1–1. STEP 1: Eliciting symptoms that indicate need for evaluation of MCI and dementia

MCI, Mild cognitive impairment

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STEP 1. Eliciting symptoms that indicate need for evaluation of MCI and dementia (Figure 1–1)

- Cognitive – Symptoms Suggestive of Cognitive Decline (SSCD) like onset, severity, and frequency of forgetfulness, word-finding difficulties, misplacing important items, or disorientation
- Behavioral – Neuro Psychiatric Inventory Questionnaire (NPI-Q) like presence or absence of delusions, hallucinations, agitation or aggression
- Function – Functional Activities Questionnaire (FAQ) like ability to keep track of current events, travel out of the neighborhood, or shop for clothes

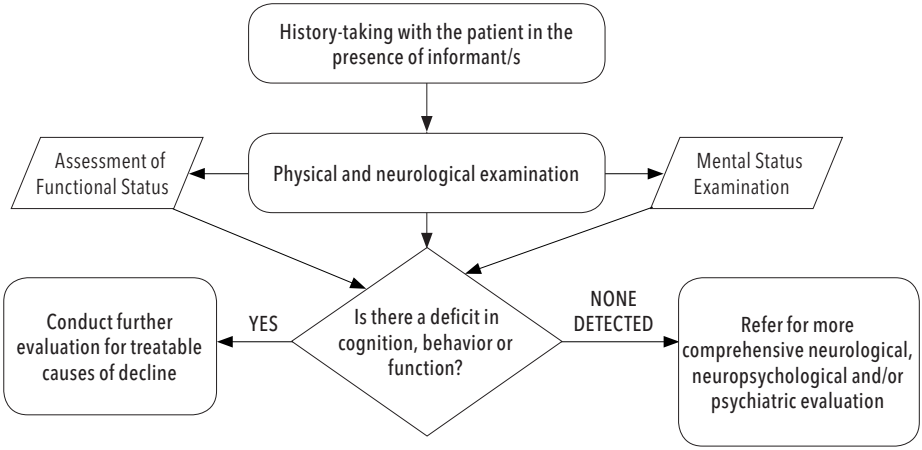

FIGURE 1–2. STEP 2: Clinical assessment and interpreting results

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STEP 2. Clinical assessment and interpreting results (Figure 1–2)[20]

- History-Taking
  - Focused on cognitive, behavioral, and functional domains
  - Emphasis on detecting change from previous status
  - Done in the presence of a qualified informant
- Physical Examination
  - Thorough and may be guided by Comprehensive Geriatric Assessment (CGA)
  - Neurological Examination
  - Establishes baseline functionality on initial visit
  - Focused on eliciting lateralizing and localizing signs to detect potentially reversible conditions
- Mental Status Examination
  - Montreal Cognitive Assessment (MoCA) or Montreal Cognitive Assessment in Filipino (MoCA-P) (Appendix Figure 1–6) and Clock Drawing Test (CDT)[4,5]
- Assessment of Functional Status
  - Adapted Functional Activities Questionnaire (A-FAQ)
- Is there a deficit in cognition, behavior and function?
  - Conduct further evaluation for treatable causes of decline
  - Refer for more comprehensive neurological, neuropsychological or psychiatric evaluation

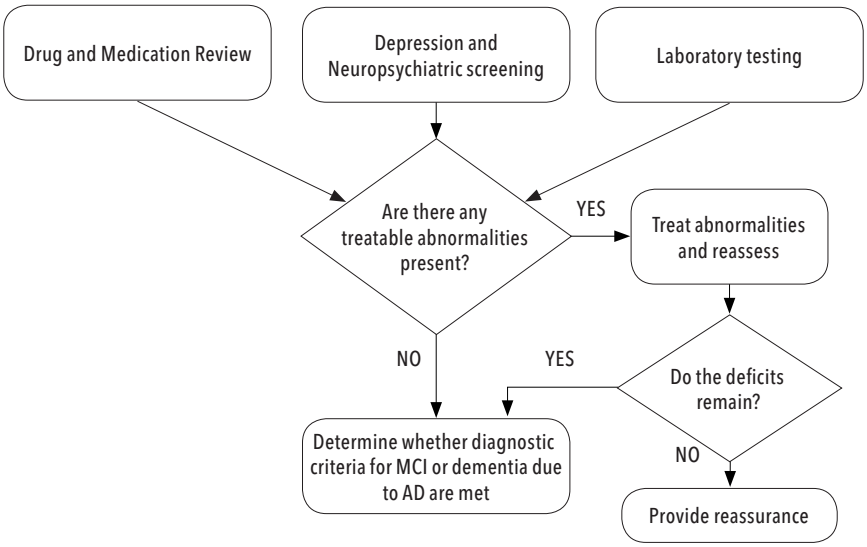

FIGURE 1–3. STEP 3: Evaluation for treatable causes of MCI and dementia

MCI, Mild cognitive impairment; AD, Alzheimer's disease

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STEP 3. Evaluation for treatable causes of MCI and dementia (Figure 1–3)

- A review of medications is also essential, as some drugs may cause delirium (e.g., analgesics, antihypertensives) or confusion (drugs with strong anticholinergic action, e.g., antihistamines)[3]
  - Updated Beers criteria (The American Geriatric Society [AGS], 2015)[6]
- Other systemic diseases must also be ruled out[3]
  - Metabolic (electrolyte and acid-base imbalance, hypoxia, hypercarbia, hypo- or hyperglycemia, uremia)
  - Infection, Sepsis, HIV
  - Decreased effective blood volume (CHF, dehydration, blood loss)
  - Urinary retention
  - Vitamin deficiencies (B12 and folate)
  - Pain
  - CNS (stroke, normal pressure, hydrocephalus, brain injury)
  - Medications
  - Environmental change (sundowning)
  - Hypo- or hyperthermia
  - Endocrine problems (uncontrolled diabetes, hypo- or hyperthyroidism)
  - Acute psychoses
  - Fecal impaction
  - Collagen-vascular (SLE)
- Psychological disorders such as depression and anxiety must be screened, and prompt referral to a psychiatrist when needed[7]
  - Zung's Depression and Anxiety Scales (Zung A and D)
  - Includes YES or NO questions that assess presence of anxiety (Do you feel nervous?) and depression (Do you feel that you lack energy?)[8,9]

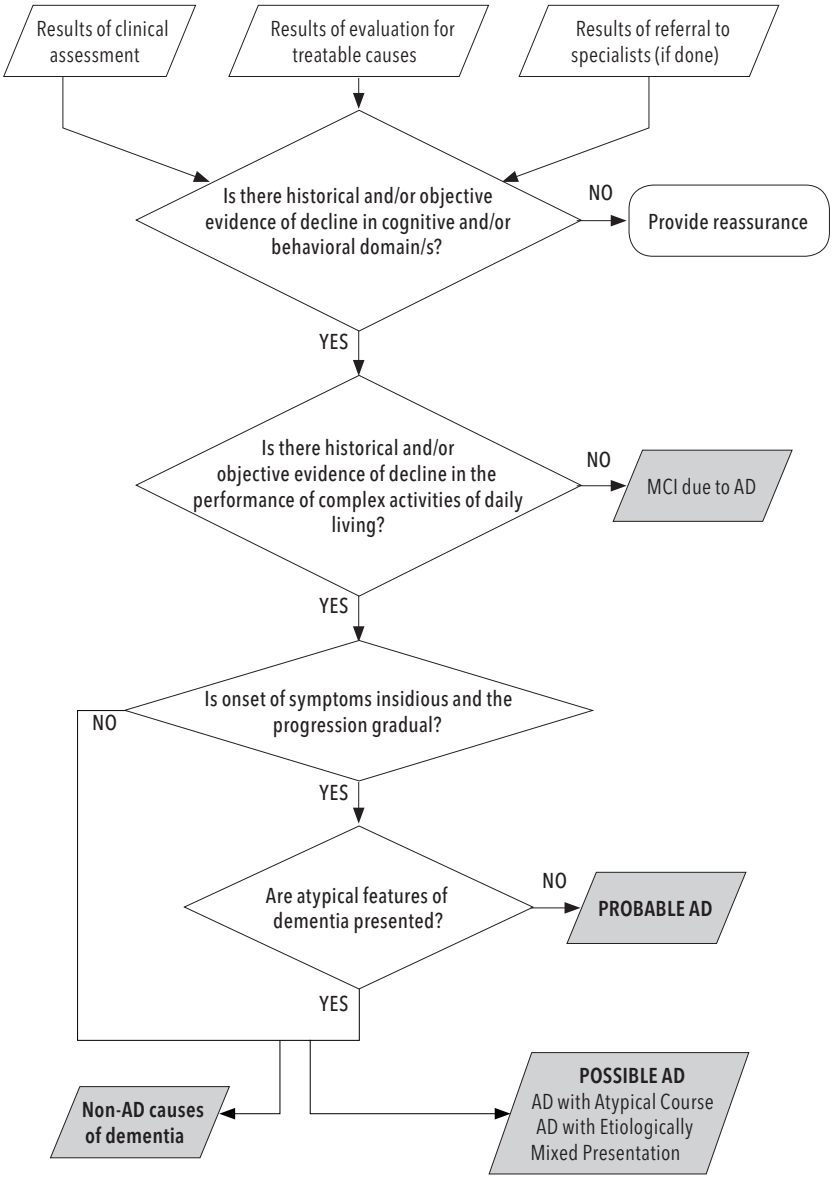

FIGURE 1–4. STEP 4 – Determining whether findings fit the diagnostic criteria for MCI or dementia due to Alzheimer's disease

MCI, Mild cognitive impairment; AD, Alzheimer's disease

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STEP 4. Determining whether findings fit in the criteria for MCI or dementia due to AD (Figure 1–4)

- After steps 1 to 3, we need to put all the findings together and determine if it is a case of MCI due to AD, probable AD, possible AD or a non-AD cause of dementia. If unsure, one should refer to a specialist.

C. Neuroimaging

- Role of structural neuroimaging (magnetic resonance imaging [MRI])
  - Excludes other potentially treatable diseases that may require surgery (e.g., chronic subdural hematoma, strokes, normal pressure hydrocephalus, and tumors)
  - Recognize vascular lesions (small-vessel ischemic white matter changes, infarcts, microbleeds)
  - Helps distinguish different types of dementia
  - Demonstrates disease progression
- Standardized MRI Visual Scoring Systems in Dementia Protocol[10]
  - GCA scale (**G**lobal **C**ortical **A**trophy)
  - MTA scale (**M**edial **T**emporal lobe **A**trophy)[11]
  - ERICA score (**E**ntorhinal **C**ortex **A**trophy)[12]
  - Koedam score (parietal atrophy)
  - Fazekas scale (white matter lesions)
  - Strategic infarcts

D. Olfactory Testing

- Pathology starts in the entorhinal cortex and transentorhinal region, which are proximal to the area of olfaction, therefore olfactory problems may be an early sign of AD.[13]
  - In one study with 250 cases of MCI, 1430 normal participants, and a 3.5-year follow-up, it was concluded that olfactory impairment predicts amnesic MCI and progression to AD. Olfactory tests are potentially useful in screening for MCI and detecting MCI that is likely to progress.

E. Gait Testing

- Quantitative gait dysfunction is associated with the risk of cognitive decline and dementia.[14]
- Based on a meta-analysis of 26 studies, dementia was associated with three factors:[15]
  - Slower pace
  - Impaired rhythm
  - Increased variability

F. Biomarkers in Dementia

- Definition of biomarker:[16]
  - Characteristic that can be objectively measured
  - Indicates normal biological or pathogenic processes or pharmacological responses to a therapeutic intervention
  - Majority of the present application of biomarkers is still limited to research, high-risk cases, and problematic cases

- Biomarkers in Dementia[17]
  1. Amyloid-beta accumulation (CSF studies and PET scan)
     - Earliest sign of dementia
  2. Synaptic dysfunction (FDG-PET and MRI)
  3. Tau-mediated neuronal injury (CSF studies)
  4. Brain structure (Volumetric MRI)

III. MANAGEMENT

- To lower the burden of dementia, there is a need for early detection and prevention.

A. Prevention of Dementia[2]

a. Primary Prevention
- Delay onset of AD pathology
- Avert the neuropathological changes in AD

b. Secondary Prevention
- Delay onset of clinical signs or cognitive impairment in individuals with evidence of pathology

c. Tertiary Prevention
- Delay onset or progression of dementia
- Can only be done with biomarkers
- Right now, the treatment that we have is tertiary prevention.

B. Factors and Prevention Strategies in Dementia

- Risk factors and protective factors fall under the categories of genetic, vascular and metabolic, diet, lifestyle and others (Table 1–1).
  - Only 35% is modifiable.[18]

TABLE 1–1. Risk and protective factors for late-onset dementia and Alzheimer's disease

CATEGORY	RISK FACTOR	PROTECTIVE FACTOR
Genetic	APOE e4 gene Familial aggregation Ethnicity	APP APOE e2 gene
Vascular and Metabolic	Hypertension* Dyslipidemia Obesity* Type 2 diabetes mellitus* Heart disease Stroke Hyperhomocysteinemia	
Psychosocial	Social isolation*	High education High occupational position Active lifestyle Extensive social network Cognitive activity/Mental stimulation
Diet	Homocysteine Saturated fats	Folate Vitamin B12 Antioxidants

TABLE 1–1. Risk and protective factors for late-onset dementia and Alzheimer's disease

CATEGORY	RISK FACTOR	PROTECTIVE FACTOR
Lifestyle	Smoking* High alcohol consumption Sedentary lifestyle*	Moderate alcohol consumption Moderate to high-intensity exercise or physical activity
Others	Depression* Head trauma Toxins	

**Modifiable*

Source: Solomon A, Mangialasche F, Richard E, et al. Advances in the prevention of Alzheimer's disease and dementia. *J Intern Med*. 2014;275(3):229-250.[17]

- Strategies to prevent dementia is outlined in Figure 1–5.

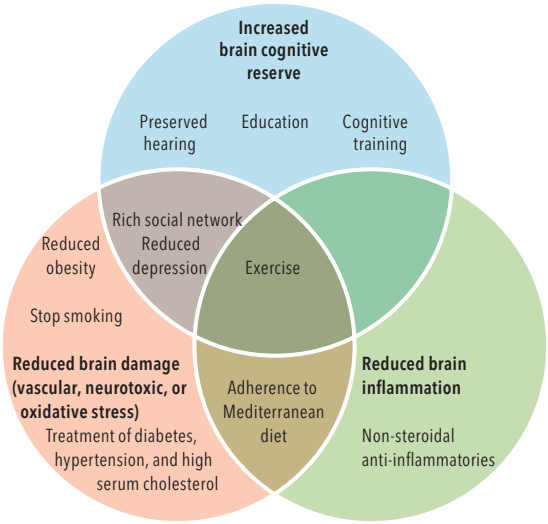

FIGURE 1–5. Potential brain mechanisms for preventive strategies in dementia

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C. Targets of Pharmacological Intervention

Currently, pharmacological intervention merely delays progression and does not fully prevent deterioration.[19]

- Transmitter-based
- Protein-focused – targets beta amyloid plaques
- Cellular processes
- Regeneration

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APPENDIX

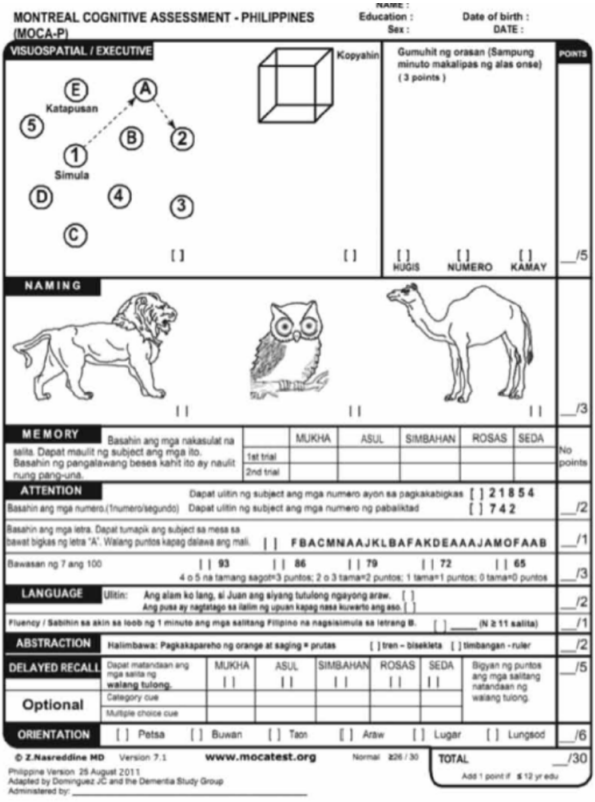

FIGURE 1–6. Filipino version of the Montreal Cognitive Assessment (MOCA)

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OPEN FORUM HIGHLIGHTS

Moderator: ANNA YORK BONDOC, MD

Q: *If your parents are suffering from Alzheimer's disease (AD), what is your risk of having the disease?*

A: Your risk increases 4 times if you have one family member who is affected. If you have two family members affected, your risk is multiplied 40 times compared to the normal population.
If you are genetically inclined to have AD, you will present with symptoms earlier.
If you have a genetic predisposition, you are the best candidate for early biomarker testing, like the APOE-e4, which is the affected gene.
Annual or biannual MRI is also suggested to detect changes.
There is also evidence for having higher risk for AD for individuals who give care to AD patients due to psychosocial stress (not because it is contagious!).

Q: *Can the Mini Mental Status Examination (MMSE) be used to diagnose dementia?*

A: Many studies have shown the limitations of the MMSE as a tool to diagnose dementia.
Since many items are language-based, if you have language problems, it unnecessarily lowers the score.
The screening test of choice now is the Montreal Cognitive Assessment (MoCA) due to the different cognitive facets that it covers.

Q: *Is amyloid-beta found in the blood as well, and not only in cerebrospinal fluid?*

A: Yes, however the present application of biomarkers is still limited to research, high-risk cases, and problematic cases.
It is also still very expensive.

Q: *Are memory-enhancing supplements useful?*

A: There is currently no evidence of their efficacy.

Q: *Can exposure to repeated anesthesia for surgeries contribute to development and progression of AD and dementia?*

A: There is no evidence for their correlation.

Q: *What practical advice can you give to caregivers of patients with dementia?*

A: To lessen the stress, one should accept the fact that he or she cannot do this alone. One must get the help of a lot of people in the caring for the patient.

Q: *What exercises can we do?*

A: You have to challenge yourself to engage in new things.
Increase level of difficulty or complexity of activities.
Multi-modal activities enhance brain stimulation.
Relaxation is essential.

Q: *Does frequent use of microwave ovens contribute to dementia?*

A: No data is available.

REVIEW QUESTIONS

1. Which of the following factors that contribute to dementia is non-modifiable?
    a. Genetic
    b. Physical inactivity
    c. Social isolation
    d. Obesity
2. Which of the following tools cannot be used to diagnose dementia?
    a. Montreal Cognitive Assessment (MoCA)
    b. Magnetic Resonance Imaging (MRI)
    c. Olfactory test
    d. Mini Mental Status Examination (MMSE)
3. Which is a protective factor for dementia?
    a. Extensive social network
    b. History of depression
    c. Sleep disturbances
    d. Dyslipidemia
4. Which of the following statements is correct about dementia and Alzheimer's disease?
    a. AD is a nonmodifiable disease
    b. Pathology in the brain occur ten years before onset of symptoms of AD
    c. Dementia is the most common cause of AD
    d. Having one family member with AD increases an individual's risk of having AD by 40 times
5. Which of the following statements about dementia is true?
    a. It is an inherited disease.
    b. It is not found in individuals younger than 65 y/o.
    c. It involves a single sphere of mental activity.
    d. It is persistent.

ANSWERS: 1. a; 2. d; 3. a; 4. b; 5. d

2 DEPRESSION AND MENTAL HEALTH ISSUES IN THE ELDERLY

Pia Natalya T. Reyes-Sia, MD, DPPA

Delivered as a webinar on November 22, 2019

https://bit.ly/ALMW_Ch2_Depression

KEY POINTS

- Older adults tend to be happier as they grow older because of the "well-being paradox."
- However, a significant minority of older adults will experience poor mental health, which can lead to negative consequences if left undiagnosed and untreated.
- Using a stepped care approach, physicians can recommend exercise and increase in social activities to help improve mental and emotional health of older adults.
- Depression in later life should be screened in the primary care setting.
- Anxiety in later life is the most common psychiatric disorder in the elderly but can be easily overlooked.
- When in doubt, refer; especially when the first line of treatment has failed or was only partially effective.
- Treatments are available and effective for depression in older adults, with similar medication doses and response rates in the younger population.
- There are resources in terms of books, apps, and online websites that can help patients understand their mental health issues.

LEARNING OBJECTIVES

- ➸ To identify the unique positive and negative aspects of ageing in terms of mental and emotional health
- ➸ To recognize and manage the symptoms of depression and anxiety in the elderly
- ➸ To know when to refer to a therapist or psychiatrist for treatment
- ➸ To determine ways to take better care of late-life mental and emotional health

I. EMOTIONAL AGEING

- Accurate expectations of ageing are critical for healthy functioning.

A. Positive Aspects of Emotional Ageing

1. "The Well-being Paradox"
   - This describes the "remarkable phenomenon of older adults maintaining well-being despite physical decline and social losses."[1]
   - In a longitudinal study across a 23-year period, negative affect decreased with age, whereas positive affect remained markedly stable.[2]

        - Older adults reported fewer minor aches and pains than young and middle-aged adults, even though they had greater numbers of chronic illnesses.
    - Survey on Filipino senior citizens in Quezon City:[3]
        - N=346 seniors 60 years of age and older
        - 70% of respondents considered themselves successful agers. They were neither depressed nor anxious, had a good quality of life, and had positive perceived health. There was no correlation between their responses and the actual number of illnesses they had.
        - A person could have many illnesses but still feel like a successful ager. On the other hand, someone with very few illnesses may not consider themselves successful agers because they are depressed.
2. Basis for Positive Aspects of Emotional Ageing
    a. **Socio-emotional Selectivity Theory** – Older adults self-regulate their own affective states by choosing to give more attention to positive stimuli and events in their daily lives than to negative ones. This skill may have been learned from their extensive accumulation of past experiences.
    b. **Ageing Brain Theory** – Ageing is associated with decreased amygdala activity and differential effects in the prefrontal cortex. These changes lead to reduced reactions to negative stimuli and less remembering of them, which result in greater subjective well-being.

B. Negative Aspects of Emotional Ageing

- Older adults may experience additional stressors that are more common in later life:[4]
    - Significant decline in physical and functional ability
    - Events such as bereavement or a much lower socioeconomic status with retirement
    - Elder abuse: physical, verbal, psychological, financial and sexual abuse; abandonment; neglect; and serious losses of dignity and respect
- Such stressors can lead to isolation, loneliness, or psychological distress in older people.

C. Assessment of the Geriatric Patient

1. Comprehensive Geriatric Assessment[5] (Figure 2–1)
    - Systematic evaluation of an older patient's functional status, psychosocial status, and medical conditions, with special emphasis on the patient's ability to perform daily activities and quality of life
    - Investigation through questions, objective testing, and systematic observation of risk factors for common pathological conditions affecting older adults (e.g., cognitive impairment, impaired mobility, falls, incontinence, and polypharmacy)
    - Speaking to and involvement of family members or caregivers in the assessment
2. Screening of Older Adults for Depression[6]
    - This is recommended when appropriate support measures are available to ensure accurate diagnosis, effective treatment, and follow-up.

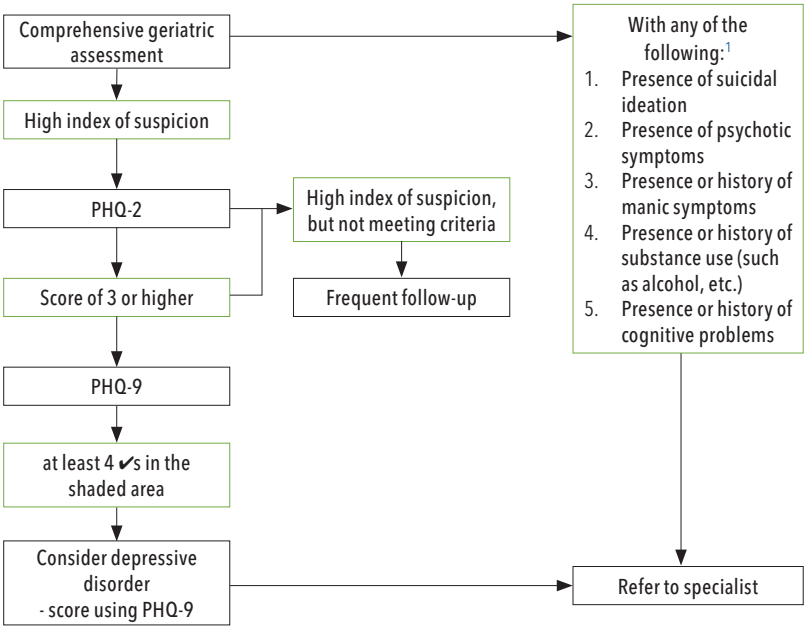

FIGURE 2–1. Flowchart for assessment of geriatric patient

Source: Hategan A, Bourgeois JA, Hirsch CH, Giroux C. *Geriatric psychiatry: A case-based textbook*. 1st ed. New York City: Springer; 2018.

II. DEPRESSION IN THE ELDERLY

A. Clinical Presentation of Depression in Older Patients

- Depression is not a part of normal ageing.[7]
- The prevalence of depression in the older adults has been estimated at anywhere between 7.2% to 38%.[8-10]
  - In the Philippines, a cross-sectional survey of older adults over 60 years of age in Rizal Province estimated the prevalence of depression at 6.6%, but could be as high as 26.5%.[11]
- Depression, presenting as either chronic depressive symptoms or a first episode in late life, has been identified as the most powerful independent risk factor for suicide in old age.[12]
  - In the US, the highest rate of suicide is in the age group of adults older than 65 years of age.[9]
  - In the Philippines, the highest rate of suicide is still in the younger population. However, as of 2011, the rate of suicide appears to be rising in the older population.[13]

TABLE 2–1. Notable Clinical Features of Depression in Older Adults

Poor memory and concentration
Decreased processing speed
Diminished executive function to the extent that the patient may be presenting with symptoms similar to a major neurocognitive disorder, known as "pseudodementia"
Symptoms decrease as the person's mood improves with treatment (unless there is a comorbid neurocognitive disorder)
Studies suggest that depression itself doubles the risk of developing major neurocognitive disorder[14,15]

Sources:
Forlenza O, Valiengo L, Stella F. Mood disorders in the elderly: Prevalence, functional impact, and management challenges. *Neuropsychiatr Dis Treat*. 2016;12:2105-2114. doi:10.2147/NDT.S94643
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- Although depression is less common among older adults than in younger adults, depressive symptoms associated with impairments in functioning may be common in late life and increase with advancing age.[16]
- In patients with late-life depression (first episode of depression in late life), significant life events precede the depression in more than 50% (Figure 2–2).[17]

FIGURE 2–2. Risk Factors for Depression

Source: Cole MG, Dendukuri N. Risk factors for depression among elderly community subjects: A systematic review and meta-analysis. *Am J Psychiatry*. 2003;160(6):1147-1156.

B. Diagnosis of Depression in Older Adults

- The Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) is still the gold standard for the diagnosis of clinical depression (also called major depressive disorder) (Table 2–2).[18]

TABLE 2–2. DSM-5 Criteria for Depression

Five (or more) of the following symptoms during the same 2-week period
Represent a change from previous functioning
At least one of the symptoms should be either: (1) depressed mood, or (2) loss of interest or pleasure
1. Depressed mood most of the day, nearly every day
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
3. Significant weight loss when not dieting, or weight gain, or decrease or increase in appetite nearly every day
4. Insomnia or hypersomnia nearly every day
5. A slowing down of thought and a reduction of physical movement (observable by others, not merely subjective feelings of restlessness or being slowed down)
6. Fatigue or loss of energy nearly every day
7. Feelings of worthlessness or excessive or inappropriate guilt nearly every day
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day
9. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt, or a specific plan for committing suicide
Must cause the individual clinically significant distress or impairment in social, occupational, or other important areas of functioning
Must also not be a result of substance abuse or another medical condition

Source: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-5).* 5th ed. Arlington, VA: American Psychiatric Association; 2013.

- The Patient Health Questionnaire (PHQ)-9[19] (Table 2–3) is more sensitive and more specific than PHQ-2.20[20] The latter consists only of 2 questions – which are the same as questions 1 and 2 from PHQ-9. However, some older adults may have a hard time recalling how often symptoms occur.
  - A PHQ-2 score of at least 3 (out of a maximum score of 6) counts as positive.
  - PHQ-9 scores correspond to the severity of the depression (Table 2–4).
- The Geriatric Depression Scale is used in patients with dementia, with the advantage of being easier to answer than the PHQ-9 since it asks questions answerable by yes/no.[21]

TABLE 2–3. Patient Health Questionnaire-9 (PHQ-9)

Over the past 2 weeks, how often have you been bothered by any of the following problems	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people have noticed. Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3

TABLE 2–3. Patient Health Questionnaire-9 (PHQ-9) (cont.)

Over the past 2 weeks, how often have you been bothered by any of the following problems	Not at all	Several days	More than half the days	Nearly every day
9. Thoughts that you would be better off dead, or of hurting yourself	0	1	2	3
Total score				

**Initial diagnosis: at least 4 ✔s in the shaded area, consider a depressive disorder*
**For scoring of severity: add up the total scores for all 9 items (Table 2–4)*
Source: Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16:606-613.

TABLE 2–4. Severity of depression based on PHQ-9 scores

TOTAL SCORE	SEVERITY
1-4	Minimal depression
4-9	Mild depression
10-14	Moderate depression
15-19	Moderately severe depression
20-27	Severe depression

PHQ, Patient Health Questionnaire
Source: Kroenke K, Spitzer RL, Williams JBW. The PHQ-9: Validity of a brief depression severity measure. *J Gen Intern Med*. 2001;16:606-613.

C. Treatment of Depression in Older Adults

TABLE 2–5. Treatment Options

1. Pharmacological treatment	Antidepressants
2. Non-pharmacological treatment	Cognitive Behavioral Therapy (CBT) Interpersonal Therapy (IPT) Behavioral Activation
3. Neurostimulation treatment	Electroconvulsive Therapy (ECT) Repetitive Transcranial Magnetic Stimulation (rTMS)

1. Considerations in Treatment[22]
   - Majority of older adults with depression are usually not treated or inadequately treated with antidepressants.
   - Other psychosocial factors that may contribute to depression and affect treatment planning include:
     - Recent life events
     - Coping with functional impairment
     - Lack of social contacts
2. Pharmacologic Treatment (Table 2–6)
   - One must master the side effects of one to two antidepressants so that they can be prescribed with confidence.
   - The response rate of the elderly to antidepressants is similar to younger patients: around 60% with treatment compared to 30% with placebo.
   a. Selective Serotonin Reuptake Inhibitors (SSRIs)
      - Escitalopram is the most commonly prescribed antidepressant by psychiatrists due to its

fairly low incidence of side effects, as well as having the lowest CYP p450 interactions of all SSRIs.

b. Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)
   - Desvenlafaxine, duloxetine and other antidepressant classes (agomelatine, bupropion, mirtazapine, and vortioxetine) are just as effective, and may be even more effective, but tend to have more side effects than escitalopram.

TABLE 2–6. Types of Antidepressants

INDICATION	CLASS	GENERIC DRUGS	ADVERSE EFFECTS
1st line	SSRIs	Fluoxetine Citalopram Escitalopram Sertraline Paroxetine	• Common side effects: nausea, vomiting, dyspepsia, diarrhea, headache, sexual dysfunction • No dose reduction in the elderly • May be associated with increased risk of falls[23] including those who have a history of a fall/fracture. • Avoid use in those at risk for bleeding (GI bleeding, on blood thinners) • Watch out for potentially life-threatening combinations, such as using an antidepressant with isoniazid (serotonin syndrome)
	SNRIs	Venlafaxine Duloxetine	• Common side effects: nausea, dry mouth, headache • No dose reduction in the elderly
	Others	Mirtazapine	• Sedation, weight gain, some anticholinergic effects
2nd line		Agomelatine Quetiapine Buspirone Impiramine Clomipramine	• No dose reduction in the elderly

Sources:
Hategan A, Bourgeois JA, Hirsch CH, Giroux C. *Geriatric Psychiatry: A Case-Based Textbook*. 1st ed. New York City: Springer; 2018.
Kok RM, Reynolds CF. Management of depression in older adults: A review. *JAMA*. 2017;317(20):2114-2122.

3. Non-pharmacologic interventions
   a. Increasing social activity
      - A systematic review and meta-analysis of prospective controlled trials showed that social activities were effective in reducing depressive symptoms compared with no intervention. However, results should be interpreted with caution due to the small number of trials.[24]
      - How the patient will increase social activities will have to be discussed with the patient and family/caregivers in a brainstorming/troubleshooting fashion.
   b. Increasing physical activity
      - A growing body of evidence indicates that physical exercise may enhance cognitive and emotional functioning in addition to its benefits for physical health.[25]

III. ANXIETY IN OLDER ADULTS

- Anxiety is a normal human emotion. Pathological anxiety, on the other hand, may lead to a lower quality of life and is associated with many other medical conditions, including cardiovascular diseases.
- It is twice more common (18.1%) than depression (9.5%) in the elderly.[10]
- Diagnosing pathological late-life anxiety may be complicated by normal ageing, challenging life events

such as bereavement and disability, minimization of symptoms, comorbidities, more frequent somatic complaints, and, potentially, cognitive impairment.

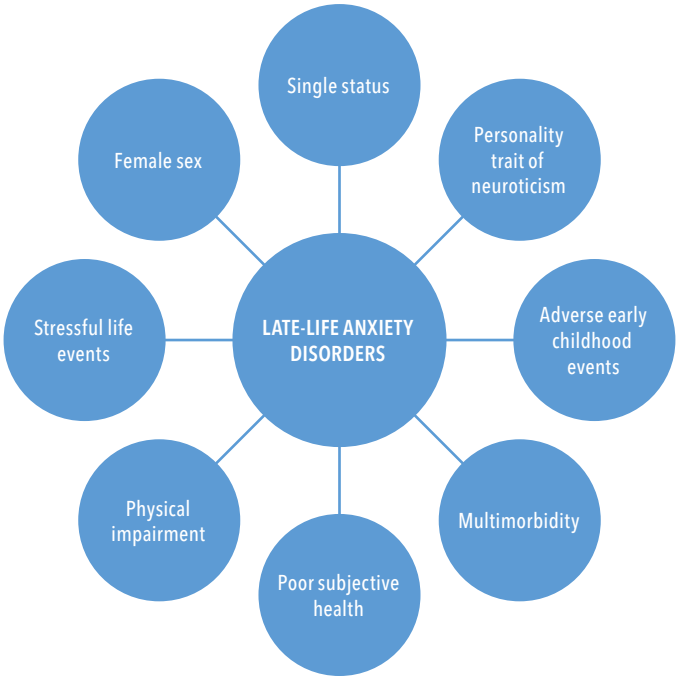

FIGURE 2–3. Risk factors for late-life anxiety disorders

Source: Hategan A, Bourgeois JA, Hirsch CH, Giroux C. *Geriatric Psychiatry: A Case-Based Textbook*. 1st ed. New York City: Springer; 2018.

- Generalized anxiety disorder (GAD) (0.7% to 9%) and specific phobias (3% to 5%) are the most common anxiety disorders among older adults, with panic disorder and social anxiety disorder (social phobia) much less common than in younger age groups.
- Prevalence rates are higher in special groups, such as patients with heart disease and atrial fibrillation, chronic obstructive pulmonary disease, and Alzheimer's disease.

A. Types of Anxiety Disorders in Older Adults[18]

1. Generalized Anxiety Disorder

TABLE 2–7. DSM-5 Criteria for Generalized Anxiety Disorder

Presence of excessive anxiety or worry, on more days than not, lasting more than 6 months
The individual finds it difficult to control the worry
Associated with three or more of the following symptoms: 1. Feeling restless, keyed up, on edge 2. Feeling easily fatigued 3. Having difficulty concentrating, mind going blank 4. Irritability 5. Muscle tension 6. Sleep disturbance
Cause clinically significant distress and impairment in important areas of functioning
The disturbance is not due to the physiological effects of a substance or another medical condition
The disturbance is not better accounted for by another psychiatric disorder

Source: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-5).* 5th ed. Arlington, VA: American Psychiatric Association; 2013.

2. Phobias
   a. Agoraphobia – marked fear of two (or more) of the following five situations:
      i. Using public transportation
      ii. Being in open spaces
      iii. Being in enclosed places
      iv. Standing in line or being in a crowd
      v. Being outside of the home alone
   b. Social phobia – also called social anxiety disorder, involving discomfort around social interaction and concern about being embarrassed and judged by others
   c. Specific phobia – fear of falling is a specific phobia that is geriatric-specific and can lead to significant functional impairment.

TABLE 2–8. DSM-5 Criteria for Specific Phobia

Marked fear/anxiety about a specific object/situation
The phobic object or situation almost always provokes immediate fear/anxiety
The phobic object or situation is actively avoided or endured with intense fear or anxiety
The fear or anxiety is out of proportion to the actual danger
Persistent, lasting more than 6 months
Causes clinically significant distress and impairment in important areas of functioning
The disturbance is not better accounted for by another mental disorder

Source: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-5).* 5th ed. Arlington, VA: American Psychiatric Association; 2013.

3. Panic disorder

TABLE 2–9. DSM-5 Criteria for Panic Disorder

Anxiety disorder based primarily on the occurrence of panic attacks, which are recurrent and often unexpected
A panic attack is an abrupt surge of intense fear or discomfort that reaches a peak within minutes, and is characterized by four or more of the following symptoms: 1. Palpitations, pounding heart, or accelerated heart rate 2. Sweating 3. Trembling or shaking 4. Sensations of shortness of breath or smothering 5. A feeling of choking 6. Chest pain or discomfort 7. Nausea or abdominal distress 8. Feeling dizzy, unsteady, lightheaded, or faint 9. Chills or heat sensations 10. Numbness or tingling sensations (paresthesias) 11. Feelings of unreality (derealization) or being detached from oneself (depersonalization) 12. Fear of losing control or going crazy 13. Fear of dying
At least one attack is followed by one month or more of one or both of the following: • Persistent concern or worry about more attacks or their consequences • A significant maladaptive change in behavior related to the attacks (avoidance, etc.)
The attacks are not due to the direct physiological effects of a substance (such as drug use or a medication) or another medical condition
The attacks are not better accounted for by another mental disorder. These may include a social phobia or another specific phobia, obsessive-compulsive disorder, post-traumatic stress disorder, or separation anxiety disorder

Source: American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders (DSM-5).* 5th ed. Arlington, VA: American Psychiatric Association; 2013.

- Disorders that involve the fear response, like panic disorder, are thought to have a particularly low incidence rate in the geriatric population and are usually associated with comorbidities.
  - This decrease in incidence may be explained by age-related dampening of physiological autonomic responses in late life.
- Therefore, any new onset panic disorder in late life should prompt a thorough search for alternative and co-morbid diagnoses with close attention to systemic medical conditions and medication side effects.

B. Screening Questions for Diagnosis of Anxiety

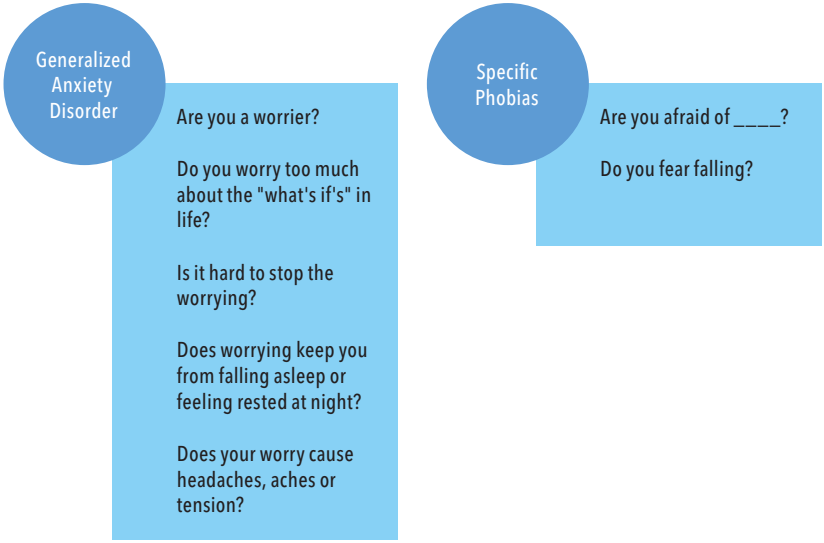

FIGURE 2–4. Screening questions for anxiety disorders[26]

Source: Cassidy K, Rector NA. The silent geriatric giant: Anxiety disorders in late life. *Geriatr Aging*. 2008;11(3):150-156.

C. Anxiety and Depression in Older Adults

- There is a high rate of co-morbidity between depression and anxiety.
  - Around 21% to 37% of community-dwelling patients with an anxiety disorder (as defined by DSM-4) experienced comorbid depression, which adds to the burden of disease.[27]
- Anxious depression in older adults appears to represent a subtype of depression that is relatively treatment-resistant, associated with an increased risk of neurocognitive decline, and perhaps most importantly, an increased risk for suicide.[28-30]

D. Treatment of Anxiety Disorders in Older Adults

1. Treatment Principles[31]
   - After diagnosis, a treatment plan should be developed in collaboration with the patient.
   - Care should be taken to provide the patient with psychoeducation about the disorder, placing emphasis on realistic goals (e.g., not to completely remove all anxiety symptoms, but to make the occurrence of anxiety feel tolerable and manageable) to minimize suffering.
   - Patient education should include information regarding treatment efficacy and tolerability, aggravating factors, and signs of relapse.
   - Minimize polypharmacy: optimize current medications and discontinue unnecessary and harmful medications including sedatives, anticholinergics, anti-histamines, and over the-counter medications.[32]

   a. Pharmacological treatment
      1. Antidepressant drugs (Table 2–10)
      2. Antipsychotic drugs and others

TABLE 2–10. Antidepressant drugs	
1st line	SSRIs SNRIs
2nd line	Agomelatine, quetiapine, buspirone, imipramine, clomipramine
Adjunctive	Pregabalin, quetiapine, risperidone

SSRI, Selective serotonin reuptake inhibitors; SNRI, Selective norepinephrine reuptake inhibitor

- While benzodiazepines can provide short-term relief of symptoms, their use should be limited to cases of extreme suffering. They should be used in a scheduled and time-limited fashion because benzodiazepines reinforce maladaptive coping behavior.
- Moreover, the benefit-risk profile worsens among the geriatric population, and therefore treatment with benzodiazepines should be avoided in older adults.[31-33]
- *"Don't take off unless you know how to land"* or *"Don't start a medication if you don't know how to stop it"*

c. Non-pharmacologic treatment

4. Cognitive Behavioral Therapy (CBT)
   - "The Anxiety and Phobia Workbook"[34]
   - Useful for psychoeducation
   - Bibliotherapy does not have strong evidence in the geriatric population, but this can still be used if the patient is cognitively intact and motivated.
   - It can be helpful for the physician and caregivers.
   * Mobile applications such as Headspace, Calm, and Insight Timer may be helpful to older adults who have trouble reading.
5. Interpersonal Psychotherapy (IPT)
6. Resources for Non-pharmacological Treatment
   - Therapy referrals are not centralized, and many are "discovered" by word of mouth.
   - In general, therapists (clinical psychologists, psychiatrists and social workers) in the Philippines practice an "eclectic" approach.
     - This means they received some training in some therapies but may not be certified in any particular one. Certification needs time, money and supervision to achieve.
     - A therapist could be excellent but not certified.
   - As much as possible, check the training of the therapist you are thinking of referring to.
     - But also bear in mind that the "fit" of therapist to patient can be as important as the training they received.
     - Ask your favorite psychiatrist.
   - Therapy Centers
     - Bulatao Center in Ateneo De Manila – mindfulness
     - InTouch
     - PsychConsult
     - Center for Behavioral Health at The Medical City

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OPEN FORUM HIGHLIGHTS

Moderator: MELISSA NADINE C. CARAAN, MD

Q: *Aside from suicide, what is the usual cause of death from depression without pathologic cause?*

A: A lot of times, depression will be accompanied by loss of appetite and problems with sleep. Depression increases the burden of whatever disease they may already have. They may have hypertensive disease, chronic kidney disease, or diabetes. All of these issues will worsen at first, and eventually they become a common cause of the demise of the patient. In some cases, the loss of appetite is very difficult to get back even after treatment, because everything has atrophied. They cannot eat as much as they used to, and the malnutrition becomes the cause of the demise.

Q: *Can the aged die just by willing to die?*

A: There is something called the "nocebo effect," and there have been great studies about how people, believing that they are going to die, just drop dead. There are case reports about this. If you believe you will have a negative outcome, you will certainly have it. The extent of the studies in terms of death in older adults is unknown. It can be possible, but usually there is an underlying medical issue such as arrythmia, heart attack, or stroke, which may be due to severe stress.

Q: *What can we say to convince a senior patient to see a psychiatrist?*

A: If people are open to talking about depression and anxiety, and not equate it to what these adults fear, the older adult can be persuaded to go. Sometimes, you will have a very stubborn older adult, usually older men who are heads of companies, who have pride and are in denial. Try to coordinate with the family practitioner they always see for their other conditions and see if they can be the one to treat them directly or introduce the idea of a psychiatric referral.

Q: *Are there studies that sertraline helps post-stroke depression among the elderly? Does it help in regaining motor ability post-stroke?*

A: A study in post-stroke patients showed that antidepressants (fluoxetine or nortriptyline) improved survival in both depressed and non-depressed patients, compared to placebo.

Q: *Can you self-claim that you have anxiety and depression without ever seeing a doctor?*

A: It's very possible, and may bear some looking into. You will never know until you ask the right questions.

Q: *Are the elderly staying in a nursing home more prone to depression or mental illness than the elderly who are being taken care of by their own families?*

A: In the United States, nursing home patients have higher incidence of depression, cognitive dysfunction, and mortality rates. In the Philippines, however, what we don't fully know are the interactions between caregiver fatigue, social isolation, and health.

Q: *Is it dangerous if you are on long-term use of sertraline?*

A: It all depends on what you mean by "long-term." When you say "long-term" in the older adult, the major issue is just making sure that the sodium levels are normal, that there would be no pharmacological interactions (i.e., blood thinners), and the patient regularly consults with their primary care physician to make sure that everything is okay with them.

Q: *What is the best treatment for major depressive disorder?*

A: The combined treatment of therapy and antidepressant will always give you the best outcome.

Q: *Can a personality disorder, like narcissistic personality, contribute to depression?*

A: Yes. If anything, narcissism has a greater contribution to a person not wanting to get treatment.

Q: *How can we motivate the elderly to be productive as they were before they got depression, with limited therapy providers here in the Philippines?*

A: Prevention is the best policy. As long as you like the work, and it is not a large source of stress for you, stay in the job for as long as you can. If you have to retire, have something set up for yourself even years before your retirement.

Q: *Have you encountered patients on antidepressants with low vitamin D, and did it improve with vitamin D supplements?*

A: There have been no studies on vitamin D deficiency in the Philippines, given that we are exposed to so much sunlight. In the US, even on vitamin D supplementation, no change in the level of depression was seen in my clinical experience. Incidentally, phototherapy helps depression.

Q: *Is there a higher incidence of anxiety in high-functioning individuals?*

A: Anxiety disorders tend to occur in patients who have a high trait of neuroticism. From neuroticism comes perfectionism and obsessive-compulsive behavior that we value in our current culture. In a way, neuroticism becomes an adaptive behavior. Therefore, we see these people as high-functioning. In that sense, yes.

Q: *In post-stroke patients with neuropathic pain and depression, do you recommend amitriptyline or duloxetine over pregabalin?*

A: Pregabalin can be used as an adjunct for anxiety. You can certainly use amitriptyline/duloxetine but watch out for the high anticholinergic effects of amitriptyline, which can worsen their cognition, and increased blood pressure with duloxetine.

Q: *Is it advisable to take St. John's Wort for the treatment of depression?*

A: It depends on how old you are and how many comorbidities you have, because St. John's Wort has many cytochrome interactions and it is hard to titrate the dose. It is not recommended for those who are post-stroke, or those who are above 65 years old with many comorbidities.

Q: *How can we increase the activity of retired patients at home if they are not willing to go out? How can we encourage them to go out? What is the best physical activity they can do at home?*

A: First, take time to get to know these older adults and try to see what they liked. In terms of exercise, do anything that will get them moving. If they're going to start at a very deconditioned state, do whatever they are willing to do. Try to involve as much of the body as possible, and then start from there.

Q: *Majority of Filipinos do not have access to laboratory facilities. So, if they present with anxiety symptoms, is it prudent to start them with anxiolytics, especially in the geriatric population?*

A: First, do a complete history and physical exam. You can always do a trial, but the older you become, the lower your sodium levels will be, so you have to see the patient regularly. You may want to lean more towards non-pharmacological therapy, rather than committing to an anxiolytic, which may give them a side effect that you cannot address quickly enough.

Q: *Would you suggest that senior citizens be periodically screened for depression?*

A: Yes, it would go a long way if the senior citizen can be screened, if there are interventions that can be put in place in the community level to address the depression.

Q: *Could hosting Christmas parties in nursing homes promote depression?*

A: It's not the activities that promote depression; it's the loss of your presence. There's always Skype, or Facebook livestream: these are ways to stay connected with older people. Something happens in the non-verbal behavior: when you see someone who is happy, it changes how you feel as well. No one is more affected by this than the older adults.

REVIEW QUESTIONS

1. Which of the following is TRUE?
    a. The Well-being Paradox describes the phenomenon of older adults maintaining well-being despite physical decline and social losses.
    b. Depression is a normal part of ageing.
    c. Mental disorders are more prevalent among older adults than younger adults.
    d. Fear of falling is NOT a geriatric-specific syndrome

2. What is the most common category of psychiatric disorders among adults aged 60 years or older?
    a. Anxiety disorders
    b. Mood disorders
    c. Drug dependence
    d. Depressive disorders

3. Which of the following is a risk factor for depression in older adults?
    a. Neurotic personality trait
    b. Sleep disturbances
    c. Male sex
    d. Marriage

4. Which does NOT characterize generalized anxiety disorder?
    a. Excessive anxiety, on more days than not, for more than 6 months
    b. Clinically significant distress and impairment in important areas of functioning
    c. Symptoms such as restlessness, easy fatigability, difficulty in concentration, irritability, muscle tension, and sleep disturbance
    d. Marked anxiety about a specific object or situation, for more than 6 months

5. What type of drug should be avoided in older adults due to its poor benefit-risk profile among the geriatric population?
    a. SSRIs
    b. SNRIs
    c. Benzodiazepines
    d. Tricyclic antidepressants

ANSWERS: 1. a; 2. a; 3. b; 4. d; 5. c

3 PERIOPERATIVE STROKE: RISKS, DIAGNOSIS, UPDATES

Grace Anne A. Banson-Herbosa, MD, DPBA, FPSA

Delivered as a webinar on June 28, 2019

https://bit.ly/ALMW_Ch3_PerioperativeStroke

KEY POINTS

- Perioperative stroke is a disabling and potentially fatal event that occurs during surgery and up to 30 days after in about 0.05 to 9.7% of surgical patients.
- Risk factors include patient-related factors (e.g., age, history of prior stroke, and other comorbidities), procedure-related factors (e.g., type of surgery, use of cardiopulmonary bypass, antiplatelet/antithrombotic interruption, and metabolic derangement), and perioperative atrial fibrillation.
- The diagnosis of perioperative stroke is challenging. A high index of suspicion should be maintained in older patients with risk factors, with the use of scales such as the NIHSS for prompt diagnosis of this condition.
- Older adult surgical patients require thorough assessment of individual health status, careful balance of bleeding versus thrombotic risks, and delayed timing of surgery for 3 months post-stroke.

LEARNING OBJECTIVES

- ➟ To define and state the prevalence of perioperative stroke
- ➟ To enumerate the risk factors for perioperative stroke
- ➟ To discuss how to diagnose perioperative stroke
- ➟ To state updates in management of perioperative stroke

I. DEFINITION[1]

- Perioperative stroke is defined as stroke that occurs during surgery and up to 30 days after.
- Systemic inflammatory responses triggered by surgery, inability to initiate thrombolytic therapy, and different types of stroke may all exacerbate cerebral injury.
- A delay in its recognition and assessment contributes to higher morbidity and mortality.
- Residual anesthetic and analgesic effects may obscure important warning signals of major stroke.

II. EPIDEMIOLOGY

- Cerebrovascular disease, including stroke, is the 3rd leading cause of mortality in the Philippines, accounting for 10.5% of all deaths for both sexes as of 2018.

- Depending on the type of surgery and patient characteristics, the incidence of perioperative stroke varies between:
  - 1.4 to 9.7% after cardiac operation
  - 2.9 to 7.4% after carotid artery surgery
  - 0.05 to 4.4% in the general surgical population
- The outcome after perioperative stroke is usually disabling and/or fatal.
  - 25 to 50% of patients die within 30 days of perioperative stroke.
  - In the remaining patients, 50% were left with major disability that adversely affected their quality of life.

III. RISK FACTORS

The following factors may contribute to the occurrence of perioperative stroke:[2,3]

1. Patient-related factors
   a. Age >62 y/o
   b. History of transient ischemic attack (TIA) or prior stroke
   c. Comorbidities (In Filipino adults, these include: hypertension, diabetes, dyslipidemia, smoking, and obesity)[4]
2. Procedure-related factors
   a. Type of surgery/procedure (e.g., coronary artery bypass graft [CABG], carotid endarterecctomy [CEA], mitral valve replacement)
   b. Use of cardiopulmonary bypass
   c. Antiplatelet/antithrombotic interruption
   d. Metabolic derangement
3. Perioperative atrial fibrillation

TABLE 3–1. Risk factors for stroke recurrence[5]

- Previous history of stroke: Most consistent independent predictor for perioperative stroke
- Age
- Renal failure
- Hypercoagulability
- Immobility
- Arrhythmia
- Mechanical cardiac valve
- Hypotension

IV. PATHOPHYSIOLOGY OF RECENT STROKE[6]

Majority of stroke is ischemic (70%) and hemorrhagic stroke only comprises 30%.[7]

A. Ischemic stroke

- Ischemic stroke is caused by a reduction in blood flow either due to a thrombus or embolus, or through hypoperfusion (Figure 3–1).
- During ischemic stroke, impairment of cerebral autoregulation occurs, which may last up to 3 months after stroke.

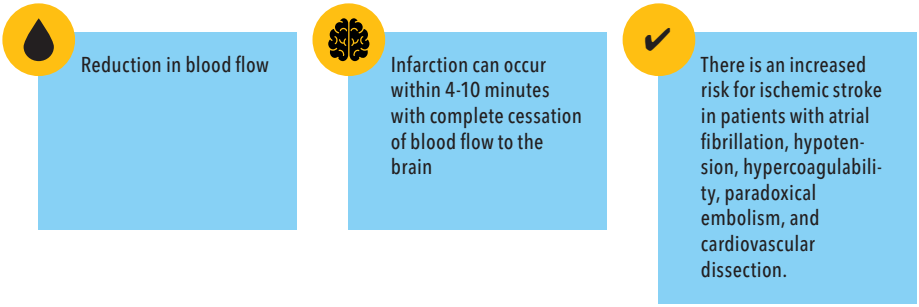

FIGURE 3–1. Pathophysiology and risk factors for ischemic stroke

- Blood pressure is the sole predictor of cerebral perfusion.

B. Hemorrhagic stroke

- Hemorrhagic stroke is characterized by bleeding, either through an intracerebral hemorrhage (ICH) or a subarachnoid hemorrhage (SAH) (Figure 3–2).

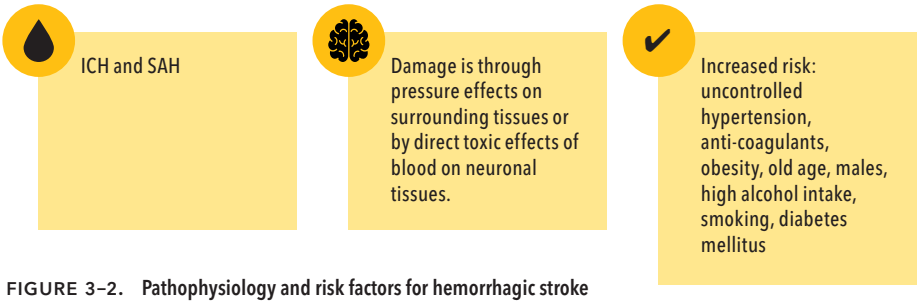

FIGURE 3–2. Pathophysiology and risk factors for hemorrhagic stroke

Recent strokes cause hemodynamic, endocrine, and inflammatory changes to cerebral autoregulation and chemo-regulation.

- Autoregulation is impaired for 1 to 3 months.
- Cerebral perfusion is dependent on systemic pressure and passive perfusion.
- The area of infarcted tissue undergoes inflammatory processes and softens, rendering the area vulnerable to hemodynamic stress.[5]

V. MANAGEMENT OF PERIOPERATIVE STROKE

- Challenges in the Philippine setting[7]
  - The neurologist-to-patient ratio in the Philippines is 1:330,000, with 67% of neurologists practicing in urban centers.
  - Health care is largely private and the cost is borne out-of-pocket by patients and their families.
  - Barriers to the delivery of adequate support to rural communities and underprivileged sectors continue to exist.
- Management of perioperative stroke can be divided into 3 phases:
  - Preoperative (Table 3–2) – to identify patients at high risk of stroke and mitigate the risk
  - Intraoperative (Table 3–3) – to mitigate the risk
  - Post-operative (Table 3–4) – to rapidly diagnose stroke and provide appropriate care
- Based on:
  - Consensus statement from the Society for Neuroscience in Anesthesiology and Critical Care (2014)[1] on perioperative care for non-cardiac, non-neurologic surgery
  - Review articles in evaluation and management of perioperative stroke (2019),[3] and specifically for elective non-cardiac surgery (2016)[5]

A. Preoperative Assessment

TABLE 3–2. Summary of recommendations for preoperative assessment for perioperative stroke

1. Clear medical history of stroke and/or TIA	Perform thorough history-taking, including previous diagnostics/ medications, and physical examination.	• Date it occurred
		• Type of stroke (ischemic or hemorrhagic)
		• Secondary prevention medications
		• Residual deficit from the stroke
		• Previous stroke-related investigations
		  ○ Brain imaging studies
		  ○ Carotid Doppler ultrasound
		  ○ Electrocardiogram
		  ○ Echocardiography

2. Timing of surgery	Delay elective surgery for 3 months since there is a defect in autoregulation, unless risk-benefit ratio is such that chances of dying from urgent surgery outweighs risk of stroke.	Elective non-cardiac surgery riskiest for major cardiovascular events (ischemic stroke recurrence, acute myocardial infarction, other cardiovascular mortality) in the first 9 months after stroke.[8,9] • *Risk is highest at 3 months* (14-fold risk) and levels off at 9 months (2-fold risk).

TABLE 3–2. Summary of recommendations for preoperative assessment for perioperative stroke (cont.)

3. Thrombotic vs bleeding risk	Weigh the thrombotic risk versus bleeding risk from surgery through careful and thorough individualized assessment.	• In addition to immobility, the pro-inflammatory and hypercoagulable state induced in surgeries places patients, who will be taken off their anticoagulants, at an increased risk for thrombosis intraoperatively.
	a. Thrombotic risk	• Low, moderate, or high risk, based on presence/absence of: ○ Mechanical heart valve ○ Atrial fibrillation ○ Venous thromboembolism • May use a scoring tool such as CHA_2DS_2VASc, which considers the following factors:[10] ○ CHF or LVEF <40% ○ Comorbidities (i.e., hypertension, diabetes, and vascular disease) ○ Age (if 65–74, or ≥75) ○ Sex (female) ○ History of stroke/TIA/thromboembolism
	b. Bleeding risk	• *Low-risk surgery:* Minor skin surgery, cataract or glaucoma, simple dental procedures, laparoscopic cholecystectomy, biopsy of a compressible site, and joint aspiration or injection • *Moderate- to high-risk surgery:* Neurosurgery, spinal/epidural procedures, urologic surgery, vascular surgery, major intra-abdominal surgery, orthopedic joint surgery, breast surgery, thoracic surgery, invasive ophthalmic surgery, reconstructive plastic surgery, pacemaker or implantable cardioverter defibrillator implantation, and liver biopsy
4. Medication review	a. Anticoagulants[6]	• Rebound hypercoagulability, characterized by increased thromboxane production and decreased fibrinolysis, can aggravate the pro-thrombotic state associated with surgery • Continuing therapy increases the risk for perioperative bleeding and affects anesthetic technique. i. Aspirin[6] ○ Moderate-to-high bleeding and thrombotic risk → continue ○ Low bleeding and thrombotic risk → discontinue 5 days ii. Clopidogrel[5] ○ Discontinue 7 days prior to non-cardiac surgery. ○ Substitute with aspirin.
	b. Antihypertensives	i. β-blockers ○ Continue β-blocker throughout the perioperative period in patients already taking them.[1] ii. ACE Inhibitors ○ Discontinue due to increased risk for stroke.
	c. Statins	Statins are beneficial and should be continued throughout the perioperative period in patients already taking them.
5. Risk communication	Get the entire surgical team on board in the individualized management plan, and in agreement with the patient and relatives.	

TIA, Transient ischemic attack; ACE, Angiotensin-converting enzyme; CHF, Congestive heart failure; LVEF, Left ventricular ejection fraction
Sources:
Mashour GA, Moore LE, Lele A V, Robicsek SA, Gelb AW. Perioperative care of patients at high risk for stroke during or after non-cardiac,

non-neurologic surgery: Consensus Statement from the Society for Neuroscience in Anesthesiology and Critical Care. *Br J Anaesth*. 2014;26(4):273-285.
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B. Intraoperative Management[1,6]

TABLE 3–3. Summary of recommendations for intraoperative management of perioperative stroke

1.	**Anesthetic Technique**	• *Neuraxial technique* may be associated with a lower incidence of perioperative stroke for hip and knee arthroplasty.[1,6]
2.	**Hemoglobin**	• For non-cardiac, non-neurologic surgical patients already taking a beta-blocker, hemoglobin <9 g/dL should be avoided to minimize risk of stroke.[1]
3.	**BP Control[5,6]**	• Maintain mean arterial BP at 50 to 150 mmHg to preserve cerebral autoregulation. • Maintain SBP at least 20% from baseline to improve perfusion pressure. (Avoid clinically significant hypotension, defined as 30% from baseline BP.)
4.	**Glycemic control[1,6]**	• Target FBS is 60–180 mg/dL
5.	**Cardiac Rhythm[5]**	• Atrial fibrillation ○ It is the most common perioperative arrhythmia, which usually occurs due to electrolyte imbalance and intravenous fluid shifts. ○ Initiate heparin therapy for intraoperative atrial fibrillation with history of stroke or TIA, and continue 30 days after return of sinus rhythm.
6.	**Management of Intraoperative Stroke[6,8]**	• Majority of intraoperative strokes in non-cardiac and non-neurosurgical surgery are ischemic. • Etiologies include ischemia due to thrombosis (68%) or emboli (16%), with only 5% occurring due to bleed. • Mortality rates of stroke following non-cardiac surgery range from 18–32%. • Goals include supportive therapy and re-establishment of blood supply to ischemic tissue. a. Use of intravenous rtPa (e.g., Alteplase) to dissolve clots is relatively contraindicated 14 days after major surgery; using mechanical catheter to remove is best method. ○ If not contraindicated, intravenous/intra-arterial rtPa or mechanical thrombolysis should be considered as soon as possible for cases of acute ischemic stroke in surgical patients. ▪ Alteplase, which usually costs Php 80,000 per vial in pharmacies, is now available to the public for free in 26 government hospitals nationwide. ○ In patients who receive rtPA (intravenous/ intra-arterial) or undergo mechanical clot retrieval, with SBP >180 mmHg and DBP >105 mmHg, treat with labetalol or nicardipine. ○ Avoid giving aspirin (or other antiplatelet agents) as an adjunctive therapy within 24 hours of intravenous fibrinolysis. b. Supplemental oxygen should be provided to maintain oxygen saturation >94%. c. Maintain airway support and ventilator assistance to treat patients with decreased consciousness or bulbar dysfunction that causes respiratory compromise. d. Perform baseline ECG and troponin level.

BP, Blood pressure; FBS, Fasting blood sugar; TIA, Transient ischemic attack; ECG, Electrocardiogram; rtPa, Recombinant tissue plasminogen activator; SBP, Systolic blood pressure; DBP, Diastolic blood pressure

Sources:

Mashour GA, Moore LE, Lele A V, Robicsek SA, Gelb AW. Perioperative care of patients at high risk for stroke during or after non-cardiac, non-neurologic surgery: Consensus Statement from the Society for Neuroscience in Anesthesiology and Critical Care. *Br J Anaesth*. 2014;26(4):273-285.
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C. Post-Operative Management[1]

TABLE 3–4. Summary of recommendations for post-operative management of perioperative stroke

1.	Organized protocol for suspected perioperative stroke	Perform emergency evaluation of surgical patients with suspected perioperative stroke.
2.	Use NIHSS score in evaluation of stroke[11]	• Easy to use • Done in 4–5 minutes • NIHSS score >16 predicts a strong probability of patient death. • NIHSS score of ≤6 indicates a strong possibility for a good recovery. • Each 1-point increase on the scale lowers the possibility of a positive outcome for the patient by 17%.
3.	Emergency imaging of the brain	Recommended before initiating any specific therapy to treat acute postoperative stroke.
4.	FAST test for post-surgical patients[12]	FACE: Uneven smile? Facial droop? ARM: Arm/leg numbness? Arm/leg weakness? ANESTHESIA: Residual anaesthetic effect? SPEECH: Slurring speech? Difficulty to speak or to understand? TIME: Get help immediately–"Time is Brain"

NIHSS, National Institutes of Health Stroke Scale

Sources:

Mashour GA, Moore LE, Lele A V, Robicsek SA, Gelb AW. Perioperative care of patients at high risk for stroke during or after non-cardiac,non-neurologic surgery: Consensus Statement from the Society for Neuroscience in Anesthesiology and Critical Care. *Br J Anaesth*. 2014;26(4):273-285.
Sun Z, Yue Y, Leung CCH, Chan MTV, Gelb AW, Hospital BC. Clinical diagnostic tools for screening of perioperative stroke in general surgery: A systematic review. *Br J Anaesth*. 2016:1-11.
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OPEN FORUM HIGHLIGHTS

Moderator: MARIA JERICA CLAUDINE Y. TORRADO-STA. ROSA, MD

Q: *For a surgery with low bleeding risk such as elective laparoscopic cholecystectomy, should we still wait three months prior to the procedure?*

A: A laparoscopic cholecystectomy is generally an elective procedure unless there are signs of cholangitis. If the patient is really in pain and if the surgery really has to be done, the recommendation is to do a carotid Doppler, just to make sure that her carotids are okay and to find out if she needs revascularization preoperatively. Otherwise, the patient and the patient's family should be made aware of the risks. For example, in a post-stroke patient with minor residuals and walks with support, some doctors just give the go-signal for the patient to undergo surgery. However, there might be a recurrence of the stroke, which may be disabling or fatal.

Q: *Is it prudent to always ask for neurologic clearance prior to surgery if there was a prior history of stroke?*

A: It depends on your practice or your center and also on your expertise as an anesthesiologist. If you are a critical care anesthesiologist then probably if the surgery is minor (wound debridement, laparoscopic cholecystectomy, and dental procedure) then you can just do it yourself and assess the patient properly. However, if the patient will undergo a major surgery with a lot of bleeding, a neurologic consult is prudent. But if you are working in a rural situation, I guess you have to do it yourself. The neurologist-to-patient ratio in a community should be considered. What is really important is communication. You have to understand your expertise and do your best with the available resources in your hospital, and communicate this with your patients and their families.

Q: *If the hemoglobin is less than 9 g/dL prior to surgery, is blood transfusion advised right away?*

A: The cut-off value of 9 g/dL has been recommended by the Society of Neuro-anesthesia (United States and Canada) in a guideline because studies have shown that this results in better outcomes. To ensure good cerebral perfusion and oxygen-carrying capacity in post-stroke patients, a level of 9 g/dL is recommended. In regular patients, however, the American Society of Anesthesiology recommends as low as 7 g/dL.

Q: *When you administer the FAST test and it turns out positive, what is considered the time of onset of the stroke?*

A: Intraoperative stroke can never be detected because the patients are under anesthesia. You will have a suspicion that the patient had stroke if there is delayed emergence and they have the risk factors for stroke. That is why they recommend the NIHSS scale for immediate postoperative patients. This should be coupled with imaging and a neurologic consult to find out if the patient really had a stroke because you have to do something about it right away. Most of the time it is ischemic and they would probably consider mechanical thrombolysis done by an interventional neurosurgeon. The FAST test is usually done when the patient is already in the wards.

Q: *What are the anesthetic medications of choice in an elderly patient who previously suffered from stroke?*

A: We prefer to use short-acting anesthetics that can be easily reversed post-operatively so that we can assess neurologic status as soon as possible. The outcomes for perioperative stroke are worse than community-based stroke, due to many confounding factors such as residual anesthesia, and post-

operative immobility due to post-operative surgical pain. Symptoms may be misconstrued as pain but may already be a stroke.

Q: *Are there specified steps in preparing our elderly patients for surgery or anesthesia to decrease the risk for perioperative stroke?*

A: Age is already a risk factor. Find out their comorbidities (previous stroke, renal failure, hypertension; especially atrial fibrillation which is a risk for thrombosis) and their baseline cognitive function.

Q: *What are the preferred drugs for postoperative pain management in the elderly?*

A: We try to do multimodal management, i.e., we give paracetamol, and NSAIDs if not contraindicated. We do blocks; a simple local infiltration will help tremendously for postoperative pain management. It would be good to do peripheral nerve block in addition to the regular anesthetic. Usually, post-stroke patients are on gabapentin due to neuropathic pain, and they just have to continue taking it. Reassurance is important especially during emergence; e.g., give them eyeglasses if visually impaired, and have someone familiar to prevent post-op delirium.

REVIEW QUESTIONS

1. Which type of stroke is the most likely to occur perioperatively in elderly patients?
   a. Ischemic
   b. Cardiac
   c. Hemorrhagic
   d. Cryptogenic

2. Up to how many months is it recommended to delay elective surgery for elderly who had stroke prior to surgery?
   a. 2 months
   b. 3 months
   c. 6 months
   d. 1 year

3. Which medication should be discontinued prior to surgery due to increased risk for stroke?
   a. Carvedilol
   b. Enalapril
   c. Losartan
   d. Simvastatin

4. What is the most common perioperative arrhythmia encountered during surgery?
   a. Sinus bradycardia
   b. Ventricular fibrillation
   c. Supraventricular tachycardia
   d. Atrial fibrillation

5. Which of the following is a component of CHA_2DS_2VASc score used in assessing thrombotic risk?
   a. Age >50
   b. Cancer
   c. Dementia
   d. Diabetes

ANSWERS: 1. a; 2. b; 3. b; 4. d; 5. d

4 AGEING AND DRY EYE DISEASE

Ma. Dominga Cecilia B. Padilla, MD, FPAO

Delivered as a webinar on February 8, 2019
https://bit.ly/ALMW_Ch4_AgeingDryEyeDisease

KEY POINTS

- Dry eye disease is among the most common conditions in the general population; more prevalent in those 50 y/o and above, and more in women.
- It is multifactorial (external, internal) and linked to disruption in homeostasis of the ocular surface.
- Dry eye disease should not be taken lightly, as it may signal other eye problems or systemic problems.
- The aim of dry eye disease treatment is to break the vicious cycle, and depends on the type of dry eye and its severity.
- Not all eye drops for dry eye disease are the same, and the correct way to use them is to preempt the symptoms.

LEARNING OBJECTIVES

- ➸ To define dry eye disease and its relationship to ageing, and discuss its common causes and pathophysiology
- ➸ To give an overview of the available and appropriate assessment and diagnostic tools for dry eye disease
- ➸ To outline the management plan for the treatment of dry eye disease among the elderly and the general population, and discuss ways to prevent having this disease

I. AGEING EYES

The eyelids and the eyes are among the tissues most affected by ageing. Effects of ageing include eye bags, drooping eyelids, cataracts, age-related degeneration of the retina, and dry eyes.

II. WHAT IS DRY EYE DISEASE (DED)?

DED is a "multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles."[1]

III. PREVALENCE AND BURDEN OF DRY EYES

- The prevalence ranges from 5 to 50% around the world. The prevalence is higher in women than men, especially in the ageing population, and higher in Asian than Western populations.
- The economic burden and impact of dry eye disease (DED) on the quality of life and productivity are significant, and can range from mild to debilitating.

IV. WHAT CAUSES DED? WHAT HAPPENS TO THE EYE WITH DED?

A. Normal Tear Film

- Forms the first refractory surface for light entering the eye; 3 μm thick
- Protects and moisturizes the cornea and conjunctiva
- Biphasic
  1. **LIPID LAYER**: Mostly wax and cholesteryl esters that protects eyes against evaporation and are spread out over muco-aqueous layer by underlying polar lipids; produced by the Meibomian glands
  2. **MUCO-AQUEOUS LAYER**: Contains 4 types of mucin and over 1500 proteins and peptides; produced by the lacrimal glands
     - Lubricants, nutrients, antimicrobials
     - Proteins, electrolytes, anti-inflammatories, growth factors
- Interaction of the entire tear film prevents tear evaporation and spilling and promotes stability.
- There is no need for eye drops if there is normal tear film.

B. The Vicious Cycle of DED (Figure 4–1)

- Anything that disrupts the homeostasis can cause hyperosmolarity of the tear film and trigger the cascade of events in the vicious cycle of DED.
- DED doesn't always mean you lack tears. More often, it is an abnormal quality of tears that causes DED. And because of the abnormal tear quality, inflammation and symptoms, reflex tearing, composed of mostly aqueous tears, can occur.

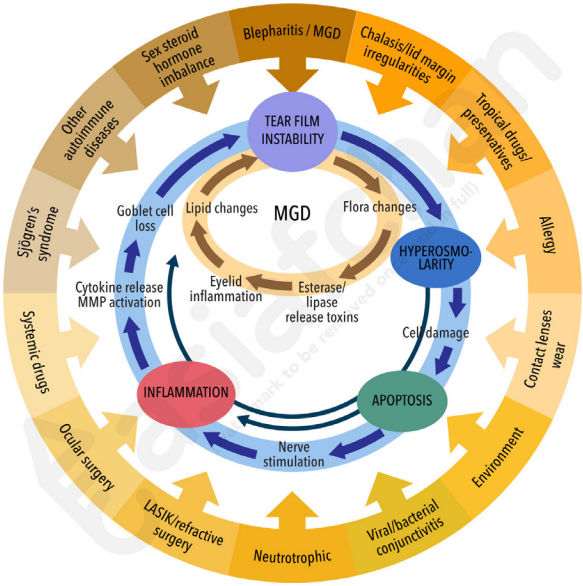

FIGURE 4–1. The vicious cycle of DED

Modified with permission from "Revisiting the vicious cycle of dry eye disease: A focus on the pathology of Meibomian gland dysfunction" by C. Baudouin et al. (2016). *Br J Ophthalmol,* 100, p303. Copyright © 2016 by BMJ Publishing Group Limited. (CC BY-NC 4.0)

- Treatment of DED aims to break this cycle, prevent hyperosmolarity, restore homeostasis and balance, and bring about relief of signs and symptoms.

V. HOW IS DED DIAGNOSED?

A. Assessing Signs and Symptoms

- Severity: Mild, moderate, and severe
- Type:
  - Aqueous-deficient dry eye (ADDE): Lack of aqueous fluid
  - Evaporative dry eye (EDE): Lack of lipid and/or mucin
  - Combined: found in most DED
- Underlying causes and risk factors:
  - Eyelid abnormalities (Meibomian gland dysfunction or MGD, ectropion, lid laxity, lagophthalmos, etc.)
  - Systemic conditions (e.g., hormonal imbalance, autoimmune diseases)
  - Medication (systemic or topical)
  - Environment (e.g., computer use, air conditioning)

B. Diagnosing DED

- Summary of the steps to properly diagnose DED are outlined in the Tear Film and Ocular Surface Society (TFOS) Dry Eye WorkShop (DEWS) II report.[2]
  1. Ask triaging questions
  2. Assess risk factors
  3. Examine the eye: Is it evaporative or aqueous?
  4. How bad is it?
- Not all clinicians will use the Ocular Surface Disease Index (OSDI), a validated 12-item questionnaire.[3] The shorter validated 5-item version, the Dry Eye Questionnaire (DEQ-5) is also available to assess symptoms of DED.[4]

TABLE 4–1. Questions to determine symptoms of DED and severity

1.	Are your eyes sensitive to light? (nasisilaw)
2.	Do you experience grittiness of the eyes? (magalas, may puwing)
3.	Are your eyes sore? (masakit, mahapdi)
4.	Do you have blurred vision or poor vision? (malabo)
5.	Is your vision made better by blinking?
6.	Do your symptoms limit your activities in any way? (driving, TV, computer work, reading)?
7.	Are your symptoms made worse by windy conditions, air conditioning, electric fan, and places with low humidity?

C. Are there risk factors?

1. Ageing and menopause (due to imbalance of sex hormones, lid abnormalities, decrease in androgen, etc.)
2. Systemic medications (Table 4–2)
3. Topical medications: Anti-glaucoma drops; decongestants, preservatives in eye drops
4. Smoking (even second-hand smoke)
5. Environmental causes: e.g. Computer vision syndrome, exposure to windy dusty conditions, air

conditioning, low humidity)

TABLE 4–2. Systemic medications that predispose to DED

- Beta-blockers
- Anti-depressants
- Diuretics
- Anxiolytics
- Antipsychotics
- Anti-Parkinsonian Drugs
- Isotretinoin
- Estrogen therapy
- Antihistamines
- Systemic chemotherapy

D. Differential diagnosis

TABLE 4–3. Some conditions that may mimic dry eye disease

1. Allergic conjunctivitis: Atopic keratoconjunctivitis, vernal keratoconjunctivitis, giant papillary conjunctivitis
2. Viral conjunctivitis
3. Bacterial conjunctivitis
4. Anterior blepharitis
5. *Demodex* infestation – incidence increases with age and may also cause **EDE**
6. Parasitic infections *(e.g. Chlamydia trachomatis)*
7. Corneal abnormalities
8. Filamentary keratitis, other keratitis (e.g., interstitial keratitis) and keratopathies (e.g., bullous keratopathy)
9. Autoimmune conditions (e.g., rheumatoid arthritis, Sjogren's syndrome, systemic lupus erythematosus). These may also manifest as severe **DED**.
10. Graft-versus-host-disease (after bone marrow transplant)
11. Psychological factors

EDE, Evaporative dry eye; DED, Dry eye disease

E. Signs of DED

- There are many tests available. But the following are recommended based on diagnostic ability, minimal invasiveness, objectivity and clinical ability (Table 4–5).

TABLE 4–4. Recommended diagnostic tests

1. Non-Invasive Tear Breakup Time (NITBUT)
2. Osmolarity
3. Fluorescein Breakup Time (FBUT)
4. Ocular Staining

  - Fluorescein Breakup Time (FBUT). This is the most practical and most accessible test to do at the clinic. If you can do only one test, do the FBUT.
    - Three normal blinks then keep eyes open
    - Number of seconds until first dark spot appears
    - Abnormal value is less than 10 seconds
    - Other studies: lower in older population (5-7 sec); Asian Dry Eye Society (ADES) pegs the cut off at 5 seconds or less

- Ocular Staining
  - **FLUORESCEIN**: corneal damage
  - **LISSAMINE GREEN**: conjunctival damage
- Eyelids are checked.
  - Meibomian Gland Dysfunction (MGD) plays a very important part in etiology of DED especially in the ageing population.
    - Hormonal imbalance of estrogens and androgens in ageing can result in DED.
    - Androgen binding in the Meibomian glands results in increased lipid production and decreased keratinization. The same protection also occurs in the lacrimal glands.
    - Androgen deficiency is a risk factor for EDE and ADDE.
- Decreased androgen occurs in:
  - Menopause (decrease in ovarian and adrenal "androgen secretion")
  - Ageing (decrease in total androgen pool in both sexes)
  - Use of anti-androgen medication (i.e. those used for prostatic hypertrophy and cancer)
  - Women with dysfunctional androgen receptors
  - Autoimmune diseases (SLE, Sjogren's syndrome, rheumatoid arthritis)[5]
- Lid wiper epitheliopathy: May indicate damage to goblet cells in the marginal conjunctiva that may result from increased friction from rubbing of the eyelids on the ocular surface
- The frothy discharge is from by-products of lipid breakdown by lipolytic enzymes of bacteria.
- *Demodex* infestation (*Demodex folliculorum and Demodex brevis*)
  - Studies show that in some populations, as high as 84% of those 60 years of age and above, and almost 100% of those aged 70 and above have *Demodex* infestations.[6]
  - The bacteria feed on sebum, and waste, leading to inflammation.
  - Tea trea oil has antibacterial, anti-fungal, anti-viral, anti-bacterial effects and is toxic to *Demodex*.[7]

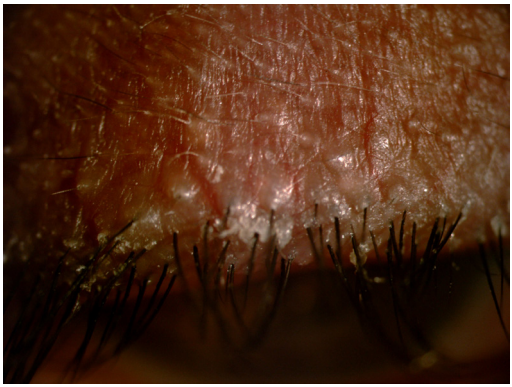

FIGURE 4–2. Anterior blepharitis in a 77 y/o man. Cylindrical deposits on the base and shaft of the eye lashes (colarettes) can be a sign of *Demodex* infestation. These deposits are regurgitated, undigested material from the mites combined with epithelial cells, keratin, and eggs. These deposits contain lipases and proteases which case eyelid Irritation. This is a common condition in the elderly population and may also be associated with dry eye disease.

VI. WHAT IS THE TREATMENT OF DED?

A. Treatment principles

- Treatment depends on cause and severity.
- The goal of treatment is to break the vicious cycle of DED by restoring homeostasis and tear stability and decreasing inflammation.
- There are many established treatment modalities that are backed up by extensive Level I evidence (e.g., tear supplements, anti-inflammatory eye drops).
- There are a lot of treatment modalities with level 2 and 3 evidence that are shown to relieve signs and symptoms of DED but still lack level I evidence and established protocols. We use them anyway. (Autologous serum, essential fatty acids, warm compress)
- More research is being done and still needs to be done to better understand how and why various types of treatment for DED work and why some do not. (Chinese herbal remedies, breast milk, and acupuncture work, but more studies are needed.)
- The treatment of DED is very much an art as it is a science. People respond differently even to established treatment protocols. Patience is often necessary.

B. Steps in Treatment

These steps are just guides. How patients are managed will also depend on the severity of the eye condition on initial presentation. Step 2 is an add-on or replacement for Step 1. However, if the DED is moderate to severe, with inflammation and pain, you will have to go to step 2 immediately. Step 3 is for severe dry eye disease in whom the measures in step 1 and 2 are not enough.

TABLE 4–5. Steps in Treatment of DED

Step 1	• Education regarding the condition, management, prognosis • Modification of local environment • Education regarding potential dietary modification (including oral essential fatty acid supplements) • Identification and potential modification/elimination of offending systemic and topical medication • Ocular lubrication of various types (if with **MGD**, consider lipid-containing tear supplements) • Lid hygiene and warm compress of various types (baby shampoo, lid wipes) • Examples of composition of various lubricants and tear substitutes: ○ Dextran ○ Carboxymethylcellulose and hydroxymethylcellulose ○ Hyaluronic acid/Sodium hyaluronate ○ Propylene glycol ○ Osmo-protectors (glycerin, erythretol, L-carnitine)

TABLE 4–5. Steps in Treatment of DED (cont.)	
Step 2	• Non-preserved ocular lubricants to minimize preservative-induced toxicity • Tear conservation (punctal plugs, moisture spectacles/goggles) • Overnight treatment (gels, moisture devices) • In-office physical heating and expression of the Meibomian glands; include device-assisted therapy (if available) • In-office intense pulsed light (IPL) therapy for **MGD** (if available) (Figure 4–3) • Prescription drugs to manage **DED**: ○ Topical antibiotic or antibiotic/steroid ointments to lid margins for anterior blepharitis ○ Topical corticosteroids for limited duration ○ Topical secretagogues (e.g., diquafasol) ○ Topical non-glucocorticoid immunomodulatory drugs (cyclosporine, tacrolimus) ○ Oral macrolide (azithromycin): Stimulate Meibomian gland function ○ Tetracycline, doxycycline, minocycline: Inhibit lipase production, decrease Meibomian lipid breakdown products, anti-inflammatory
Step 3	• Autologous/allogenic serum eye drops ○ Concentration may range from 20 to 50% ○ Promote epithelial healing, neutralize inflammatory cells ○ Rich in albumin, growth factors, fibronectin • Therapeutic bandage contact lens options
Step 4	• Topical corticosteroids for a longer duration • Amniotic membrane grafts • Surgical punctal occlusion • Other surgical approaches (e.g., tarsorrhaphy, salivary gland transplant)

DED, Dry eye disease; MGD, Meibomian gland dysfunction

Source: Jones L, Downie LE, Korb D, et al. TFOS DEWS II management and therapy report. *Ocul Surf.* 2017;15(3):575-628.[8]

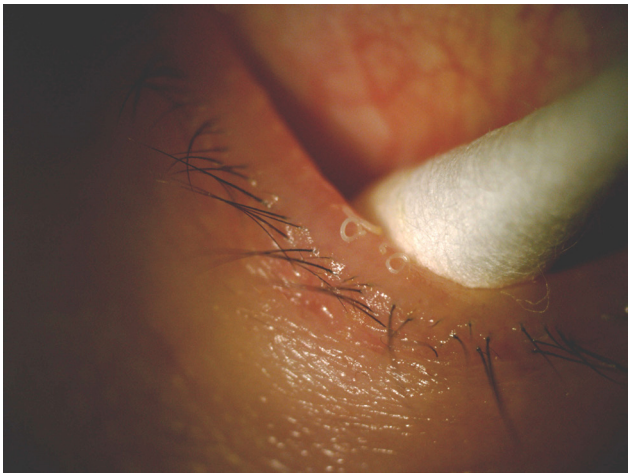

FIGURE 4–3. Meibomian gland dysfunction in a 65 y/o woman. This figure shows the thick, "toothpaste like" secretion that is expressed from abnormal Meibomian glands. Expression of the Meibomian glands, preferably after warm compress, should be done regularly as part of the clinical management.

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OPEN FORUM HIGHLIGHTS

Reactor: ELEANORE B. IGUBAN, MD
Moderator: ALNETTE L. TAN, MD

- *Reaction from Dr. Eleonore Iguban:*
  Dry Eye Prevention
  Do not forget to BLINCC:
  - **B** – Take regular breaks from visual work (i.e. reading, computer)
  - **L** – Lubricate your eyes (but consult your ophthalmologist first)
  - **I** – Increase your intake of water
  - **N** – Nourishment (Omega Fatty Acids)
  - **C** – Clean your lids
  - **C** – Appropriate environmental conditions

Q: *Is Dry Eye Syndrome caused by prolonged use of computer? Is it reversible?*

A: Yes. Habits can bring about dry eye. When people use a computer for a long time, studies have shown that people do not blink completely. That can cause dry eye syndrome.
If you use a computer for more than 20 minutes, an easy guide to remember is 20/20. Every 20 minutes, take a 20-second break. Look away at an image far away or you can even close your eyes. The symptoms are reversible. All you have to do is change your habit.
Your computer screen should be at a level a little below your eyes.
Is electric fan or aircon breeze hitting your eyes directly? If so, change the direction of the wind.
Incomplete blinks are worse when using small gadgets.
Playing video games wherein people do not blink enough for fear of losing points can cause dry eye. Dry

eyes is one of the components in computer vision syndrome.
When reading an e-book, the pixels are always moving and leads to eye strain due to constant adjustment.

Q: *What are the differences between eye drops and ointments? Which one do you prefer?*

A: Eye drops are more liquid and less viscous but are not as long lasting as eye gels. However, when using polymers, the more viscous the eye drops, the more likely they will blur the vision.
Ointments are more oil-based used for inflammation and scrubbing the eyelids.
Whether to use drops, gels and/or ointments will depend on the doctor, on the eye condition and on the comfort of the patient.

Q: *Do places with hot temperatures cause dry eyes?*

A: Heat may cause evaporation that will cause dry eyes. However, if it's hot and humid, it's not as bad as hot and dry locations such as deserts.
Bring glasses and avoid too much sun exposure.

Q: *When should expression of Meibomian glands be performed? How frequent should it be done, how should it be done, and what should be the endpoint?*

A: There is no gold standard: the endpoint is when the patient is no longer symptomatic. If severe, it may be done once a week; if not too bad, once a month.
Patient can do the warm compress first for 5-10 minutes and massage at home, but it is recommended that the and ophthalmologist do manual expression of the meibomian glands in the clinic. It may also be good for the actual warm compress to be done also at the clinic right before the manual expression of the Meibomian glands.
Oral antibiotics may be given for MGD: minocycline and tetracycline. Azithromycin may also be given, and it may also increase Meibomian gland secretion.

Q: *Are people taking estrogen therapy or using contraceptives at high risk for developing dry eyes?*

A: Yes, estrogen and progesterone can inhibit production of lipids in the Meibomian glands that may cause or worsen DED. Breast cancer patients on hormonal chemotherapy may also be at higher risk of DED. The body can sometimes restore balance through a paradoxical increase in testosterone production responding to the damaged Meibomian glands.

Q: *After LASIK surgery, my eyes have always been dry, is there any alternative to artificial tears?*

A: You will likely need to use some topical lubricants, especially in the beginning of treatment or early after the LASIK. The following can be adjuvant treatments:

- Supplements such as omega-3 fatty acids 1000 to 3000mg/day. This however is based on level II evidence and not level I.
- Punctal plugs before and after LASIK may be used.
- Mild dry eye is not an absolute contraindication to LASIK but there are patients who need to be pre-treated when contemplating LASIK. Secretagoues like Diquaasol sodium drops can be given. Those with severe dry eye should not undergo LASIK.
- Check on other factors that could be the cause of the dry eyes as well.

Q: *Is there a correlation between contact lens use and dry eyes?*

A: Chronic contact lens use can damage the goblet cells and conjunctival cells that produce the mucin and aqueous fluid and cause DED. But the irony is that contact lenses are also used to treat dry eyes.

Q: *Can DED be found in children?*

A: It can be, but usually secondary to other diseases such as atopic keratoconjunctivitis (allergies).

Q: *Do Visine and Eye Mo have a role with the treatment of dry eyes?*

A: You can use these once in a while, but if the drops contain decongestants, then these decongestants that are used to treat red eyes may cause dry eyes. Preservatives such as benzalkonium chloride may also cause dry eyes.
Consult an ophthalmologist on the use of these eye drops, especially if there is dependence.

REVIEW QUESTIONS

1. Which of the following does not describe a normal tear film?
   a. It is triphasic: mucous, lipid, and aqueous layers
   b. It protects and moisturizes the cornea.
   c. It forms the first refractory surface for light entering the eye
   d. Interaction of its components prevents evaporation

2. Which type of DED is due to lack of mucin and/or lipid?
   a. Aqueous type
   b. Combined type
   c. Evaporative type
   d. Inflammatory type

3. How is Meibomian dysfunction initially treated?
   a. Lubricants with decongestant
   b. Lid scrubs combined with warm compress and lubricants
   c. Immediate oral antibiotics
   d. Plucking of eye lashes

4. Which of the following systemic medications can cause dry eye disease?
   a. Beta blockers
   b. ACE inhibitors
   c. Antibiotics
   d. Omega-3 fatty acids

5. In the prevention of DED, which of the following is a part of the mnemonic BLINCC?
   a. Take regular breaks from visual work
   b. Increase intake of vitamin supplements
   c. Break the habit of scratching your eyes
   d. Clean your contact lenses

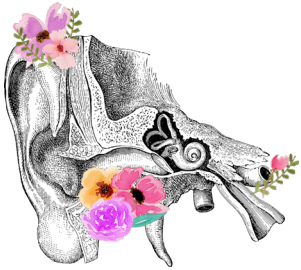
ANSWERS: 1. a; 2. c; 3. b; 4. a; 5. a

5 HEARING LOSS IN THE ELDERLY

Teresa Luisa G. Cruz, MD, MHPEd

Delivered as a webinar on August 9, 2019

https://bit.ly/ALMW_Ch5_HearingLoss



KEY POINTS

- Normal hearing is dependent on normal anatomy and functioning of the ear and the central nervous system.
- Hearing loss can occur if any component of the ear or central nervous system is abnormal due to:
  - Genetics
  - Congenital anomalies
  - Infections
  - Tumors
  - Systemic diseases
  - Trauma
  - Noise
  - Ototoxicity
- The ageing population is significantly burdened by hearing loss: physically, mentally, and emotionally.
- Management of hearing loss depends upon the specific cause.
- For presbycusis or age-related hearing loss, a holistic approach must consider all aspects of the condition to manage the burden.
- Future efforts must focus on research, education, and policy formulation to address prevention and management of hearing loss in the ageing population.

LEARNING OBJECTIVES

- ➸ To describe the normal anatomy and physiology of hearing
- ➸ To give an overview on the epidemiology and risk factors for hearing loss in the elderly
- ➸ To discuss the types of hearing loss in the elderly
- ➸ To outline the diagnostic and therapeutic plan for hearing loss in the elderly
- ➸ To discuss the impact of research, education, and policy in management of hearing loss

I. NORMAL HEARING

A. Anatomy

- The ear has 3 divisions: outer ear, middle ear, inner ear (Figure 5–1).
- Majority of the ear is located inside the skull.
- The tympanic membrane, or the eardrum, is the boundary between the outer and middle ear.
- The middle ear is an air-filled space that is connected to the nose, the back of the nose, and the throat by means of the Eustachian tube.
- The inner ear is the one responsible for transforming mechanical energy to electrical energy that is transmitted to the brain.

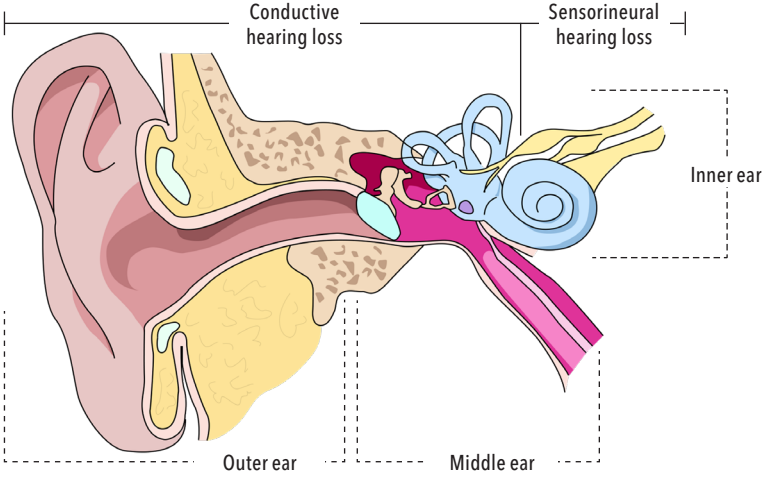


FIGURE 5–1. Normal anatomy of ear and types of hearing loss

Adapted with permission from "A self-instructional manual on disorders of hearing: Diagnosis, prognosis and principles of therapy for LU IV medical students" by Department of Otorhinolaryngology, Philippine General Hospital, University of the Philippines Manila, 2008, H-1

© Jose Florencio F. Lapeña, Jr., MD, 2008[1]

B. PHYSIOLOGY

- The process of hearing involves the ears up to the brain so that we can hear and understand what we hear (Figure 5–2).
- Any lessening of capacity to hear normally is called *hearing loss*.

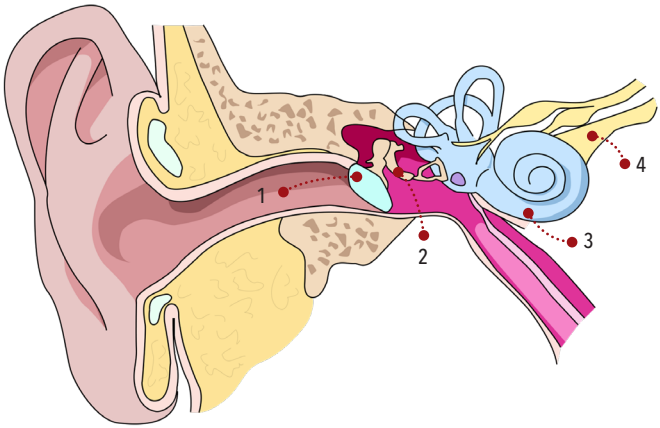


FIGURE 5–2. Normal pathway of sound

1. Sound waves are collected by the pinna, enter the ear canal, and strike the ear drum.
2. This leads to the movement of the malleus, incus, and stapes in the middle ear that serves as a conductive mechanism.
3. Mechanical waves are conducted to the fluid inside the cochlea, resulting in the movement of hair cells that will transform mechanical energy to electrical energy.
4. This electrical energy will be detected by the vestibulocochlear nerve and directed to the brain.

Adapted with permission from *"A self-instructional manual on disorders of hearing: Diagnosis, prognosis and principles of therapy for LU IV medical students"* by Department of Otorhinolaryngology, Philippine General Hospital, University of the Philippines Manila, 2008, H-1 © Jose Florencio F. Lapeña, Jr., MD, 2008[1]

II. EPIDEMIOLOGY[2]

- Around 6% of the world's population or 466 million people have disabling hearing loss:
  - Adults: 432 million
  - Children: 34 million
- By 2050, it is estimated that over 900 million people will develop disabling hearing loss.
- Approximately one third of people over 65 years of age are affected by disabling hearing loss. The prevalence in this age group is greatest in South Asia, Asia Pacific, and sub-Saharan Africa.[3,4]

III. LEVELS OF HEARING LOSS

- The levels of hearing loss are based on the threshold of environmental noise that a patient can still hear and/or repeat (Figure 5–3).
- A patient with slight hearing loss (WHO Grade 1) is still able to hear and can repeat words in a normal voice at 1 meter.
- In moderate hearing loss, from 41 to 60 dB (WHO Grade 2), a patient can only hear or repeat words in a raised voice at 1 meter. This level is already considered a hearing disability.
- Hearing damage occurs above 85 dB and causes severe hearing loss that ranges from 61-80 dB (WHO Grade 3). A patient can only hear words if shouted into the better ear.
- Profound hearing loss, over 81 dB (WHO Grade 4) is when a patient cannot hear or understand shouted voice.

- There is a lower threshold for moderate hearing loss in children (30 dB) compared to adults (40 dB), emphasizing the importance of normal hearing in a child's optimal development.

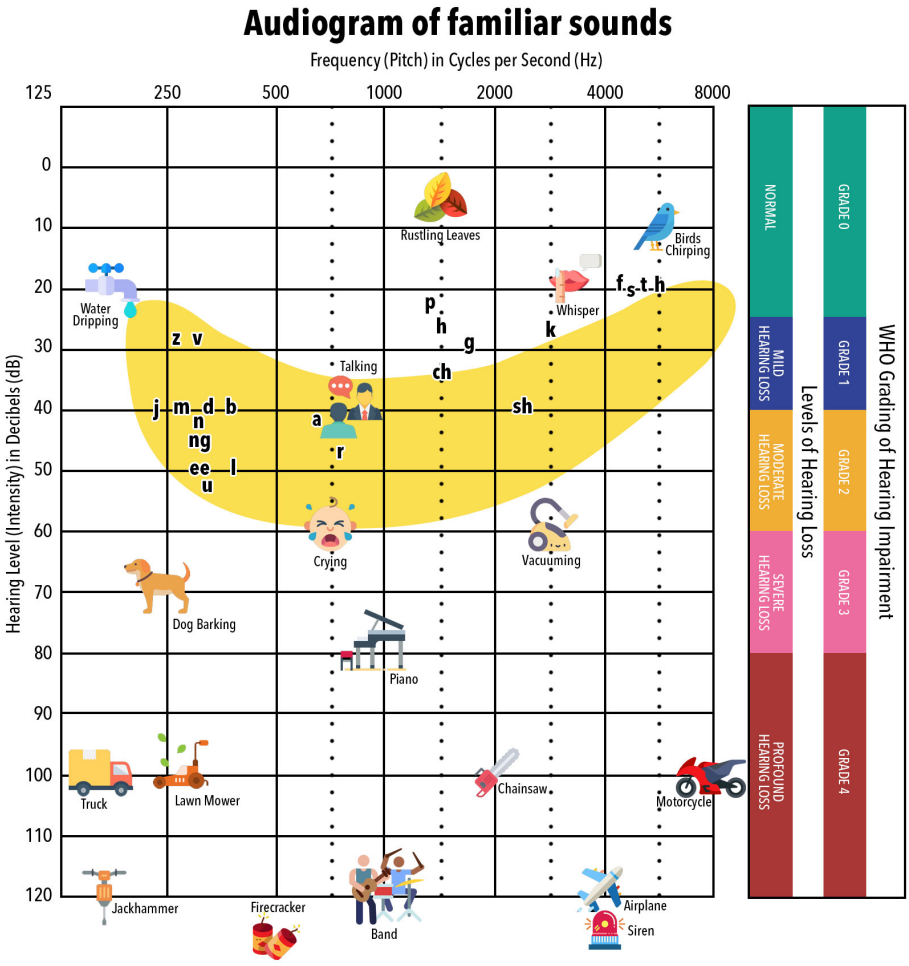


FIGURE 5–3. Classification of hearing loss and common sound levels from environment

Sources:

American Academy of Audiology www.audiology.org/sites/default/files/publications/Audiogram2012_EngSample.pdf[5]

World Health Organization. Grades of hearing impairment. www.who.int/pbd/deafness/hearing_impairment_grades/en/. Accessed March 30, 2020.[6]

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IV. CAUSES OF HEARING LOSS

Types of Hearing Loss – based on location (Figure 5–1)

1. Conductive hearing loss – when the condition affects the outer (Table 5–1) or middle ear (Table 5–2)
2. Sensorineural hearing loss – when the condition affects the inner ear; more difficult to treat
3. Mixed hearing loss – when both conductive and sensorineural hearing loss are present
   - The deeper the problem, the more challenging the solution.

TABLE 5–1. Outer ear conditions (conductive hearing loss)

DISEASE	CLINICAL PRESENTATION	TREATMENT
1. Impacted cerumen	Cerumen is a normal product of the ear glands, but excessive production and use of cotton buds push the cerumen inwards.	Softening and removal of the impacted cerumen by an ear, nose, and throat (ENT) specialist to free up the ear canal can dramatically improve hearing.
2. Foreign body obstruction	Cotton coming loose from a cotton bud, animated objects such as ants or cockroaches or sand after swimming; may cause pain once they get into the ear canal.	ENT specialist removes the foreign body with special instruments, drowns the insects before removal, or flushes out sand.
3. Otitis externa	Fungal (otomycosis) (Figure 5–4) • Deep seated itching, discomfort, discharge, foreign body sensation, pain, and edema that is less severe than with bacterial external otitis • Usually affects medial area • Appearance varies per organism (fine coal dust or wet newspaper-like with *Aspergillus*, soft, white and sebaceous-like with *Candida*)	Topical antifungal medication for 2–3 weeks after ear canal cleaning by an ENT specialist
	Bacterial • Ear pain, pruritus, discharge, and hearing loss; • Tragal tenderness or pain with ear-pulling; • Ear canal is erythematous, edematous, and typically with yellow/brown/white/gray debris	Topical antibacterial medication to cover for skin pathogens like *S. aureus*
4. Diffuse otitis externa	Swelling of ear canal commonly due to excessive use of cotton buds, or swimmer's ear, causing pain	• Topical antibiotic ear drops are often adequate. • Systemic oral antibiotics may be necessary if with extensive infection and massive swelling.
5. Malignant otitis externa	• Usually presents with severe pain and ear discharge; • In association with poorly-controlled diabetes mellitus	• Usually requires oral antibiotics • Sugar control also needs to be achieved
6. Osteomas	• Benign • Occurs in fishermen and people with chronic water exposure in ears	• May not need treatment if hearing loss is mild • May be surgically removed if hearing loss is disabling

TABLE 5–1. Outer ear conditions (conductive hearing loss) (cont.)

DISEASE	CLINICAL PRESENTATION	TREATMENT
7. Malignant ear canal tumors	• Include squamous cell carcinomas and adenocarcinomas • Usually arise from ear canal skin	Biopsy and appropriate medical and surgical management

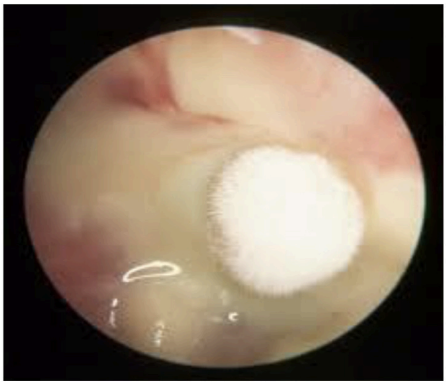

FIGURE 5–4. Otoscopic picture showing white creamy debris in ear of patient with otomycosis

Reprinted from 'Hospital based study on etiopathogenesis and treatment of otomycosis: Ethnic Kashmiri population' by Sumbria D, Yousuf A, Ahmad R. *Int J Otorhinolaryngol Head Neck Surg*. 2019;5(5):1190-1196.[8]

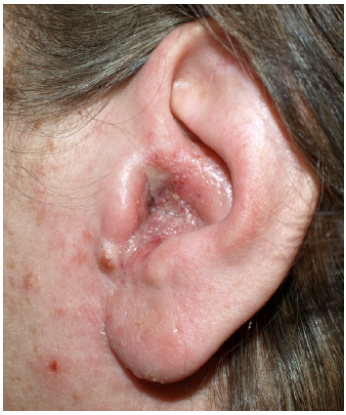

FIGURE 5–5. Otitis externa (swimmer's ear) may also be caused by *P. aeruginosa* or other bacteria commonly found in water. Inflammation of the outer ear and ear canal can lead to painful swelling.

Reprinted from 'Bacterial Infections of the Skin and Eyes.' Openstax. https://openstax.org/books/microbiology/pages/21-2-bacterial-infections-of-the-skin-and-eyes. Published 2016.

TABLE 5–2. Middle ear conditions (conductive hearing loss)

DISEASE	CLINICAL PRESENTATION	TREATMENT

1. Acute otitis media (Figure 5–6)	• Presents with pain and hearing loss
	• In the exudative stage of Acute Otitis Media (AOM), air is replaced by mucus and presents with increasing pain
	  ○ Increased pressure in the middle ear creates a hole in the eardrum and the mucus will egress into the ear canal, leading to ear discharge
	  ○ Common in pediatric population
		Oral antibiotics

2. Cholesteatoma	• If left untreated in areas without access to healthcare, longstanding infection can progress to chronic suppurative infection with cholesteatoma. • Cholesteatoma has enzymes that can cause lysis and necrosis of bony structures around ears; • The most feared complication is intracranial space invasion if the tegmen is breached, which can lead to meningitis.	Surgical management
3. Otitis media with effusion	Fluid or mucus inside middle ear but no infection	Myringotomy to suction out fluid and mucus from the middle ear
4. Tumors	Glomus tumor or paraganglioma	Surgical treatment
5. Otosclerosis	Abnormal bony consistency in foot plate of stapes with failure of ossicles to conduct sound waves	Surgical treatment

Note: Any condition in the nasopharynx can spread to the middle ear through the Eustachian tube

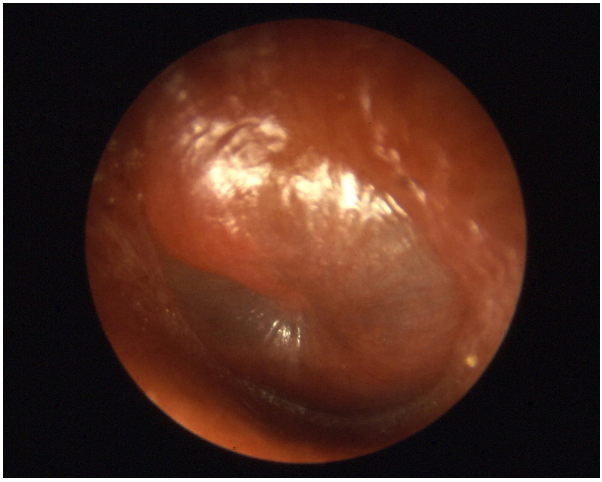

FIGURE 5–6. Otitis media

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TABLE 5–3. Inner ear conditions (sensorineural hearing loss)

CONDITION	CLINICAL PRESENTATION
1. Genetic[9]	• >40 genes cause deafness • 300 syndromes • Mutations, chromosomal abnormalities • Mitochondrial mutations: late-onset hearing loss, pathophysiologic mechanisms for age-related presbycusis
2. Congenital	• If no timely intervention, leads to a life of deafness 1. Maternal infections – babies develop profound hearing loss ○ Congenital rubella syndrome ○ Cytomegalovirus ○ Toxoplasmosis 2. Hypoplastic auditory nerves 3. Cochlear abnormalities
3. Ototoxicity	• Prevention is key since damage is irreversible • May damage hair cells of inner ear • May be caused by medications or chemicals (Table 5–4)
4. Inner ear diseases	1. Meniere's disease 2. Sudden sensorineural hearing loss 3. Head trauma/Temporal bone fracture 4. Superior semicircular canal dehiscence syndrome ○ Most patients with vertigo, ear fullness ○ Often misdiagnosed as Meniere's disease 5. Autoimmune 6. Tumors ○ Acoustic neuroma/Vestibular schwannoma – benign, but can be life threatening due to location
5. Other Diseases	1. Diabetes mellitus[10] 2. Hypertension 3. Hypothyroidism 4. Bacterial meningitis 5. Stroke 6. AIDS 7. Parotitis 8. Measles 9. Syphilis

TABLE 5–4. Medications and chemicals that cause ototoxicity

MEDICATIONS	CHEMICALS
Aminoglycosides (streptomycin for tuberculosis – most notorious)	Butyl nitrite
	Carbon disulfide
Hydrocodone	Styrene
Methotrexate	Carbon monoxide
Loop diuretics	Heavy metals: tin, lead , manganese, mercury
Sildenafil	Hexane
NSAIDs	Ethylbenzene
Quinine	Toluene and xylene
Macrolides	Trichloroethylene
Carboplatin	Organophosphate pesticides

NSAIDs, Non-steroidal anti-inflammatory drugs

V. NOISE

- Possible sources of noise:
  - Ambient environmental noise
  - Personal audio electronics - iPods have no decibel levels and should be kept at 30%–40% on the dial to enjoy listening to music without limit.[11]
  - Acoustic trauma
  - Workplace noise

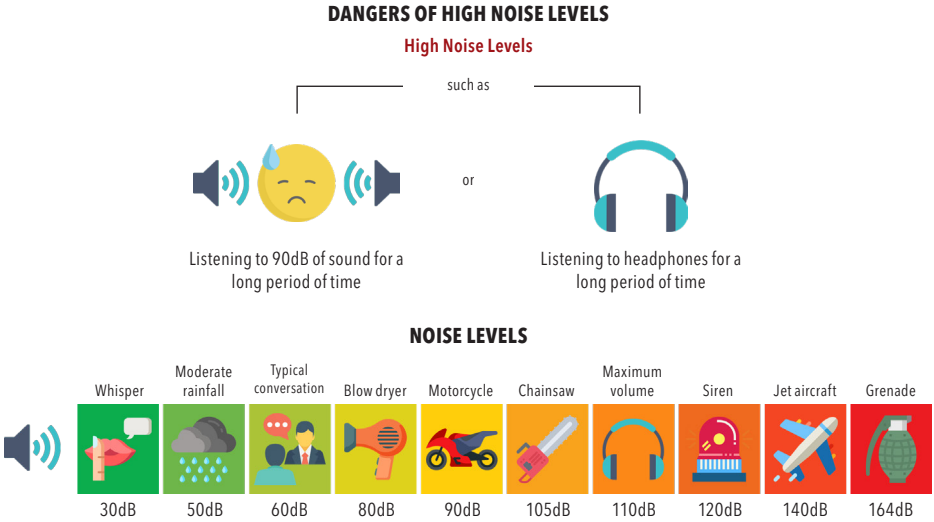

FIGURE 5–7. Noise levels from environment

Adapted from jehsomwang@shutterstock.com. Royalty-free stock vector ID: 389924158
Images from www.flaticon.com (Whisper, rain, dryer, motorcycle, and aeroplane from Freepik; typical conversation from Vectors Market; chainsaw from Nikita Golubev; headphones from Good Ware; siren from Smalllikeart, and grenade from photo3idea_studio)

TABLE 5–5. Noise levels

ALLOWABLE NOISE	UNSAFE LEVELS OF NOISE
• 85 dB (engine noise in big ships; heavy city traffic) for 8 hours • 90 dB (heavy city traffic) for 2 hours • Up to 100 dB (power tools) for 25 minutes	• Continuous exposure at 70 dB • Long exposure to loud noise on headphones • 125 dB – noise becomes painful

- Noise is the most studied environmental risk factor for hearing loss in adulthood.
  - Exposure to industrial, recreational, military, and social or community noise
- Global burden of noise-induced hearing loss: ~16% of the adult population affected[12]
- Compliance with recommendations, such as ear protection, is generally low due to lack of awareness. Affected people also do not feel the hearing loss, which is gradual and insidious in onset over 20 years.
- Hazards of of industrial noise have been reduced due to:
  - Hearing conservation regulations[13]
  - Increasing automation at work
  - Shift from noisier industrial to quieter information-based economies

VI. PRESBYCUSIS

A. Overview[14]

- Age-related hearing loss
- Progressive, bilateral, symmetrical
- Factors:[15]
  - Genetic predisposition
  - Physical and environmental insults
  - Physiologic stressors
  - Lifestyle behaviors
- Loss of higher frequencies
  - Involvement of consonants, not vowels that make up most of the spoken word
  - The elderly usually complain that they can hear sound but cannot understand the words (i.e., poor speech discrimination).
- It begins in the 4th decade, with the sharpest rise in prevalence rates at ages over 80 years, affecting 50–80%.
- It is projected to be one of the top 15 leading causes of burden of disease by 2030.[16]
- It has negative effects on:
  - Mental health
  - Emotional well-being
  - Self-esteem
  - Interpersonal relations
  - Health-related quality of life
  - Work possibilities and career
- Population-based studies show that hearing loss is associated with more rapid cognitive and physical ageing.[17,18]
- Age-related sensory loss, including hearing loss, is associated with dementia and falls.[19]

TABLE 5–6. Types of presbycusis

TYPE	PATHOLOGY	CLINICAL COURSE
1. Sensory presbycusis (Cochlear presbycusis)	Due to degeneration of the organ of Corti	• Hair cell loss specific to the extreme apical (low-frequency) and basal (high-frequency) regions of the cochlea • Speech discrimination is often preserved.
2. Neural presbycusis	Due to degeneration of cells of the spiral ganglion	1. Atrophy of nerve cells in the cochlea and central neural pathways ○ It is estimated that 2100/35000 neurons are lost every decade; loss begins early in life and may be genetically predetermined.[20] ○ Effects are not noticeable until old age because pure tone average is not affected until 90% of neurons are gone. 2. Atrophy occurs throughout the cochlea. 3. The basilar region is slightly more predisposed than the remainder of the cochlea. 4. Disproportionate decrease in speech discrimination may be observed before hearing loss is noted.

TABLE 5–6. Types of presbycusis (cont.)

TYPE	PATHOLOGY	CLINICAL COURSE
3. Metabolic/strial presbycusis	Characterized by atrophy of the stria vascularis that normally maintains the chemical and bioelectrical balance and metabolic health of the cochlea	• Hearing loss is represented by a flat hearing curve because the entire cochlea is affected. • Speech discrimination is preserved. • The process in younger population (age 30–60 yrs.) is that of slow progression and may be familial.
4. Mechanical/ Cochlear conductive presbycusis	• Due to thickening and secondary stiffening of the basilar membrane thus affecting its movement • More severe thickening in the basal turn of the cochlea where the basilar membrane is narrow	• It correlates with gradually sloping high frequency sensorineural hearing loss that is slowly progressive. • Speech discrimination is average for the given pure tone average.

Source: Lee K. Pathophysiology of age-related hearing loss (peripheral and central). *Korean J Audiol*. 2013;17:45-49. [21]

B. Diagnosis And Treatment[22]

1. **Diagnosis**
   - History taking
   - Physical examination
   - Pure tone audiometry with speech audiometry
   - Imaging is rarely needed, unless with unexplained one-sided hearing loss.
   - Other laboratory tests
2. **Treatment**
   - Presbycusis cannot be reversed, ameliorated or cured.
   - There are no approved or recommended pharmaceutical treatments for presbycusis.
   - Stem cell therapy has not been proven to be effective.
   - Rehabilitation options
     - Sensory management
       - Hearing aids, cochlear implants
     - Instruction
       - How to use technology
       - How to create optimal listening environments by reducing background noise
     - Perceptual training
       - Improve types of listening skills needed to enhance speech perception
     - Counseling
       - Encourage participation
       - Deal both emotionally and practically with residual limitations
   - Largely unrecognized by policy makers
   - Concerns of advocates of Hearing Health:
     - How hearing loss affects healthy ageing
     - The current deficits in and barriers to hearing health care (HHC)
     - How presbycusis can be addressed as a public health issue (Table 5–7)

TABLE 5–7. Barriers and efforts to achieving hearing health

BARRIERS	EFFORTS
Lack of human resources	NHSRC, PNEI, PSO-HNS, PANORS,PSAUD
Higher priority of other health issues	Researches, advocacies, policy proposals
Lack of public awareness about hearing loss	Missions, trainings, popular & social media
Lack of awareness about the profession of audiology	UPCM and UP CAMP: Master of Clinical Audiology
Lack of audiology education programs	
Lack of government funding for Hearing Health Care	DOH, PCSO, PhilHealth
High cost of hearing aids	More providers
Limited access to Hearing health care	Community-based strategies

NHSRC, Newborn Hearing Screening Reference Center; PNEI, Philippine National Ear Institute; PSO-HNS, Philippine Society of Otorhinolaryngology-Head and Neck Surgery; PANORS, Philippine Academy of Neurotology, Otology & Related Sciences; PSAUD, Philippine Society of Audiology; UPCM, University of the Philippines-College of Medicine; CAMP, College of Allied Medical Professions; DOH, Department of Health; PCSO, Philippine Charity Sweepstakes Office; PhilHealth, Philippine Health Insurance Corporation
Source: National Academies of Sciences, Engineering and Medicine. *Hearing Health Care for Adults: Priorities for Improving Access and Affordability.* (2016). (Blazer DG, Domnitz S, Liverman CT, eds.). Washington, DC: The National Academies Press.[23]

VII. PRIORITIES FOR FUTURE SERVICE DELIVERY AND RESEARCH[24]

- Development and training of all levels of HHC providers
- Provision of incentives to halt exodus of professionals to developed countries
- Creation of education models that address needs
- Development of consumer electronic approaches toward over-the-counter hearing aids
- Adoption of patient-centered, community-delivered approaches
- Reduction of hearing aid stigma: universal design
- Conduction of educational programs for people with hearing loss and their family members/caregivers
- Greater use of the web to provide education, hearing screening, assessment, and treatment

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OPEN FORUM HIGHLIGHTS

Moderator: CHRISTINE JOY S. ARQUIZA, MD

Q: *How can we prevent hearing loss from ambient noise?*

A: Use common sense. If you go to a rock concert, even if the ticket is cheap, do not get seats located beside the speakers emitting 90–110 dB. Analyze the situation. For those who do not have a choice because of your profession/occupation, please wear a hearing protection aid. What is the best? Earbuds and headphones; wear them together. Together, they can provide a 40–50 dB lessening or attenuation.

Q: *Is there a difference if you listen to something over headphones versus speakers?*

A: Headphones are better than earphones, because earphones transmit vibrations that can cause hearing loss. Distance from the source of sound should be considered.

Q: *What is the genetic predisposition to hearing loss?*

A: More than 40 genes [associated with hearing loss] have been identified, but the predisposition to acquire these genes have not been identified. They found a gene that was linked with chronic suppurative otitis media.

Q: *What is the effect of prolonged intake of aspirin tablets on hearing?*

A: It's really also the constitution of the person. Usually aspirin is toxic to the cochlea. But there are other medications that are more vestibulotoxic, such as vancomycin.

Q: *When can the elderly be brought for hearing screening?*

A: There's not much on hearing screening recommendations. If there's no complaint, and it's not really a life-threatening condition, then there's no recommendation. It is important in pediatric patients – that is why there's pediatric hearing screening.

Q: *What is the use of hearing aids?*

A: Hearing aids are very useful for the rehabilitation of patients with hearing impairment, especially the elderly. These have been proven to help the elderly hear better. Cochlear implants are an accepted modality for hearing rehabilitation; cochlear implantation is a surgical procedure. It has shown good results.

Q: *Do hearing aids provide 100% restoration of hearing?*

A: Hearing cannot be restored, only aided. A hearing aid is a high-tech microphone. It is not the cure for a disease.

Q: *Is there a difference in hearing aids for pediatric patients versus geriatric patients?*

A: It is difficult for the pediatric population to use hearing aids because they have not learned to hear. The prognosis is a little bit more guarded, especially if you diagnose them at a later age.

Q: *How do you propose they clean their ears? How often should they go see an ENT?*

A: Do not be so obsessive-compulsive about earwax. Earwax is not a disease. It's a normal product of the ear. Just towel-dry the outside of your ears; do not use cotton buds every day. The more we interfere with this normal physiology, the more we are prone to impacted cerumen. Go to the ENT when you have a complaint.

Q: *Is baby oil recommended for the removal of insects from the ear?*

A: If the patient has a history of ear discharge, it is better to use hydrogen peroxide since it is more sterile, considering that it will reach the middle ear. Otherwise, baby oil is alright.

REVIEW QUESTIONS

1. Which of the following may cause hearing loss?
   a. Congenital rubella syndrome
   b. Carbon dioxide
   c. Exposure to short-term noise at 70 dB
   d. Exposure to continuous noise at 60 dB

2. In which category of hearing loss is level of noise >60 dB classified?
   a. Mild
   b. Moderate
   c. Severe
   d. Profound

3. Which of the following medications may cause hearing loss?
   a. Cetirizine
   b. Methotrexate
   c. Isoniazid
   d. Metformin

4. Which can cause sensorineural hearing loss?
   a. Meniere's disease
   b. Cholesteatoma
   c. Otitis media
   d. Otitis externa

5. Which of the following is true regarding presbycusis?
   a. It cannot be reversed, ameliorated, or cured.
   b. It usually affects hearing of higher frequencies in the mid-range.
   c. Mechanisms include the degeneration of the ossicles, organ of Corti, cells of the spiral ganglion and softening of the basilar membrane.
   d. It is usually unilateral.

ANSWERS: 1. a; 2. c; 3. b; 4. a; 5. a

6 HOW TO TAKE CARE OF AGEING SKIN

Aileen Adela J. Montero, MD, FPDS

Delivered as a webinar on Oct 11, 2019
http://bitly.com/ALMW_Ch6_AgeingSkin

KEY POINTS

- Skin naturally breaks down over time. Chronic ultraviolet exposure compounds the process.
- Dermatologists cannot overemphasize the importance of sun avoidance, proper use of sunscreens, and a healthy lifestyle.
- Skin care practices should be age-appropriate and address skin needs of patients.
- Prescription-strength retinoids are the most studied and have the best evidence for skin ageing.
- Careful skin examination should be done to differentiate benign from premalignant and malignant lesions.

LEARNING OBJECTIVES

- ➸ To differentiate between chronologic ageing and photoageing of the skin
- ➸ To discuss histological changes in ageing skin
- ➸ To give an overview on anti-ageing skin treatments
- ➸ To identify common skin disorders in the elderly

I. AGEING SKIN

- Very few patients die of old skin or succumb to skin failure.
- The importance of skin ageing is primarily psychological.
- Emotional impact of skin ageing should not be underestimated.

A. Chronologic versus photoageing

- ○ The skin undergoes changes with time and in response to environmental factors and hormonal influences (Figure 6–1 & Figure 6–2; Table 6–1)
- ○ Effects of Ultraviolet (UV) Radiation on Skin:
  - ▪ UVA reaches the dermis, which damages to collagen and leads to the skin ageing. It makes the ageing process more prominent in people habitually exposed to sunlight.
  - ▪ UVB activates collagenase, which increases collagen breakdown.

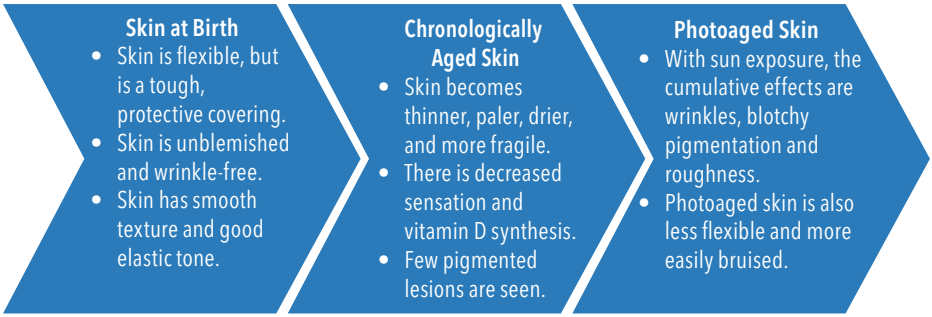
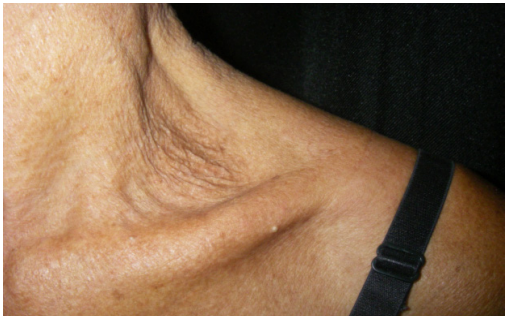


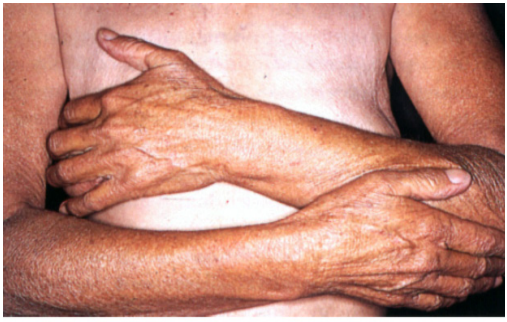
FIGURE 6–1. Changes in skin with age and sun exposure

TABLE 6–1. Histologic changes in skin ageing

- Thinning of epidermis
- Flattening of epidermal-dermal junction
- Loss of elasticity of the dermis and reduction and disorganization of the extracellular matrix
  - Increased collagenase, a protein which breaks down collagen
  - Fragmented collagen fibers
  - Collapsed fibroblasts



(a)



(b)

FIGURE 6–2. (a) Photoaged versus sun-protected skin. Dry, yellowish, more wrinkled appearance of both forearms, in contrast with the equally chronologically aged, sun-protected skin of the abdomen and chest; **(b) Photoaged versus chronically aged skin of an elderly woman.** Extremely wrinkled and lax skin on habitually sun-exposed area, in contrast with the covered skin at the lower neck and shoulder of a 67-year-old street vendor

1. **INTRINSIC AGEING** – gradual, influenced by genetics and hormones
   - Thinner skin with fine wrinkles
   - Fine wrinkles, sagging/laxity
   - Pale color with occasional purpura

(a) (b)

FIGURE 6–3. (a) 80-year-old with sagging and wrinkling of the face, (b) Sagging and wrinkling of facial skin of a 75-year-old elderly male with multiple seborrheic keratoses

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2. **EXTRINSIC AGEING** – caused by sun/UV light exposure
   - Dyspigmentation (e.g., solar lentigo)
   - Laxity
   - Yellow hue
   - Wrinkles
   - Telangiectasia – visible blood vessels under skin
   - Leathery appearance
   - Cutaneous malignancies

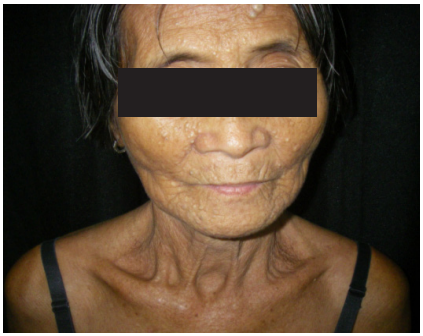

FIGURE 6–4. Waxy, yellowish discoloration and papular appearance of skin. This is a 67 y/o street vendor who spent hours under the sun most of her days selling cigarettes and rags.

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FIGURE 6–5. Folds, furrows and sagging of the skin of a 74-year-old male patient

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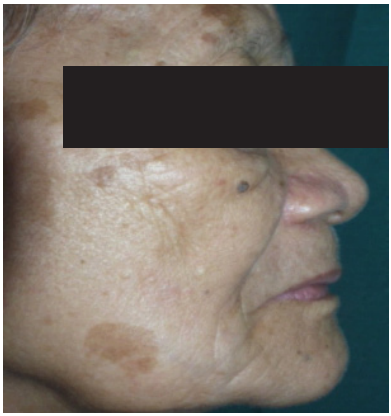
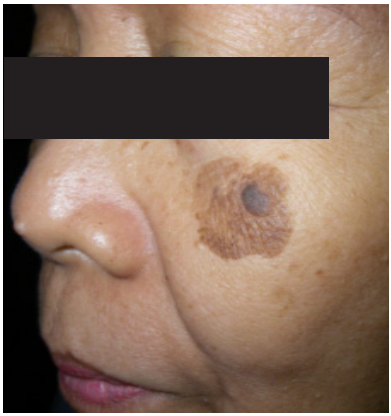


(a)



(b)

FIGURE 6–6. (a) Multiple light brown patches (solar lentigos) on the right cheek and frontal areas of the face of a 72-year-old female; (b) Light brown patch (solar lentigo) topped with slightly raised rough-surfaced dark brown thin flat papule (seborrheic keratosis) on the left malar area of a 64-year-old female

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II. SKIN REJUVENATION

A. Principles of skin rejuvenation

- Broad-spectrum sunscreens prevent ultraviolet damage on the skin.
- Antioxidants react with radical oxygen species to reduce oxidative stress.
- Fillers plump up the skin and increase mechanical tension.
- Retinoids stimulate collagen production and minimize wrinkles.

B. Prevention – "Start young to stay young"

1. Sunscreens – broad-spectrum protection against UVA, UVB and infrared radiation
   - Unilateral dermatoheliosis – aged skin on one side more exposed to sun reiterating importance of sun protection[1]
2. Proper nutrition and sleep
   a. Diet rich in fiber, fruits and vegetables – best source of antioxidants; the more colorful the better
   b. Less inflammatory food - meat should be limited to once or twice a week
   c. Adequate water intake
   d. Adequate sleep
   e. Supplements
      - Supplements are recommended only if required nutrients are not taken in enough amounts in the diet.
      - Supplements, with the proper ingredients and dosage, can help improve the appearance of ageing skin.[2]
3. No smoking and heavy alcohol use - Smoking and alcohol consumption significantly but differentially affect skin and volume-related facial ageing.[3]
   a. Smoking
      - Smoking increases matrix metalloproteinases, which degrade collagen and matrix proteins.
      - It is associated with an increased severity of forehead lines, crow's feet, glabellar lines, under-eye puffiness, tear-trough hollowing, nasolabial folds, oral commissures, and perioral lines.
      - It is also associated with reduced lip fullness, but not midface volume loss or visible blood vessels.
   b. Heavy alcohol use (more than 8 drinks/week)
      - Alcohol intake at more than 8 drinks/week is associated with increased upper facial lines, under-eye puffiness, oral commissures, midface volume loss, and prominent blood vessels.

C. Skin rejuvenation

TABLE 6–2. Common rejuvenation treatments

1.	Retinoids
2.	Topical antioxidants
3.	Peptides
4.	Plant extracts
5.	Oral antioxidants
6.	Botulinum toxin injections
7.	Chemical peels
8.	Lasers

TABLE 6–3. Categories of topical agents for skin use

TYPE OF TOPICAL AGENT	DEFINITION	EXAMPLE
Drug	"intended for use in diagnosis, cure, mitigation, treatment, or prevention of disease," i.e., it affects the structure or function of the body.	Prescription retinoids (e.g., tretinoin)
Cosmetic	"intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or party thereof for cleaning, beautifying, promoting attractiveness, or altering the appearance of skin," i.e., the product cannot alter the structure or function of skin.	Moisturizers
Cosmeceutical	"improve the appearance of skin, but is not for therapeutic purposes"[5]	Retinol, retinaldehyde, and retinyl esters

Sources:
US Federal Food, Drug, and Cosmetic Act; 1938.[4]
Kligman AM. Cosmeceuticals: A broad-spectrum category between cosmetics and drugs. In: Elsner P, Maibach HI, eds. *Cosmeceuticals and Active Cosmetics*. Second. Boca Raton: Taylor & Francis Group, LLC; 2005:1-6.[5]

1. **Retinoids**
   - The retinoids are a family of vitamin A derivatives that is considered the gold standard for skin rejuvenation.
   - Tretinoin is considered a drug (vs. retinol, which is found in cosmeceuticals).
   - Retinoid application increases procollagen in skin after 6 months.
   - Retinoids needs to be continuously used to get the desired effect, and is not a miracle cure.
2. **Cosmeceutical Agents**
   - Cosmeceuticals are "in-between" products that may have biologically active ingredients.
   - Some may actually change the structure and/or function of skin, and could be categorized as drugs (as per regulatory definition).
   - Their efficacy is often not assessed; although most undergo safety testing

   a. ***How do cosmeceutical agents work?***

TABLE 6–4. Different classes of cosmeceutical agents and examples

CLASS	EXAMPLES
Anti-inflammatory	Salicylic acid, alpha hydroxy acids, chamomile
Depigmenting agents	Arbutin, kojic acid, tranexamic acid, licorice extracts, other plant phenols, vitamin C, turmeric
Moisturizers	Ceramide
Peptides	Pentapeptides (Pal-KKTKS), acetyl hexapeptide, octapeptide – will increase collagen deposition
Growth Factors	TGF-ß, EGF, KGF, placental extract

TGF-ß, Transforming growth factor-beta; EGF, Epidermal growth factor; KGF, Keratinocyte growth factor

b. ***Do they work?***

TABLE 6–5. Three major questions used to evaluate cosmeceuticals[6]

1.	Can the active ingredient penetrate the stratum corneum and be delivered in sufficient concentrations to the intended target in the skin?
2.	Does the active ingredient have a known specific biochemical mechanism of action in the target cell or tissue in human skin?
3.	Are there published peer-reviewed, double-blind, placebo controlled, statistically significant, clinical trials to substantiate the efficacy claims?

Source: Levin J, del Rosso JQ, Momin SB. How much do we really know about our favorite cosmeceutical ingredients? *J Clin Aesthet Dermatol.* 2010;3(2):22-41.[6]

c. ***How much do we really know about our favorite cosmeceutical ingredients?***

TABLE 6–6. Characteristics of different cosmeceutical ingredients

INGREDIENT	DOES IT PENETRATE?	DO WE KNOW HOW IT WORKS?	DOES IT SHOW CLINICAL SIGNIFICANCE?
Retinoids (retinaldehyde, retinol)	Yes	Yes	Limited data; has been shown to decrease fine lines and wrinkles but have to be used for a long time
Kinetin	No studies	Partially	Partially
Niacinamide	Yes	Yes	Yes; need further studies to establish optimal concentration
Soy isoflavones	Limited data	Yes	Lacks clinical trials with adequate sample size
Soy protease inhibitors	No studies	Yes	Yes
Green tea	Limited data	Yes, antioxidant and anti-inflammatory	No clinical trials showing significant clinical improvement of signs of ageing

Source: Levin J, del Rosso JQ, Momin SB. How much do we really know about our favorite cosmeceutical ingredients? *J Clin Aesthet Dermatol.* 2010;3(2):22-41.[6]

- **Retinoids** – There is some evidence to support the use of retinaldehyde and retinol to decrease fine lines and wrinkles.
- **Niacinamide** – It is shown to be effective for anti-ageing, but need further studies to establish optimal concentration in products.
- **Soy** – Although it has a lot of research on its antioxidant effects, it lacks clinical studies greater than 50 patients.
- **Green tea** – Preclinical studies showed its antioxidant and anti-inflammatory activities, but there are no clinical trials showing significant clinical improvement of the signs of ageing.
- **Retinaldehyde** – Clinical trials for acne have more participants, which is why this vitamin A derivative has been proven to work.
- Other researches on herbals were also done and has shown a number of products that increase collagen, which decrease inflammation found in aged skin.[7,8]

○ All of them seem to work but the problem is the small number of participants in most studies and finding products with the proper concentration of active ingredients.

TABLE 6–7. Commonly used antioxidants used in skin care formulations

CLASS	SPECIFIC COMPOUNDS	COMMON SOURCES
Vitamin E	Alpha tocopherol	Vegetable oils (olive, sunflower, safflower), nuts, whole grains, leafy vegetables
Benzoquinones	Coenzyme Q_{10} or ubiquinone	Oily fish (such as salmon and tuna), organ meats (such as liver), and whole grains
	Idebenone	Synthetic quinone
Tripeptide	Glutathione	Ubiquitous in all mammalian cells
Vitamin C	L-ascorbic acid	Citrus fruits, tomatoes and tomato juice, and potatoes
Carbohydrate derivative	N-acetyl-glucosamine	Occurs throughout nature and in all human tissues
Vitamin B3	Niacinamide	Meat, fish and wheat
Polyphenols	Genistein	Soy beans
	Ferulic acid	Whole grains, spinach, parsley, grapes, rhubarb, and cereal seeds
	Isoflavone	Tea
	Silymarin	Milk thistle plant
	Coffeeberry	Coffee plant
	Resveratrol, oxyresveratrol	Red grape, cranberry
	Anthocyanin	Pomegranate
Carotenoids	Lycopene	Watermelons, tomatoes
Procyanidin	Pycnogenol	French maritime pine bark

Sources:
Addor FAS. Antioxidants in dermatology. *An Bras Dermatol*. 2017;92(3):356-362.[9]
Petruk G, Giudice R Del, Rigano MM, Monti DM. Antioxidants from plants protect against skin photoaging. *Oxid Med Cell Longev*. 2018.[10]
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TABLE 6–8. Cosmeceutical ingredients that have undergone clinical trials

INGREDIENTS	INDICATIONS
Salicylic acid	Acne
Glycolic acid	Acne, photodamage, discoloration, stretch marks, hyperpigmentation, melasma
Ceramide	Atopic dermatitis
Ascorbic acid	Hyperpigmentation, wrinkling, stretch marks, melasma
Phosphatidylcholine	Lower lid bulging
Oligopeptide	Wrinkles, skin ageing
Peptide primers	Wrinkles
TGF- β1	Wrinkles
Pal-KTTKS	Wrinkles, fine lines
Retinaldehyde	Acne
Vitamin K	Post-laser purpura

TGF- β, Transforming growth factor-beta; Pal-KTTKS, Palmitoyl pentapeptide

Source: Tsai TC, Hantash BM. Cosmeceutical agents: A comprehensive review of the literature. *Clin Med Insights Dermatology*. 2008;1:1-20.[12]

3. **Dermatological Procedures – to promote youthful skin**
    - Chemical peels
    - Botulinum neurotoxin injections for frown lines
    - Soft tissue fillers
    - Lasers

III. COMMON SKIN CONDITIONS IN THE ELDERLY

1. Pruritus – due to dry skin; cracking, with possibility of secondary bacterial infection
2. Eczemas
3. Stasis dermatitis
4. Seborrheic dermatitis or dandruff

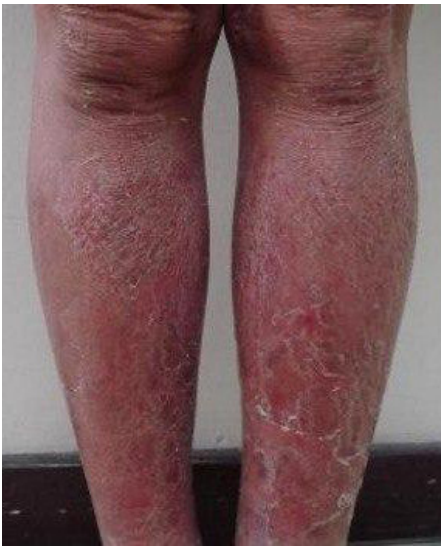

FIGURE 6–7. Eczematous patches on legs with generally dry and cracked skin

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5. Xerotic eczema (Figure 6–7)
6. Incontinence-associated dermatitis – especially for bedridden patients
7. Infections
    - Candidiasis – common in patients with diabetes mellitus, usually found in intertriginous areas

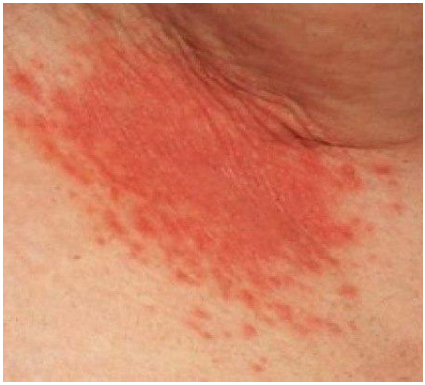

FIGURE 6–8. Candidal intrertrigo

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8. Skin Tumors
   - Benign
     - Seborrheic keratosis – benign skin growths usually found on back or face; common in Filipino skin color

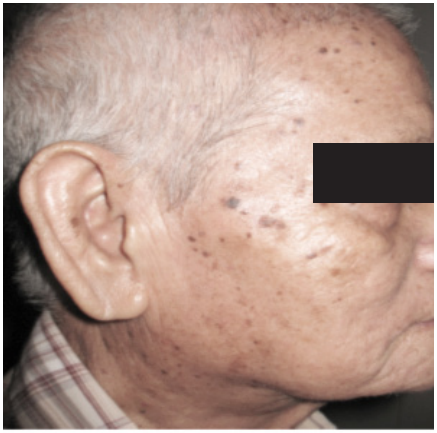

FIGURE 6–9. Multiple brown flat warty papules on the face having a 'stuck-on' appearance on the face of an elderly male

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   - Premalignant
     - Actinic keratosis – common in patients with prolonged exposure to sunlight
   - Malignant
     - Basal cell carcinoma (Figure 6–10)
     - Melanoma

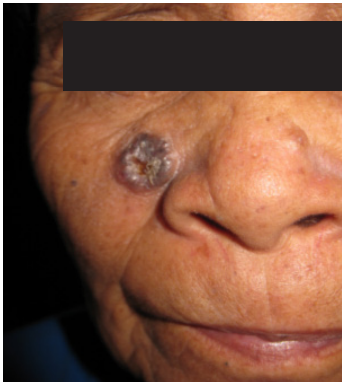

FIGURE 6–10. Solitary well defined ulcerated pigmented plaque with rolled edges in a 78-year-old female with history of chronic sun exposure

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9. Skin discolorations
   - Solar lentigo
   - Melasma

IV. CARING FOR THE SKIN

TABLE 6–9. Skin care across the ages

AGE GROUP	SKIN APPEARANCE	SKIN CARE
Twenties	• Smooth skin and even color • Little need for emollients • Acne may be present	• Simple skin care • Gentle cleanser • Sunscreen
Thirties	• Thinning of skin beneath the eyes, skin is less elastic • Fine wrinkles around the mouth and eyes	• Sunscreen • Moisturizers with antioxidants • May start retinoids
Forties	• Skin is sallow, less supple, skin surface not as smooth • Pigmented lesions, angiomas start to appear • Lines appear even at rest, sagging skin	• Sunscreen • Retinoids (prescription) • AHA's • Moisturizers with antioxidants, and/or peptides • Office procedures such as laser rejuvenation or botulinum toxin injection
Fifties, Sixties, Seventies	• Wrinkles are deeper • More sun spots, skin becomes rough, dermis markedly thinner, volume loss	• AHA's • Sunscreens • More hydrating moisturizers (used twice a day) • Antioxidants • Prescription retinoids • Office procedures such as laser rejuvenation or fillers

TABLE 6–10. Tips on how to look younger

- Dress appropriately to your age.
- Wear the right eyeglasses.
- Less makeup is always better.
- Treat yourself better.
- Smile.

What matters most is how you see yourself. If you are happy looking at yourself in the mirror, then you will be happy for the rest of your life.

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OPEN FORUM HIGHLIGHTS

Moderator: SHEENA MAUREEN T. SY, MD

Q: *What is the appropriate SPF of sunscreen and how should it be applied?*

A: SPF stands for sun protective factor. Before companies put the SPF label on their sunscreens, they undergo regulated tests. SPF 30 is the minimum. When the companies mark them as SPF 50, 30, or 15, the recommended amount of sunscreen that should be put onto the face is 2.5 ml or half a teaspoon on the face. However, if you use 2.5 ml of sunscreen on the face, it will appear very greasy. For women, I advise a tinted sunscreen so that it blends with the skin when applied. If the amount is too thin, even if the SPF is 50, it could be just equivalent to SPF 10. Studies do not recommend an SPF of 100 or 80 or beyond 50, because the difference between an SPF 50 and 30 is only 5%. Additionally, there is no sunscreen with 100% SPF. The only 100% SPF available is when you're inside a room under the blanket in your bed and without any sun exposure.

Q: *Do oral sunblock capsules such as beta-carotene work?*

A: As of now, there is one that works. These capsules contain a plant-derived ingredient from *Polypodium leucotomus* that has been shown to work as a sunscreen. They have to be taken at least 5 days before sun exposure and every day when at the beach. They do work; but the protection is not total. Topical sunscreens are still needed on top of it. Additionally, apply sunscreens every hour, if possible, because sunlight, water, and sweat may dissolve the sunscreen.

Q: *Does kojic acid as a whitening agent have systemic side effects when used as a soap or a cleanser?*

A: When you use a soap or cleanser as a method for applying something on the skin, remember to wash it off after a certain contact period. Thus, a minute after the soap is applied, it is washed off, to minimize absorption or systemic effect. Kojic acid does work, especially in cream form and applied on hyperpigmented areas. You don't want to whiten the entire skin. Our melanin serves a purpose by protecting the nucleus of our keratinocytes from sun damage. It has been shown that when you expose your skin to sunlight, the melanin granules inside the cell actually move to cover the nucleus. When UVA rays enter the skin, they are reflected off by the melanin granules. When you try to decrease the melanin granules on your normal skin, more UVA goes into the nucleus to damage the DNA; this makes you more prone to skin cancers.

Q: *What is the advantage of using astaxanthin on normal skin?*

A: There are so many herbal ingredients right now in the market. A lot of research has shown that most of them do work but we do not know the effective concentrations on the skin. If you don't know whether a specific herbal ingredient works, it is better to just eat a healthy diet.

Q: *How long should you apply topical retinoids? Which formulation is more effective for photoageing – tretinoin or adapalene? And at what percentages?*

A: The concentration of adapalene for anti-ageing is higher (0.3%) than what is being used for acne. For tretinoin, even 0.025% has beneficial effects. For younger individuals, you can use the cosmeceutical form, retinol 1% retinaldehyde 0.04%. To see effects, a study showed that it should be used around 6 months and maintained because ageing is a continuous process. The minute you stop, the normal process of collagen degradation with ageing will proceed.

Q: *Which is more effective – bakuchiol or retinol?*

A: I have not seen a study that compared the two products. Topical vitamin A, such as retinol, retinaldehyde, or tretinoin, is still the most studied and proven effective, and serves as the gold standard for other anti-ageing treatments.

Q: *What should we look for in moisturizers especially for use in the hot and humid climate of the Philippines?*

A: This is a case-to-case basis. The most important features to look for in moisturizers are : 1) non-irritating, 2) no perfumes, 3) with active ingredients that really work (such as ceramide) and 4) with added anti-inflammatory ingredients (such as antioxidants that fight the effects of pollution). To avoid the sticky feeling from the use of heavy oil-based facial moisturizers in hot weather, choose moisturizers that are lightweight and water-based.

Q: *Which topical antioxidants or vitamins do you recommend?*

A: I recommend vitamin C, since it has the most studies. Vitamin C is a chemical that is extremely fragile. If you see vitamin C being sold to you in a clear bottle, that's not vitamin C, since it degrades in sunlight. It should be placed in amber-colored bottles. The L-ascorbic acid is the best form of vitamin C because it is easily absorbed by the skin.

Q: *It is possible to apply vitamin C serum and retinol together at night?*

A: Yes, you can. There are even formulations that have ferulic acid and other substances that can improve the appearance of the skin, together with vitamin C.

Q: *What is the appropriate amount of sun exposure for a person to get adequate vitamin D?*

A: At our age, we rarely go out under the sun. We are usually inside our offices wearing our jackets leading to less sun exposure needed for the production of vitamin D. This is why in some journal articles, vitamin D supplementation is recommended. The sun is a good source of vitamin D but it really causes a lot of damage on the skin that accumulates from birth to later years. The less sun exposure you receive, the better your skin will look. However, the amount of sun exposure one chooses to receive is a personal choice. If you're happy swimming or doing outdoor activities, go ahead and do those. Just use sunscreen to prevent skin cancer. In that case, the most important concern is the appearance of skin cancer, not the aesthetic appearance of the skin.

Q: *Is glutathione harmful or beneficial for us?*

A: I am taking this opportunity to remind the audience that under our FDA, intravenous glutathione is only approved for use to treat persons undergoing chemotherapy who need antioxidant rescue. Intravenous glutathione for skin whitening is not approved. Glutathione is a very good antioxidant. However, it has to be taken at the right amount. Anything in mega doses is not good for the body. If you take glutathione in very high amounts, it becomes an oxidant rather than an antioxidant. Antioxidants, such as glutathione, vitamin C and vitamin E, work together. but they have to be given in the right amounts. However, it is still better to get our antioxidants from the food we eat.

Q: *Please comment on facial yoga for the prevention of wrinkles or acupuncture to minimize the lines.*

A: I have not yet read anything nor have any personal experience about facial yoga. There are so many things that have not yet been studied and discovered, so it doesn't mean that facial yoga will not help. Wrinkling on the face is usually because of movement such as smiling, or frowning. If you don't have any facial expressions, then you actually won't have any wrinkles. In chronologic ageing, the wrinkles appear on the area of the corners of the cheeks because of loss of fat in this area, leading to drooping and wrinkle formation. However, the lines beside the eyes and forehead are due to movement of the facial muscles.

Q: *If you predominantly sleep on one side, will it affect the skin?*

A: Yes, it will because if you sleep for 7–8 hours, you predominantly sleep on one side, which will make the nasolabial fold on that side more prominent. If you're watching TV or reading, and you're unconsciously frowning, it will make those lines deeper. If you put something on these areas that could remind you to relax these areas, that will actually prevent wrinkles on your glabellar area from developing.

Q: *Which one is better for wrinkles – chemical peeling or laser resurfacing?*

A: We usually do lasers for deeper or more prominent lines. If the lines are finer, you can get away with chemical peeling. The difference would be the price of the procedures. It would depend on the capacity of the patient.

Q: *Is there a way to make sunscreen less sticky or more absorbable?*

A: You can try to use sunscreens in gel forms because they are less oily and feel better on skin. After you have perspired a lot, you have to reapply your sunscreen. Facial sunscreens usually give good effects for only 3–4 hours even if they are SPF 40 or 50.

Q: *How much time between reapplication of sunscreen?*

A: Reapply every 3–4 hours. When you are in your office the entire day, then you don't really need to reapply. But when you go in and out of the office and you perspire, then you need to reapply every 3–4 hours.

Q: *How about umbrellas with UV protection?*

A: Yes, they can help. But you have to be aware of reflected UV rays from the cement pavement, or from the sand on the beach, which reflects back 80% of sun rays. For someone without skin pigmentation problems, and who is walking on the street, using a sunscreen and UV umbrella are fine. But if you have a problem with skin pigmentation, such as melasma triggered by sunlight, I suggest that aside from sunscreen and UV umbrella, use a fan or handkerchief to cover the pigmented area to completely block out the sun. There is no perfect sunscreen, and thus, there is a need to do additional sun protection measures if you have pigmentary problems.

Q: *What ingredients do people with sensitive skin need to avoid in cosmetic products?*

A: Avoid perfumes and pigments in skin creams. You also need to avoid retinols and AHA's which may trigger skin reactions. When you buy a product and you have sensitive skin, do not apply to the entire face immediately. Apply only on a small area for a couple of weeks; so that in case of problems, only a small area, and not the entire face, has to be treated.

REVIEW QUESTIONS

1. What type of skin ageing is characterized by dyspigmentation, laxity, wrinkles, telangiectasia, leathery appearance with yellow hue, and is associated with cutaneous malignancies?
   a. Intrinsic ageing
   b. Extrinsic ageing
   c. Photoageing
   d. Catabolic ageing

2. Which of the following is not an anti-ageing treatment?
   a. Oral antioxidants
   b. Sunscreens
   c. Retinoids
   d. Honey

3. What age is it best to start prescription retinoids for ageing skin?
   a. 40s
   b. 30s
   c. 20s
   d. 50s

4. Which of the following is false?
   a. Smoking causes midface volume loss and visible blood vessels.
   b. Heavy alcohol use is associated with increased upper facial lines, under-eye puffiness, oral commissures, midface volume loss, and visible blood vessels.
   c. A diet rich in dairy and sugar will improve the appearance of ageing skin.
   d. Broad spectrum sunscreen should be used to prevent skin ageing.

5. Which is a premalignant skin condition?
   a. Actinic keratosis
   b. Seborrheic keratosis
   c. Melanoma
   d. Basal cell carcinoma

ANSWERS: 1. b; 2. d; 3. a; 4. c; 5. a

7 ROLE OF ENVIRONMENT AND DIET IN SKIN AGEING

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KEY POINTS

- The Filipino brown skin is a multiheritage skin wherein the lighter skin phototypes are prone to photoageing and skin cancer.
- Electromagnetic radiation, through sun exposure and indoor man-made devices, may lead to oxidative stress, inflammation, and skin ageing.
- Environmental pollution, poor sleep quality, and stress may disrupt the skin barrier and lead to skin ageing and skin diseases.
- We recommend an anti-inflammatory diet, a healthy lifestyle, and the use of tested and hypoallergenic protective barrier products.
- Meditate and pray to help reduce stress: "May you be happy, healthy, safe, and at peace."

LEARNING OBJECTIVES

- ➸ To describe the different Filipino brown skin phototypes and its responses to internal and external exposomes
- ➸ To discuss the mechanisms by which these exposomes lead to skin ageing
- ➸ To choose lifestyle practices that minimize skin ageing and other systemic conditions associated with chronic inflammation

INTRODUCTION

Our genome, from inherited genes, and our *exposome* from our non-genetic *exposures from the environment*, have complementary roles in the development of chronic diseases, including skin ageing.[1]

Recognizing mechanisms on how exposomes act on the skin allows us to more effectively delay the onset and treat the appearance of ageing skin. The two top exposomes most associated with ageing are: the environment and the diet.[2]

I. THE ENVIRONMENT AND SKIN AGEING

A. Electromagnetic Radiations (EMR)

1. Filipino Brown Skin and its Phototypes

   The Filipino brown skin is a multiheritage skin color that varies from very light to very dark brown shades (also called *overtones*), with *undertones* ranging from orange or blue, red, and yellow or pale violet (Table 7–1).[3,4] A study showed a similar wide range of Japanese skin phototypes, and

that light to tan skin phototypes have particularly high risks of UVA-induced DNA damage that makes them prone to skin cancer and an early onset of photoageing.[5]

TABLE 7–1. Questionnaire for the Phototyping of Multi-heritage Asians. A Modification of the Fitzpatrick Questionnaire.

Your Skin Color overtone is…	White ☐	Ivory White ☐	Light Brown ☐	Medium Brown ☐	Dark Brown ☐	Darkest Brown to Black ☐
Your Skin Color undertone is…	Reddish ☐	Pink or yellow to mauve ☐	Pinkish or yellowish ☐	Shades of red, yellow, or orange ☐	Orange ☐	Blue ☐
Within 30 minutes of noon sun exposure, your skin reddening is…	Very marked ☐	Marked ☐	Moderate ☐	Mild ☐	Very mild ☐	Very mild if at all ☐
Within 30 minutes of noon sun exposure, your skin darkening is…	None ☐	None ☐	Immediate and mild+ ☐	Immediate and moderate++ ☐	Immediate and marked+++ ☐	Intense but not obvious ☐
When you do develop a tan, it lasts…	Zero to one week ☐	Two weeks ☐	One to two months ☐	Two to six months ☐	More than six months ☐	Indefinitely ☐
Your heritage is mostly…	Pure Caucasian White ☐	Pure Asiatic White (PAW) or Pure Caucasian White (PCW) ☐	Mixtures of Pure Caucasian White and Asiatic White (PCW + PAW) ☐	Mixtures of: Caucasian Brown (PCB) and/or Asiatic Brown (PAB) and/or Asiatic White ☐	Pure Asiatic Brown ☐	Pure Black: Asiatic Aboriginal or African ☐
YOUR SKIN PHOTOTYPE IS (Add the check marks and the column with the most checks is your skin phototype	**I**	**II**	**III**	**IV**	**V**	**VI**

PAW: Pure Asiatic White: Predominantly Chinese, light Indian, Japanese, Korean
PAB: Pure Asiatic Brown: Predominantly dark Indian, Indio-Malay
PCW: Pure Caucasian White: Predominantly Northern European
PCB, Pure Caucasian Brown
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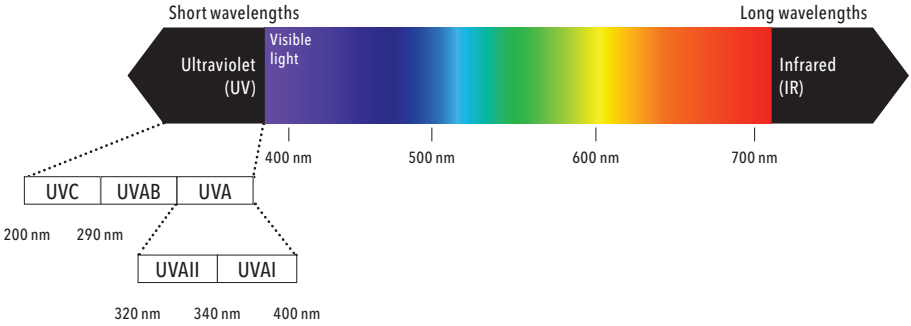
Filipinos and other people of color generally prefer an evenly distributed and slightly lighter shade of their natural brown skin color.[6] Quality of life is markedly reduced in those with

discolorations from post-inflammatory hypo-/hyperpigmentation and melasma, which are often also considered features of ageing skin.[7,8] Melasma, post-inflammatory hyperpigmentation, and facial spots, including dermatosis papulosa nigra and seborrheic keratoses, are among the top 10 skin problems of Filipinos.[9] Many of these changes are induced or aggravated by the sun and man-made sources of electromagnetic radiation.

2. Electromagnetic Radiation Spectrum
   - From the shortest and most intense, to the longest and least intense wavelengths of radiation that affect skin ageing, the spectrum consists of: ultraviolet, visible light, and infrared energies (Figure 7–1).



UV, Ultraviolet; VL, Visible light; IR, Infrared; nm, Nanometer

FIGURE 7–1. Electromagnetic radiations and spectral wavelengths. UVB (290–320 nm); UVA-II (320–340 nm); UVA-1 (340–400 nm); VL (400–760 nm); IR (760nm–1 mm)

Reprinted with permission from 'Skin in the Tropics: Sunscreens and Hyperpigmentation' by V.M.Verallo-Rowell, Pasig City, Philippines, 2001, Anvil Publishing, Inc., p17.

   - Being in the equatorial belt, 5–21° north of the equator, the sun shines directly at us in the Philippines, thus our UV indices are high (Figure 7–2).[10]

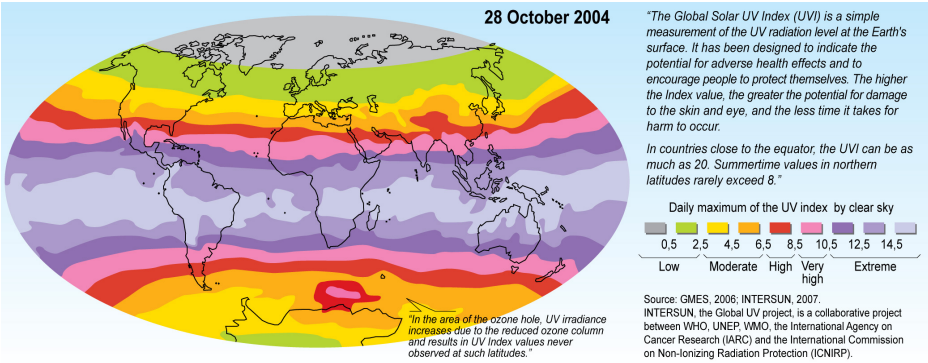


FIGURE 7–2. The UV Index Worldmap. The Philippines' solar UV index belongs to the extreme category, being part of the equatorial belt.

Reprinted with permission from 'UV Index Worldmap'. Vital Ozone Graphics 2.0 - Climate Link. 2009. by Emmanuelle Bournay, GRID-Arendal. www.grida.no/resources/7130

TABLE 7–2. Mechanisms of Skin Ageing from Solar and Indoor Radiation

EMR SOURCE		MECHANISMS	AGEING EFFECTS ON SKIN
SOLAR	**UVB**	Intense energy to epidermal cells causes:[11] • Damage of mitochondria • Aryl hydrocarbon receptor signaling • Receptor-initiated signaling • Telomere-based DNA damage • Protein oxidation	Acute exposure Erythema to blistering Chronic exposure[12] • Photoaged skin - dyschromias of hypo-/ hyper-pigmentations reddish, with dilated tiny vessels • Rough, dry, flaky skin texture, large pores • Wrinkles around the mouth, eyes, and cheeks • Warty growths, benign and solar keratoses • Skin cancers
	UVA **VL** **IR**	• Oxidation, oxidative stress, reactive oxygen species formation result in • Matrix metalloproteinases, type 1 procollagen gene expression, inflammatory cells infiltration • Stratum corneum barrier disruption.[13,14]	UVA-1,VL • Post-inflammatory, dose-related, persistent hyperpigmentation, which is darker in brown vs white skin • Contribute to formation of skin neoplasms[15-17] Infrared and heat • Redness with no hyperpigmentation, best seen in 'baker's arms', and thighs from prolonged laptop use • Wrinkles, large pores, dry, rough, aged-looking, dull skin[17]
INDOOR	**Artificial lighting**	Fluorescent lights • Besides emitting VL, the mercury gas also forms non-visible UV • In non-enveloped CFLs, the phosphor lining is apparently thinner and permits exit of some UV.	• In vitro study on skin fibroblasts and keratinocytes exposed to CFLs:[18] ○ decrease in proliferation rate ○ significant increase in production of reactive oxygen species ○ decrease in their ability to contract collagen • These are tiny, sub-threshold amounts, lessened further by movement and distance, but over time, may reach cumulative skin effects.[19]
	Skin treatment devices (to treat wrinkles, photoageing and skin tumors)	Lasers • *VL*: Argon, alexandrite krypton pulsed • *Short IR*: Nd:YAG, Er:YAG • *Mid-IR*: CO_2[20] Non-laser[20] • LED-based • UV • VL • Near IR *Note*: Treatment times are in nano- to picoseconds, and are intense and repetitive.	Absorbed energies[21] • Destroy pigments: Superficial &/or deep dermal red hemoglobin in vessels, light to dark melanin, tattoos, others • Coagulate water in tissues to alter dermal connective tissue and biological target genes of fibroblasts and other cells *Note*: May be double-edged, with dose and frequency-related effects such as erythema, edema, crusting, and post-inflammatory hypo- or hyperpigmentation. Careful consideration of skin color and dosage, enough to produce corrective but not overly destructive results, are important.[22]
	Electronic visual displays (e.g., smartphones, tablets, computers, TV)[23]	VL Irradiation: Induce reactive oxygen species in 1-hr. petri dish-cultured fibroblasts[24]	Low energies, often LED and pure VL, over time may contribute towards wrinkles, freckling, skin dryness and photosensitivity.[25]

EMR, Electromagnetic radiation; UV, Ultraviolet; CFL, Compact fluorescent lights; Nd, Neodymium-doped; YAG, Yttrium aluminum garnet; CO_2, Carbon dioxide; LED, Light-emitting diode; TV, Television

3. Photoprotection

   Adequate photoprotection poses many challenges in people with brown skin, since they do not burn as quickly as those with white skin, and thus, have a hard time learning the habit of daily sunscreen use.

   a. *General Challenges of Topical Sunscreens*
      - Need to apply and re-apply a sunscreen daily[26]
      - Photosensitivity to some active ingredients
        - Para-aminobenzoic acid [PABA] and derivatives, benzophenones
      - Increased melanoma over time
        - If sunscreen absorbs UVB, but not UVA that is now known to be a big contributor to skin cancer formation
      - Recent issues on absorption of active ingredients, estrogenicity, risk of vitamin D deficiency, bleaching of coral reefs
        - Oxybenzone, octinoxate [ethylhexyl methoxy cinnamate][27]
      - Recent review of all approved organic ingredients by the United States Food and Drug Administration
        - Only inorganic zinc oxide and titanium dioxide are approved; Can be cosmetically unappealing, depending on formulation[28]
      - Lack of VL photo protection in sunscreens
        - Large molecules of zinc oxide and titanium dioxide protect against UVB, UVA-PF, and some VL. Iron oxide pigment in colored products also protect against VL.[29-31]
        - A Filipino brown skin study measured actual amounts of powder, foundation, and sunscreen that people use.
          - Participants used significantly less amounts than the standard 2 mg/cm^2 dosage. By layering of sunscreen and cosmetics/skin care products, higher UVB-sun protection factors (SPF), protection factor for UVA (UVA-PF), and VL protection factor (VL-PF) were achieved[32]
        - A more recent 2017 study showed that layering with newer products containing higher iron oxide content, to color, contour, and camouflage skin, achieved higher UVA-1, VL and IR protection.[33]

B. Environmental Pollution and Skin Ageing[34]

Pollution is environmental contamination by chemical, physical, or biological agents, and is monitored regularly by Clean Air Agencies. Among the four types of environmental pollutants, particulate matter (PMs) affect people the most (Table 7–3).

TABLE 7–3. Types of Environmental Pollutants

TYPES	DESCRIPTION	CHARACTERISTICS
Particulate matter (PM)[35-37]	Ultra-fine PM (<0.1 μm)	From combustion (e.g., diesel exhaust) or industrial processes (e.g., rubber)[38] • May enter lung and blood vessels
	Fine PM (<2.5 μm)	• Usually from combustion • Able to penetrate, disrupt the skin barrier, and produce ROS-dependent inflammatory cytokine production[39,40] • Produce dry, flaky, rough and itchy skin that is easily penetrated by more pollutants
	Coarse PMs (2.5 to 10 μm)	From mechanical processes
	Traffic soot	From diesel exhaust; made of a mix of carbon particles covered by organic PAHs
Gaseous pollutants[41-43]	CO and CO_2	Products of combustion reactions, from coal, wood, natural gas burning, or combustion engines of cars
	SO_2	Power plants' burning of sulfur-containing fuel such as coal and oil
	NO_2	From vehicle exhaust, electric power plants (burning of coal, oil, diesel fuel, natural gas), cigarettes, gas stoves, and silos emissions
	Peroxyacetyl nitrates	From heat and ultraviolet light photochemical reactions
	Volatile organic compounds	From burning of gasoline, coal, wood, or natural gas, cigarettes
	Ground level ozone (O_3)	From complex photochemical chain reactions of sun + pollutants, regular contact with O_3 depletes stratum corneum antioxidants, forms facial wrinkles, peroxidizes lipids, and oxidizes proteins.
Heavy metals from metal and industrial processing plants	Lead	From the combustion of leaded gasoline where used
	Airborne mercury	From the earth's mantle, the sea surface through evaporation, or combustion of coal and other fossil fuels *Note*: Bleaching skin products with mercury are banned but are still available.[44]
Persistent organic pollutants (POP)[45]	Dioxin	From defective processes in the manufacture of herbicides and pesticides, fertilizers, paper bleaching, incineration and incomplete combustion of solid waste Note: More than 90% of human exposure is through dairy products, seafood and meat.

PM, Particulate matter; ROS, Reactive oxygen species; PAH, polycyclic aromatic hydrocarbons; CO, Carbon monoxide; CO_2, Carbon dioxide; SO_2, Sulfur dioxide; NO_2, Nitrogen dioxide

1. Epidemiological studies on ageing and air pollution
    a. Particulate matter, traffic-related nitrogen dioxide (NO_2) and ground level ozone
        - Cohort studies on Caucasian women in Germany, and Caucasian and Asians in China:[47,48]
            - Increase in soot and particles from traffic was associated with 20% more pigment spots on forehead and cheeks (Germany).[46]
            - More numerous senile lentigos in high PM2.5
            - NO_2 exposure groups (China).[47,48]
        - A Public Health and Air Population in Asia (PAPA) studying Bangkok, Hong Kong, Shanghai and Wuhan, compared concentrations of these pollutants:[49]
            - **PM10:** Similar in Bangkok and Hong Kong; lower in Shanghai and Wuhan; much higher in North America and Western European cities

- **NO_2:** Higher in Hong Kong and Shanghai than between Bangkok and Wuhan; similar between North America and Western Europe
- **SO_2:** Higher in Shanghai and Wuhan; similar between Bangkok and Hong Kong.
  - There was consistently strong correlation between daily concentrations of NO_2 and PM10 and face pigment, seborrheic keratoses, and deep naso-labial folds and wrinkles in all four cities (Spearman coefficient, 0.6 to 0.8). Pronounced nasolabial folds and wrinkles were observed in all four cities.

b. Tobacco smoke[50-53]
   - One cigarette inhalation has >3,800 harmful chemicals, including nicotine, formaldehyde, carbon monoxide, tar, cyanhydric acid, ammonia, mercury, lead, and cadmium.
   - Blood flow in the microcirculation is immediately reduced. Maximum effect is seen after the first 2 minutes, regardless of nicotine concentration.
   - Smoker's facial skin shows altered skin hue and wrinkling in the perioral area, upper lip, and eyes. Heavy smokers have oral mucosa melanosis or hyperpigmentation.
   - Twin studies show increased wrinkles, tissue laxity, pigmentary changes – roughly 2 ½ years difference in appearance–in the smoker versus non-smoker twin.

2. Summary of Environmental Pollution in the Philippines:
   - The Philippines is a rapidly developing economy. Similar to Bangkok, the added humidity, heat, and UVR were shown to increase inflammatory diseases, that include ageing. Pollutants are now a significant health burden not just to highly industrialized countries, but also to ours.
   - In urban areas, day and night traffic is pervasive, populations are dense, and small and large medium businesses are located even in some residential areas.
   - In rural areas, small businesses and homes may be using fossil or solid fuels.
   - In both areas, usage of manufactured chemicals is rampant.
   - Smoking and vaping are less rampant but still prevalent.

3. Treatment and prevention of ageing skin from the environment

TABLE 7–4. How to Prevent and Correct Skin Ageing due to the Environment

O	• Practice sun avoidance: Seek shade whenever possible. Wear rash guards.
U	• Use sunscreens that also have UVA-PF and VL-PF, aside from SPF.
T	• Minimize exposure to environmental pollutants from traffic and cottage industries.
D	• Avoid large public vehicles; stick to smaller ones.
O	• Live in less crowded areas if possible.
O	• Go to the province and start an organic farm.
R	• Regularly remove dust particles from your home and surrounding areas.
S	• Minimize dust-collecting clutter, give away or share stuff you no longer need.

TABLE 7–4. How to Prevent and Correct Skin Ageing due to the Environment (cont.)

INDOORS	• Avoid staying under incandescent, compact fluorescent lights. • Shine light sources directly on reading/work material, not on skin. • Instead of blue lights, prefer yellow lights such as LED-yellow. • Lessen use of devices with electronic visual displays (e.g., iPhone, iPad). • Put a UV film protector on your computer monitor. • Stay several meters away from TV flat screen monitors. • Apply an opaque, black film on window beside where you usually sit. • Avoid or be careful with use of cosmetic devices that emit UV, VL, IR, and RF. • Lessen use of antimicrobial sprays, insecticides, disinfectants, and fragrances. • Use more natural non-irritating hypoallergenic cleansers like baking soda, non-scented alcohols, and simple bar soaps. • Use local alcohols, vinegars, VCO, and monolaurin as disinfectants. • Use crushed charcoal to absorb odors. • Avoid bleaching agents, steroid and other active creams unless prescribed and monitored by a PDS board-certified dermatologist.
BOTH	• Apply barrier creams containing large molecules such as zinc oxide, titanium dioxide, and iron oxide in high percentages to avoid indoor and outdoor pollutants, UV, VL, and IR (from solar and man-made devices) • Use protective masks, clothing, and other gear as needed, even post-COVID. • Role of Antioxidants[54] ○ **Melatonin**[55,56] ▪ Known to many as a sleep inducer, melatonin is now being studied for its anti-ageing antioxidant effects, including in oncology. ▪ May be contained in cosmetic products, but one should read the label on how it was packaged, since antioxidants are easily damaged with processing and the presence of additives. ○ **Retinoids**[57] ▪ Old reliable gold standard for skin ageing, and at the right amount, with barrier-repairing ingredients ○ **Barrier repair products** ▪ VCO has barrier-repairing fatty acids. ○ **Vitamins**[58,59] ▪ Antioxidant vitamin preparations are easily damaged by pressure, heat, additives, other processing methods and packaging. See Diet, next section.

UVA, Ultraviolet A; PF, Protection factor; VL, Visible light; SPF, Sun protection factor; IR, Infrared; RF, Radiofrequency; VCO, Virgin coconut oil; COVID, Coronavirus disease; PDS, Philippine Dermatological Society

II. INTERNAL EXPOSOMES ON SKIN AGEING

A. Psychological Stress[60-62]

a. Although patients immediately state that their skin disorders are caused and worsened by stress, to date, underlying mechanisms are ill-defined and no conclusive evidence directly links stress with skin ageing.

b. Most studies do show that stress induces a decline in epidermal permeability barrier function (EBPF).

- Healthy female students (N=16) were assessed at periods of perceived high stress (final exams and after a long vacation), and low stress as control.
  - Transepidermal water loss (TEWL) showed significant deterioration during both periods with higher stress.
  - The authors concluded that psychological stress causes a decline in EPBF by deterioration in barrier disruption and recovery, which was visible as dry, rough, and

aged-looking skin.

c. Changes from chronic stress appear to be an important factor in determining vulnerability to ageing and age-related comorbidities.[63]

B. Sleep Quality[64-66]

a. We know that chronic lack of sleep from overnight work, studying, and other activities make us look terrible.

b. Studies were able to quantify changes that contribute to skin ageing.
   - Quasi-experimental study of 60 healthy Caucasian women given simulated solar radiation[65]
     - Poor sleepers had increased signs of intrinsic ageing, impaired skin barrier function, and poorer perception of their appearance and physical attractiveness.
     - Used validated assessments tools (Pittsburg Sleep Quality Index, [PSQI]; Score of intrinsic and extrinsic skin ageing [SCINEXA])
   - Quasi-experimental study that took photographs of 23 sleep-deprived adults[64]
     - Sleep-deprived people appear less healthy, less attractive, and more tired compared with when they are well rested.
   - Survey of 630 night-shift call center agents in Manila[66]
     - Poor sleepers had significantly more prevalent and severe self-reported acne vulgaris, seborrheic dermatitis, atopic dermatitis, skin dryness, and pruritus; but not hair and nail concerns.

c. Poor sleep may potentiate the effects of stress on the skin. A link between stress and poor sleep has been seen with chronic skin diseases and specific inflammatory dermatoses, such as acne vulgaris, atopic dermatitis, and psoriasis.

d. Both stress and poor sleep quality diminish skin barrier function; seen as dry and rough skin, and perceived as aged-looking skin.

C. Diet, Supplements and the Antioxidant Paradox

- Antioxidants are needed for innate detoxification pathways, in the transcription of vitagenes, or have a direct role in events and functions taking place in the mitochondria.
- Japanese twin studies show that those on an antioxidant-rich diet and who avoid excess alcohol are perceived to be younger. Nutrition was estimated to account for up to 30% of wrinkle formation in women.[67]
- However, there are no available clinical data that demonstrate the effects of intake of supplements with antioxidants on visible ageing.[68]
- In addition, other large long-term studies conclude that antioxidants in supplements do not provide substantial and consistent health benefits to prevent or treat chronic diseases. Halliwell calls this the 'Antioxidant Paradox.' Some points given to explain the paradox, are in Table 7–5.[69,70]

TABLE 7–5. Antioxidants in Supplements versus Diet[71-73]

IN SUPPLEMENTS	IN THE DIET
Often present in one form	• Often present in many forms such as the oxidized and the reduced antioxidants • May differ in chemical composition for different roles in oxidative disease genesis, such as to boost innate antioxidant defense mechanisms

TABLE 7–5. Antioxidants in Supplements versus Diet[71-73] (cont.)

IN SUPPLEMENTS	IN THE DIET
Often present in high amounts. Consumers who believe that more is better take higher doses than recommended	• Often present in smaller doses • Optimum range, above which effects go down steeply
May undergo heat, pressure, and chemicals to deodorize, bleach, or to further refine the final processed product	• From sources that practice, preferably, yearly inspection and are certified organic, meaning - no inorganic insecticides, fertilizers, antiseptics, antibiotics; follow natural soil enrichment; composting from farm vermiculture and from the farm's own plant products; and no genetically modified plants. • Best eaten unprocessed, or as natural and organic as possible
Heat- and light-sensitive antioxidants may be destroyed by shipping and packaging	• Best harvested, cooked with similarly sourced products, and eaten as close to table as possible and/or stored properly in cool shaded places or fresh frozen; to minimize antioxidant deterioration.
Flavors, colorants, preservatives, solvents can be photoallergens	• Best eaten fresh, needing no artificial colorants and flavors.

D. Antioxidant Studies on some Philippine Edible Plants:

Under the intense equatorial sun with higher amounts of UV, VL, and heat, tropical plants are shown to develop more antioxidants that can be beneficial as part of the diet.[74-76] They help combat oxidative stress from our exposomes and inflammation, the common mechanism in ageing.

1. Virgin coconut oil (VCO)
   - Antioxidant assays showed presence of antioxidants in VCO.[77-79]
   - A recent in *vitro* genetic study reported that VCO has anti- inflammatory and skin barrier protective properties.[80]
   - RCT comparing VCO vs corn oil in diet
     - In the diet, coconut oil is more anti-inflammatory, while corn oil is more pro-inflammatory.
     - 28-day trial: 20 patients with psoriasis were given the same common food ingredients and needs weekly (Table 7–6). All were given lectures on how to avoid inflammation-causing lifestyle.
     - Ten were blinded to only use cold-pressed VCO, the other ten, to only use corn oil in their food preparations.
     - Immunohistochemistry of skin biopsies at baseline and after 28 days:
       - Expression of CD3 for T cells, CD11c for myeloid dendritic cells, K16 for epidermal hyperplasia, Ki67 for cell proliferation showed that VCO is more than 50% *anti*-inflammatory and corn oil is 40% *pro*-inflammatory.[81]
     - RNA sequencing of the same skin biopsy specimens is pending

TABLE 7–6. Our Proposed Anti-Inflammatory Diet Plate

DIET	RECOMMENDATIONS
Fluids	Drink filtered water (80%), tea, coffee, fresh juice (20%), with little or no refined sugar. Limit fruit juices or make with veggies in a shake. Limit milk/dairy to 1–2 servings.

TABLE 7–6. Our Proposed Anti-Inflammatory Diet Plate (cont.)

DIET	RECOMMENDATIONS
Fats and Oils	• Use VCO, preferably cold-pressed, organic, to cook/bake/drizzle on food • For deep-fry cooking, may use RBD coconut oil. • Use less monounsaturated virgin olive oil for light cooking, in salads and toppings. • No canola oil, which is from genetically modified rapeseed oil. • Margarine, shortening, corn oil, and other PUFAs are omega-6 rich, which make more pro-inflammatory eicosanoids. • Recommended amount of TFAs >0.5 g per serving of processed food.
Carbohydrates	• No refined carbohydrates: white sugar, bread, pasta, rice, artificially sweetened drinks, pastries, cookies, cakes, ice cream, candies, chocolates, French fries, and potato chips • Whole grain (brown bread, pasta, oats, rice), tubers (potatoes, ube, camote, taro), legumes (green, baguio beans), nuts (peanuts, cashew, pili) and seeds (watermelon, pumpkin)
Vegetables	• Leafy greens of: alugbati, cabbage, chili, malunggay, mongo sprouts, pechay, saluyot, camote tips, singkamas, and kolitis • Asparagus, bell peppers (red, orange, yellow), carrots, celery, cucumber, eggplant, green beans, mushrooms, okra, banana (heart and blossoms), string beans, winged beans, and tomatoes
Fruits	• Fruits of varied colors: banana, chico, grapes, guava, guyabano, jackfruit, lanzones, mango, oranges, papaya, pineapple, star apple, and watermelon • Coconut products: Water, gata (milk), flesh of buck or kinudkud (shredded)

VCO, Virgin coconut oil; GM, Genetically modified; RBD, Refined bleached and deodorized; PUFA, Polyunsaturated fatty acids; TFA, trans fatty acids; GM, Genetically modified

Source:

Harvard School of Public Health and Medicine. *Comparison of the Healthy Eating Plate and the USDA's MyPlate*. 2017.[82]

2. Philippine Edible Tuber
    - Native yams across the Philippines were found to have high antioxidant capacities in total phenolics, flavonoids, anthocyanin, and are kept at the University of the Philippines-Los Baños Germplasm Bank.[84,85]
    - We are planning to conduct repeat laboratory assays and animal toxicity studies to confirm this reported antioxidant capacity. We also plan to conduct clinical trials to test whether this translates to effective and safe antioxidant effects on normal Filipino skin and later, on post-inflammatory hyperpigmentation/melasma with oxidative stress and inflammation due to UV, VL, and heat.

III. DAILY SKIN CARE TO DELAY SKIN AGEING IN FILIPINO BROWN SKIN[85-87]

- In general, use hypoallergenic products for personal care or use at home and office.
- Always read labels to avoid those with photosensitive ingredients:
    - Fragrance (often with different names; "well-documented" and "fragrance-free" may be the best guide)
    - Preservatives
    - Colorants
    - Some sunscreen agents (e.g., benzophenones)
- See your dermatologist if the labels are not clear to you and seek guidance on active ingredients in skin care products to help exfoliate, nourish, and repair skin tissues.

TABLE 7–7. Simple Daily Skin Care

AREA	MORNING	NIGHT
Body	• Hypoallergenic wash: removes surface, lower skin particulates and microbes once or twice daily • Body oil (e.g., VCO): breaks down in the skin to fatty acids that help repair the lipid bilayer of replenishing epidermal cells • And/or a lotion with cholesterol and ceramide, the two other main ingredients for stratum corneum barrier repair	• Repeat morning routine. • Add an exfoliant with active ingredients (e.g., retinoids, antioxidants, peptides, or hyaluronic acid).
Face, neck, photo-exposed skin	**As base:** • Mild cleanser, with no or mild scrubs • Moisturizer with humectant, barrier repair, and antimicrobial functions (e.g., cold pressed VCO) **On top (prevent/treat skin ageing):** • EMR screen with photoprotection factors (PF) to UVB (SPF >30), UVA (PF-A >10, at least 1/3 of the SPF), critical wavelength >370 nm • Iron oxide in tinted colorant/concealer/foundation, with VL-PF of at least 3 (1/3 of PF-A), alone or layered. • Pressed powder with iron oxide (reapply as needed) • For dyschromias, wrinkles, barrier problems - apply a barrier base with zinc oxide and/or titanium dioxide ○ Layer products for more VL protection.	• Mild cleanser, with no or mild scrubs • Moisturizer with humectant, barrier repair, and antimicrobial functions (e.g., cold-pressed VCO)

VCO, Virgin coconut oil; EMR, Electromagnetic radiation; PF, protection factor; UV, Ultraviolet; SPF, Sun protection factor; VL, Visible light

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OPEN FORUM HIGHLIGHTS

Moderator: MARIA ASSUMPTA CECILIA R. SERRANO, MD, FPDS

Q: *Is there a difference between people with a normal sleep pattern and those with a reverse sleep pattern (i.e., sleeps in the day, awake in the night) or is it just the amount of sleep that affects skin disease severity?*

A: In reverse sleep pattern (also called irregular sleep-wake syndrome), the five stages of sleep are compromised. Due to interference with body repair and tissue regrowth, which occurs during sleep, there is accelerated ageing of tissues, similar to nocturnal interrupted sleep. Even with 7–8 hours daytime sleep, the circadian rhythm is also compromised.
It has been shown in the study of Dr. Lu that sleep for people who are graveyard workers have generally poor sleep quality and skin diseases, when present, are more severe.

Q: *What kind of prophylaxis do you suggest for people with chronic occupational exposure, such as to strong detergents?*

A: **Skin barrier protection**. There are a lot of barrier creams now with iron oxide, titanium dioxide, long chain silicones, and exopolysaccharides. The nice thing about them is that they are large molecules and they just sit on the surface of the skin. Some, put on thickly, initially appear white, but blend with the skin color when rubbed well into the skin to protect you from chronic particulates exposure.
For those with atopic dermatitis, barrier creams are available containing a 3:1:1 ratio of ceramides, cholesterol, and fatty acids that is the same proportion found in normal healthy skin. These comprise the

main ingredients of the barrier layer and can help restore a compromised skin barrier.
Layering technique ensures adequate barrier protection. At my clinic, I have a big computer monitor on my right. Since I have both photo-contact and photo-drug dermatitis, my right side has darkened and is drier due to the visible light. I now apply four layers: 1) a sunscreen which protects against UVA and UVB, 2) a titanium dioxide and zinc oxide barrier cream, 3) a thin base coat of iron oxide, and 4) a thicker liquid foundation. To shape and contour, I use products with even more iron oxide.

Q: *What is your advice for males who do not want to use sunscreen?*

A: What I do is I scare them. You know you have a beautiful wife. You know what's going to happen when you turn 60? She'll still look 30. That is why you want to use this. I have a lot of male patients who use liquid foundation after trying on the shade and texture they prefer. When they put it on their skin, it doesn't look like makeup. It looks natural yet they are protected. For men I give a **simpler 2- to 3-step regimen** of layering on the face: 1) a sunscreen with high: SPF, for UVB; PFA, for UVA; 2) zinc oxide and titanium dioxide for UVB, UVA, and VL protection because they tend to be more sun-exposed, and 3) topmost, I give a light-to- sheer foundation with a high iron oxide content.

Q: *Is it true that males prefer to use gels than cream because it looks better on their skin? Is there an advantage to the use of gels?*

A: The problem with gels and sprays is that the delivery of the sunscreen **can be uneven**. Some areas may have the gel with sunscreen, while other areas may mostly be just gelatin or liquid. Another problem with gels and sprays is that people **tend to apply a little amount**–less than the standard sunscreen protection factor test dose of 2 mg/cm^2.
Fortunately, there now are products with silicones that make the product feel very light, apply smoothly, and thus, for males, very acceptable to apply on their skin.

Q: *Please comment on the oral photo-antioxidants that are marketed as oral sunscreens.*

A: The general consensus among dermatologists is that since the 'oral sunscreen' products available provide a low level of sun protection (studies mention SPF2–4), they cannot replace topically applied sunscreens. Instead, they may be given as an adjunct, prior to sun exposure. Oral sunscreens from our own edible tropical plants may give higher antioxidant and protection factors. We are now exploring this.

Q: *What is the best percentage of sunblock to use?*

A: If the question is on how much sunblock to use, the testing dose for sunscreens is 2 mg/cm^2 per 9% of the body surface area (Figure 7–3). This amount is roughly a finger strip from the palmar crease to the fingertip on the index and middle fingers. However, this amount is too copious; thus, one may initially apply one fingertip unit, followed by another fingertip unit after 30 minutes. A fingertip unit is from the distal crease to the tip of the finger.

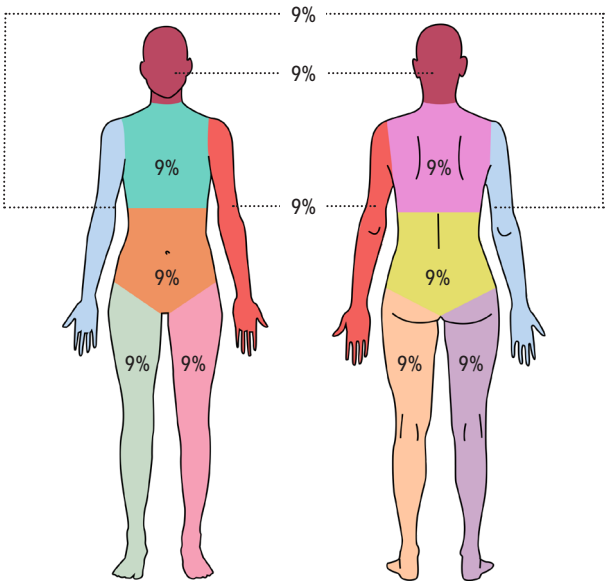

FIGURE 7–3. Rule of Nines

If the question is on the percentage of active ingredients in the sunscreen, these vary in any given formula. Protection Factors (PFs) are the measure for their effectivity. For UVB PF, The European Cosmetic and Perfumery Association (COLIPA) and FDA Guidelines mandate in vivo tests done with an indoor solar simulator. FDA-approved sunscreens can claim 'broad-spectrum' if the SPF is 50+.

UVA-PF determination is done in vitro using a spectrophotometer. A sunscreen can be labeled 'broad-spectrum' if it is able to reach a *critical wavelength* of >370 nm.

There are no standard tests for visible light and infrared PFs. In our Photodermatology Laboratory at VMV Skin Research Centre + Clinics (VSRC), we use a pure visible light-emitting lamp (400–760 nm) and follow the UVB methodology.

Thus, besides texture and color, read the label for ingredients and on how PFs were tested. Note that some sunscreens base their PF claims just on the basis of the percentage of the active ingredients present in the sunscreen. Such claims are generally faulty because interactions with the rest of the inactive ingredients may vary the final PF of the product.

Q: *Are there herbal alternatives to sunscreen products?*

A: The alternative to topical sunscreen products is oral intake, because it is more convenient for people to take a pill than to apply and reapply a sunscreen.

Dermatologists who practice or go on missions to the Cordilleras anecdotally say they rarely see skin cancers among patients, including indigenous people. Intake of herbs and other native foodstuff may be the reason for this paucity.

Tubers have been shown to have high antioxidant capacity. These are readily available edible plants on which we now are doing further laboratory and translational studies. As our study progresses, I will want to look at the dosage and the amount of tubers that people can include in their food. These may help our people on oxidative processes and inflammation, which is the basic mechanism for most of the current

common diseases; from diabetes, hypertension, depression, Alzheimer's disease and ageing from our exposomes.

Q: *Nurses and other health care workers are used to night shift work. In my case, I observed that after my shift, I feel that I have dry skin. Is it normal? What would be the best way to recover and maintain a healthy skin?*

A: Yes, your observation is correct. First, low humidity from air-conditioning, often kept at low temperatures, lowers the amount of water in the air. Second, the barrier of the skin is compromised due to lack of sleep as well as work stress. I love VCO as a moisturizer to prevent and treat dry skin. When its triglycerides break down into fatty acids, glycerin is also formed and this is a huge absorber of water. VCO's fatty acids are saturated and medium length, so they line up to make a great palisade that acts as an occlusive to prevent water loss and to also protect your skin from the outdoors. (This property is why coconut oil becomes like white butter in temperatures below 25°C). These fatty acids contribute to the lipids of the destroyed barrier and to the repair of cell membranes. They also have broad-spectrum antimicrobial action against hospital and community-acquired microbes.
Apply VCO on your skin - as an occlusive moisturizer, humectant, barrier repair and antimicrobial oil. If you want something fancier, do so but with your exposomes in mind. If you have a tendency for allergy, avoid products that have preservatives, dyes or fragrance, to avoid making your problem worse.

Q: *May I ask if applying BB or CC cream products for those 70 years old and older is good and recommended to improve ageing skin?*

A: BB stands for Blemish Base; CC for Color Corrector. Good advertising, but be wise about your skin. Don't go by hearsay. Always read the ingredients list in the bottle or packaging. If it does not have any of the things that I mention above, they may not improve ageing skin, and may have ingredients that cause skin allergy, irritation, and barrier disruption that contribute to skin ageing.

Q: *Do you offer special sun exposure instructions for people with low vitamin D levels?*

A: Our literature search shows no studies on the ageing effects on our brown skin photo types by our perceived high prevalence of *low* serum 25-hydroxyvitamin D levels.
Individuals of African ancestry living in the US, also have lower (~2-fold) serum 25-hydroxyvitamin D levels, while levels in white skin Caucasians are higher. This is attributed primarily to photoprotection from dark skin pigment. Another reason is polymorphism of genes controlling skin melanin content. An earlier study showed that SLC24A5 111^{Ala} allele was associated with lower serum 25-hydroxyvitamin D3 and lower levels of 24, 25-dihydroxyvitamin D3, independent of melanin index. The same authors recently showed a CYP3A43 genotype, previously implicated in cancer, strongly associated with biomarkers of vitamin D metabolism.
On vitamin D and ageing, albeit in mostly white skin, causal associations between serum vitamin D (25(OH)D) concentrations and features of facial skin ageing were studied. Associations between the ageing features and 25(OH)D were done using single nucleotide polymorphisms identified from previous genome-wide association studies. Meta-analysis of the two cohorts, associated *higher* serum 25(OH)D with a higher perceived age (P-value = 3.6 × 10-7), more skin wrinkling (P-value = 2.6 × 10-16), but not more pigmented spots (P-value = 0.30). In contrast, a genetically determined 25(OH)D) concentration was not associated with any skin ageing feature (P-values >0.05). The authors conclude that the study did not indicate causal associations between 25(OH)D and features of skin ageing.[3]
A vitamin D study on ageing in Filipino brown skin is obviously needed.

Q: *Are collagen supplements safe to take even if you are hypertensive?*

A: In Section II-C. I talked about the Antioxidant Paradox, so I also became curious about collagen supplementation, which is newer, but use is rising. A 2019 systematic review by Francesca Choi, my Taiwanese-Filipina dermatology colleague, working from the University of California Irvine, gives me pause, that it may have some value. Her review includes randomized controlled trials on efficacy of collagen supplementation on skin quality and anti-ageing. Included were 11 studies with 805 participants. Eight studies used collagen hydrolysate 2.5g/d to 10g/d for 8 to 24 weeks, to treat skin ageing, xerosis, cellulite and pressure ulcers. Two studies used collagen tripeptide 3g/d for 4 to 12 weeks, with notable improvement in skin elasticity and hydration. One study using collagen dipeptide suggested anti-ageing efficacy proportionate to collagen dipeptide content. They concluded that short- and long-term use of oral collagen supplements for skin ageing is promising and safe. There was increased skin elasticity, hydration, and dermal collagen density with no reported adverse events.[4]
On the question asked on safety in patients with hypertension, I have not found any such study.

Q: *When is the best time to apply coconut oil as a moisturizer?*

A: As a moisturizer, first, look for an **organic and cold-pressed** VCO because the minimal processing and least exposure of the coconut plant to chemicals assures you of its high antioxidant content. Next, your exposomes. Let's say you're a police officer out there in EDSA–apply coconut oil, four times a day. For us, working ladies, who habitually avoid sun exposure–apply in the morning, again at night, and gently massage into the skin. For those who regularly go outdoors for exercise or sports, apply at least twice a day then reapply after sweating and physical activities that wipe off the VCO.

Q: *Is it advisable for someone with lupus to use sunblock that has SPF130? How long does the effect last?*

A: A very high number like SPF130 only indicates UVB protection. For patients with active lupus disease, the sunscreen I recommend is broad-spectrum against UVB and UVA, by having physical (zinc oxide and titanium dioxide) and some chemical sunscreen ingredients. You have learned in Section A1 the need to protect against VL, for which products with zinc oxide, titanium dioxide, and iron oxide are needed and for which are needed and for which layering is advised. Avoidance of IR radiation and heat is also in the same section.

Q: *What is your opinion regarding the use of Chin Chun Su? It is a cream available at leading drugstores for pimples, with sulfur as active ingredient.*

A: I know some people use them. I searched for its declared ingredients list but could not find any, except that it supposedly has salicylic acid and sulfur. Without an ingredient list I would not recommend it to anyone. Effectiveness and safety of active and other ingredients need to be assessed.[29]

Q: *Is it true that sweets, such as cake and chocolates, cause ageing? What variety of food do you recommend to have a healthy skin?*

A: It is unfortunate but true. Many clinical studies now confirm that low-carbohydrate diets reduce body weight, decrease levels of serum leptin, insulin, fasting glucose and triglycerides, all of which are implicated in metabolic defects and ageing. Conversely, high glycemic index and high-carbohydrate diets positively correlate with age-related diseases including diabetes and heart diseases. Thus, a low-carbohydrate diet may delay ageing in humans by preventing metabolic diseases and improving general health of the skin.
See our proposed anti-inflammatory diet in Section C, based on our VCO versus corn oil diet study,

pending the final RNA sequencing study results. Note that a recent in vitro genetic study shows the barrier repairing effects of VCO.

REVIEW QUESTIONS

1. What is the primary mechanism by which solar radiation causes skin ageing?
   a. Generation of reactive oxygen species that results in the expression of enzymes forming wrinkles
   b. Decreased epidermal permeability
   c. Chemicals in the air activated by heat energy causing inflammation of the skin
   d. Thermal energy causes fragmentation of collagen fibers

2. Which combination of forms of solar radiation causes hyperpigmentation but not erythema?
   a. UVB + UVA_2
   b. UVA_1 + Visible light
   c. UVA_2 + Infrared
   d. UVA_2 + UVA_1

3. Which additive in sunscreens protects against visible light?
   a. Carbon dioxide
   b. Carbon monoxide
   c. Iron oxide
   d. PABA

4. Antioxidants in supplements do not provide substantial health benefits. True or False?
   a. True
   b. False

5. Which of the following is consistent with an anti-inflammatory diet?
   a. Using virgin olive oil more than coconut oil
   b. Consuming dairy at least 3 times a day
   c. Limiting red meat to 2-3 servings/week, choosing lean cuts with no marbling
   d. Frying food using canola oil

ANSWERS: 1. a; 2. b; 3. c; 4. a; 5. c

8 MULTIDISCIPLINARY CARE IN HEAD AND NECK CANCER

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Delivered as a webinar on August 30, 2019
https://bit.ly/ALMW_Ch8_MultidisciplinaryCare

KEY POINTS

- Head and neck cancers are the 6th most common cancer, and risk factors include smoking include: alcohol, betel nut chewing, and poor oral hygiene.
- Early detection of head and neck cancers by thorough history and physical examination, confirmed by appropriate diagnostic procedures such as imaging and metastatic work-up is key. If one is unsure, refer to the experts.
- The best initial treatment is almost always surgical resection, but chemotherapy or radiation may play a role as definitive or adjuvant options depending on the situation.
- A multidisciplinary team approach to the management of head and neck cancers is important to restore quality of life and function in society.

LEARNING OBJECTIVES

- ➸ To review the incidence and risk factors for head and neck cancers
- ➸ To discuss the clinical presentation of common head and neck cancers
- ➸ To know the standard procedures used in diagnosing head and neck cancers
- ➸ To explain to a patient how a head and neck tumor can be managed

I. EPIDEMIOLOGY OF HEAD AND NECK CANCERS

- 90% of head and neck cancers are due to squamous cell carcinoma (SCCA), which is the 6th most common cancer worldwide.[1,2]
- There is a rising incidence of head and neck cancers, especially in young adults, non-smokers, and non-drinkers.[3]

TABLE 8–1. Risk factors for head and neck cancers

- Age
- Tobacco
- Alcohol
- Betel nut chewing
- Poor oral hygiene, ill-fitting dentures
- Occupational exposure (chronic inhalants)
- Genetic predisposition
- Nutritional
- Infections (viral infections such as HPV, EBV)

HPV, Human papillomavirus; EBV, Epstein Barr virus

II. SPECIFIC TYPES OF HEAD AND NECK CANCER

TABLE 8–2. Common locations of head and neck cancer

1. Nose, paranasal sinuses (frontal, maxillary, ethmoid, sphenoid) and anterior skull base
2. Nasopharynx
3. Oral Cavity- lip, tongue, floor of mouth, buccal mucosa, alveolus, hard palate
4. Oropharynx- tonsil, soft palate and base of tongue
5. Larynx and hypopharynx
6. Skin of the face and neck
7. Ear and temporal bone
8. Salivary gland
9. Thyroid gland

III. DIAGNOSIS OF HEAD AND NECK CANCER

A. History and Physical Exam

a. Timeline of symptoms and signs
b. Family history
c. Risk factors
d. Complete ear, nose and throat (ENT) physical exam

B. Clinical Presentation

- A progressive and chronic clinical course may point to a diagnosis of cancer (Table 8–3). Cancers can grow and get bigger in size, and may spread to the neck nodes, lungs, bones, liver, brain and other parts of the body.

TABLE 8–3. Common signs and symptoms of head and neck cancer

1. Painless growth in the neck, lateral or anterior location
2. Intermittent epistaxis, especially if persistently on the same side
3. Bleeding from mouth or ear
4. Non-healing ulcer in the oral cavity; >2 weeks duration; most often on the tongue
5. Persistent nasal obstruction, especially on the same side
6. Slowly progressive odynophagia and/or dysphagia
7. Slowly progressive dyspnea, and stridor
8. Loosening of dentition
9. Any growth / bulge in the mouth, face and neck area
10. Otalgia that is not infectious in etiology
11. One-sided facial palsy

C. Diagnostic Workup

TABLE 8–4. Diagnostic tools for head and neck cancer

1. Endoscopy ○ Nose & Sinuses ○ Nasopharynx ○ Larynx ○ Trachea	• Locates the cancer • May use flexible scopes or rigid scopes • May be done in the clinic or operating room
2. Biopsy	a. Source of Tissue Sample: → Primary mass/tumor → Suspected lymph node b. Method → Fine-needle aspiration biopsy (FNAB)* – Clinic procedure → Core-needle biopsy - Clinic procedure → Incisional biopsy or Excision biopsy - may be done as a clinic procedure or in the operating room setting c. Specimens are sent for: Gross, microscopic and immunohistochemical examination
3. Imaging a. CT scan	As needed depending on presentation and spread of the cancer For assessment of bone involvement
b. **MRI***	For assessment of soft tissue and nerve involvement
4. Metastatic work-up a. Chest x-ray vs. chest CT scan b. Liver ultrasound c. Bone scan d. PET Scan	Completes the picture to establish the cancer stage at diagnosis, which will guide appropriate treatment Chest x-ray may be used to screen for lung metastases, especially when conserving resources; but chest CT scan is more useful in discovering actual lesions.

FNAB, Fine Needle Aspiration Biopsy; CT, Computed Tomography; PET, Positron Emission Tomography; MRI, Magnetic Resonance Imaging

IV. MANAGEMENT OF HEAD AND NECK CANCER

A. Treatment Principles

- ○ The earlier a cancer is detected, the more treatment options are available, and the greater the chance for a cure.
- ○ The appropriate treatment depends on important considerations (Table 8–5)

TABLE 8–5. Treatment considerations in head and neck cancer

1. Resectability of cancer
2. Prognosis of cancer
3. Functional deficits, cosmetic deformities, psychological impact of treatment
4. Patient's general health condition to tolerate treatment and its side effects
5. Cost of treatment
6. Family/caregiver support

- There is a need for a multidisciplinary team approach to treatment (Figure 8–1)

FIGURE 8–1. Multidisciplinary Team for Head & Neck Cancer Treatment

B. Treatment Options

1. *Surgery*
   - The best initial treatment is almost always upfront surgery.
   - Surgery is recommended if the cancer is resectable and one can operate with no significant functional morbidities.
   - In a few select tumors that are unresectable or with significant debilitating and deforming outcomes, chemotherapy and radiation are preferred.
2. *Radiation Therapy*
   - Radiotherapy may be done with or without chemotherapy.
   - It may be delivered in the adjuvant, definitive or palliative setting (Table 8–6).

TABLE 8–6. Indications for radiation therapy

1. Aggressive, high grade, high stage (3 & 4) or bulky tumors
2. Positive surgical margins
3. Presence of unfavorable features (lymphovascular space invasion, extracapsular spread, extranodal spread)
4. May be given for palliation in unresectable, symptomatic and disseminated cancer

3. *Chemotherapy*
   - Chemotherapy acts as a "radiosensitizer."
   - It may be employed together with radiation to help control the tumor
   - It is never used alone in most head and neck cancers, except maybe in lymphomas and in disseminated cancer, for palliation.
4. *Rehabilitation And Psychosocial Support*

V. SPECIFIC TREATMENT FOR COMMON HEAD AND NECK CANCERS[4]

A. Thyroid Cancer

- >90% are either papillary or follicular carcinomas which are generally "compatible with life."
  - Papillary carcinoma
    - Usually spread to lymph nodes in the neck
  - Follicular carcinoma
    - Commonly spread by blood to other parts of the body, usually lungs and bones
- Management
  - Surgery is composed of a thyroidectomy (usually total); and a neck dissection if there are enlarged lymph nodes.

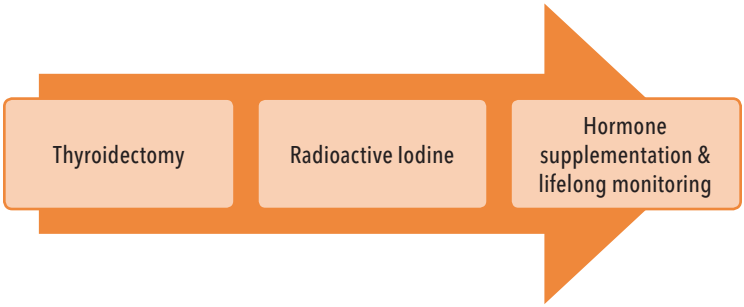

FIGURE 8–2. Management of Thyroid Cancer

B. Laryngeal Cancer

- Vital Structures
  a. Air and food passages
  b. Voice box
- Treatment Options:
  a. *Early Cancer (Stage 1 & 2)* (Figure 8–3):
     → Non-Surgical (external beam radiotherapy) versus surgical (laser surgery or conservation

laryngectomy)
→ Voice is retained (although with changed quality)
→ No need for permanent tracheostomy

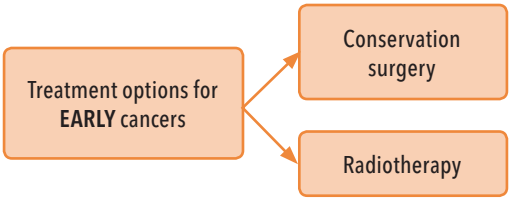

FIGURE 8–3. Treatment for early laryngeal cancer

b. *Advanced Cancer* (Figure 8–4)
   1. Surgery is done followed by radiation ± chemotherapy.
      - Total laryngectomy ± neck dissection
        - Removal of the larynx
        - Permanent hole in the center of the neck (stoma) where air flows in and out
        - Loss of voice
        - Requires adjustments in swallowing
   2. Definitive concurrent chemoradiation (chemotherapy + radiotherapy)
      - If this fails, salvage surgery is recommended
   3. Speech Rehabilitation
      a. Esophageal speech
      b. Electrolarynx
   4. Swallowing Rehabilitation

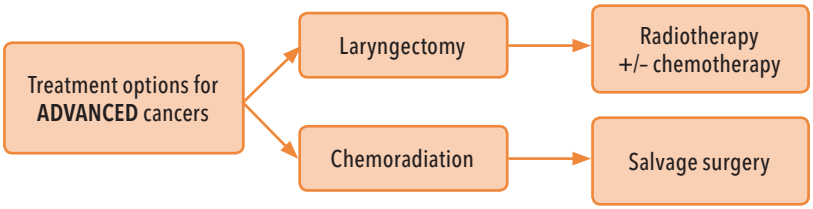

FIGURE 8–4. Treatment for advanced laryngeal cancer

C. Oral Cavity Cancers

- Surgery is the initial treatment of choice.
  - Neck dissection is almost always part of the surgery.
  - Surgery will affect:
    - Speech
    - Chewing and swallowing
    - Breathing

- Radiation with chemotherapy
  - May be recommended as adjuvant treatment after definitive surgery
  - May be used as definitive treatment for stage 3 and 4 cancer, where it may be the only treatment offered

D. Nose and Sinus Cancers

- Surgery is recommended if possible.
- If tumor is inaccessible, options are radiotherapy and chemotherapy.

E. Nasopharyngeal Cancers

- Nasopharyngeal cancers are not amenable to primary surgery.
- These are treated with definitive radiotherapy and chemotherapy.
- Possible salvage surgery should be considered for residual neck nodes.

VI. TREATMENT PRINCIPLES OF RADIOTHERAPY[5]

- Radiation therapy is defined as the use of ionizing radiation to treat cancer (Figure 8–5)
- Certain machines, such as the Helical Tomotherapy® machine and TruBeam®, have more advanced capabilities, which provide greater precision and fewer side effects as compared to conventional medical linear accelerator (LINAC).

5a. Linear accelerator 5b. Tomotherapy

FIGURE 8–5. Radiotherapy Machines

A. How is radiotherapy given?

TABLE 8–7. Use of radiotherapy in head and neck cancer treatment

ROLE IN TREATMENT	
Neoadjuvant	Before the curative treatment
Adjuvant	After curative treatment; most common use
Definitive	Radiotherapy IS the curative treatment
Palliative	To control symptoms or slow down progression of tumor in advanced stages
PRECISION IN TREATMENT	
Conventional radiotherapy	Least precise
3D conformal radiotherapy (3DCRT)	Adequate for big tumors; not ideal for smaller tumors of the head and neck
Intensity modulated radiotherapy (IMRT)	The dose of radiation delivered can be tailored (modulated) to the patient's anatomic features.
Image-guided radiotherapy (IGRT)	Most precise and makes allowances for movement (e.g., swallowing and breathing)

B. What happens during radiotherapy?

- **CT simulation** – the patient undergoes a CT Scan with immobilization devices and the proper positioning, much like a dress rehearsal.
- **Treatment planning** – the radiation oncologist and medical physicist will come up with a good daily treatment plan that hits the critical areas and avoids the organs at risk.
- **Daily treatment** – the patient comes in daily during weekdays to get small doses of radiation that, when accumulated, are designed to either obliterate a tumor or control symptoms.

C. How long does radiotherapy take?

- **Daily** – a few minutes per day
- **Overall** – depends on the intent
  a. **Definitive or adjuvant** – generally longer treatment duration
  b. **Palliation** – generally shorter overall treatment duration

D. Will there be side effects?

- Yes, the kind and manner of side effects depend on the area treated.
- Yes, the longer the treatments and the higher the dose, the more side effects are expected.

TABLE 8–8. Common side effects of radiotherapy to the head and neck

- Dryness of the mouth and throat, including loss of saliva
- Oral ulcers
- Dysphagia and taste changes, such as loss of taste
- Fatigue
- Hair loss
- Skin changes, such as darkening
- Taste changes
- Throat changes, such as trouble swallowing
- Less active thyroid gland

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OPEN FORUM HIGHLIGHTS

Moderator: JEAN ANNE B. TORAL, MD

Q: *Is there a screening tool for head and neck cancers?*

A: There is none. Check for risk factors in the history (e.g., smoking), and check for palpable masses and lymph nodes in the neck. There are no biomarkers or blood tests for screening. You should have a high index of suspicion.

Q: *Can you describe the procedure of laryngoscopy? Are there any complications?*

A: We have an examining mirror that we use in the clinic, but it does not have magnification, and the patient often gags. Laryngoscopy is the examination of the larynx to visualize the vocal cords, when the patient has a hoarse voice. We insert either a rigid scope through the mouth or a flexible scope through the nostril. It has a camera and light source that allows us to see the structures with a TV monitor. It can be done in the clinic and it is uncomfortable but not painful. Operating room laryngoscopy is done under general anesthesia for greater visualization and biopsy collection.

Q: *Are singers prone to get laryngeal cancer?*

A: No, but voice overuse can cause nodules.

Q: *What is the prognosis of for thyroid cancer? Is there such a thing as a 'friendly cancer'?*

A: Papillary thyroid cancer generally has excellent prognosis, although there are some aggressive subtypes. A low-risk patient is typically a female under 55 years of age, with good prognosis (expected survival 98%-100%). Thyroid cancer is a little more aggressive among males and the elderly.

Q: *What are the risk factors for thyroid cancer?*

A: Family history of cancer may be a risk factor. But there is no proven dietary risk (e.g., iodine deficiency) or work-related risk.

Q: *Is the use of e-cigarettes associated with head and neck cancers?*

A: Studies are inconclusive, but as a foreign substance in the body, it has the potential to cause cancer.

Q: *Is there any cancer risk with laryngopharyngeal reflux or reflux esophagitis?*

A: Yes, there have been studies supporting this association. I see a lot of patients who complain of foreign body sensation or feeling of phlegm in the throat.[6]

Q: *What do you do with radiation-induced dysphagia?*

A: While patients are undergoing radiotherapy, patient should gargle often, and hydrate with water, fruit and buco juice, or any liquid. Some patients have loss of sense of taste, dry mouth or oral ulcers, and so fruit juice may have an unacceptable bad taste. When we anticipate further difficulty in swallowing, we can put a feeding tube or a nasogastric tube. Loss of happiness derived from eating adds to psychological side effects.

Q: *Do nasal polyps increase the risk of nasopharyngeal cancer?*

A: No, there is no malignant transformation of biopsy-proven nasal polyps after excisional surgery. But sometimes only the surface is biopsied and the deeper part has something else. Inverting papilloma might look like a nasal polyp, but has malignant potential.

Q: *What is the relationship between HPV and head and neck cancers?*

A: HPV strains that cause head and neck cancers are different from those that cause certain gynecological cancers. Only oropharyngeal cancer is said to be related to HPV.

Q: *Do you have prosthetics in ENT? How about radiology?*

A: Yes. We use prosthetics in ENT for defects of the ear, nose and sinuses. This improves the quality of life of patients with head and neck cancer, which we must always consider.

Q: *What is the role of plastic surgeons in head and neck cancers?*

A: Plastic surgeons perform flaps to cover soft tissue and bone defects for reconstruction.

Q: *Is minimally invasive surgery performed for head and neck cancers?*

A: Yes, but only for small tumors.

Q: *How long are the surgeries for head and neck cancers?*

A: Anywhere from 6 hours to 15 hours.

Q: *What imaging is cost-effective for head and neck cancers?*

A: CT scan is cost-effective since you can see soft tissue and bone. With MRI, bone is less visible. The proper technique for CT scan should be followed.

REVIEW QUESTIONS

1. What is the most common pathology for head and neck cancer, comprising about 90% of cases worldwide?
    a. Basal cell carcinoma
    b. Squamous cell carcinoma
    c. Melanoma
    d. Adenoma
2. What is usually the best initial, upfront mode of treatment for head and neck cancers?
    a. Excisional surgery
    b. Chemotherapy
    c. Radiotherapy
    d. Immunotherapy
3. What is NOT a recommended treatment for nasopharyngeal cancer?
    a. Excisional surgery
    b. Chemotherapy
    c. Radiotherapy
    d. Possible salvage surgery for residual neck nodes
4. What is the use of endoscopy in the diagnosis of head and neck cancer?
    a. Locates the cancer
    b. Determines bony involvement
    c. Determines soft tissue spread
    d. Locates the sites of metastases
5. When is radiation necessary in the treatment of most head and neck cancers?
    a. Aggressive, high grade, high stage (3 & 4) or bulky tumors
    b. Positive surgical margins
    c. Presence of unfavorable features (lympho-vascular space invasion, extracapsular spread, nodal spread)
    d. All of the above

ANSWERS: 1. b; 2. a; 3. a; 4. a; 5. d

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SECTION 2

CARDIOVASCULAR, PULMONARY, ENDOCRINE AND RENAL SYSTEMS

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9 HYPERTENSION IN THE ELDERLY

Esperanza A. Icasas-Cabral, MD

Delivered as a webinar on March 29, 2019
https://bit.ly/ALMW_Ch9_Hypertension

KEY POINTS

- Hypertension is highly prevalent in the elderly, and is a major, treatable risk factor for cardiovascular disease.
- Multiple comorbidities make the management of hypertension in the elderly challenging.
- Hypertension in the elderly should be treated to reduce complications such as stroke and myocardial infarction.
- Patients should be free to make informed choices on treatment options.
- Lifestyle modification is useful, together with drug therapy.
- Start with low doses of medications and titrate slowly.
- The usual target BP is 140/90 mmHg, but an SBP of 150 mmHg is an acceptable goal for elderly patients.

LEARNING OBJECTIVES

- ➸ Discuss epidemiology and importance of hypertension
- ➸ Define hypertension in the elderly
- ➸ Discuss pathophysiology of hypertension in the elderly
- ➸ Discuss complications of hypertension and prevention of stroke and cardiovascular events
- ➸ Outline the treatment of hypertension in the elderly

I. EPIDEMIOLOGY OF HYPERTENSION IN THE ELDERLY

- Approximately 25 % of adults (around 12–13 million people) in the Philippines have hypertension (HTN).
- The prevalence of HTN in the Philippines increases markedly with age.
  - ~45% by 60 years
  - ~55% by 70 years
- In the U.S. Framingham Study, HTN eventually developed in more than 90% of participants with normal blood pressure by 55 years of age.[1]

II. IMPORTANCE OF HYPERTENSION IN THE ELDERLY

- Older people are the fastest growing segment of the population.
- The prevalence of HTN is very high in the elderly.

- Unique issues in managing HTN in the elderly:
  - Systolic HTN is more frequent.
  - Elderly patients are more likely to have comorbidities.
  - Many clinical trials in HTN have excluded patients, particularly those 80 years of age and older.
  - The elderly are more susceptible to certain adverse effects (e.g., orthostatic hypotension).

III. DEFINING HYPERTENSION IN THE ELDERLY

- 'Elderly' is defined as >65 y/o; 'Really old' is defined as >80 y/o
- HTN is defined as: Systolic blood pressure (SBP) >140 or diastolic blood pressure (DBP) >90 mmHg
- There is continued increase in SBP with age; on the other hand, DBP decreases with age after 50 y/o.
- Systolic hypertension is defined as an SBP >140 mmHg and DBP <90 mmHg.
  - It is the most common cause of hypertension in patients over 50 years of age, and accounts for around 75% of hypertension in those over 65 y/o.
  - After age 50, systolic hypertension is a much more important risk factor for cardiovascular events than diastolic hypertension.
  - It is more often poorly controlled than diastolic hypertension.
- Diastolic hypertension is more common in the young.

IV. PATHOPHYSIOLOGY OF HYPERTENSION IN THE ELDERLY

- Multiple changes occur in arteries with ageing, such as reduced elastin content and increased non-distensible collagen and calcium, which result in arterial stiffening.
- Age-associated arterial stiffening results in an increase in SBP and a decrease in DBP.
- Flow-mediated arterial dilation declines with ageing.
- Older patients with hypertension have increased plasma norepinephrine, low renin, and low aldosterone levels.
- Many so-called "normal ageing changes" in arterial structure and function are blunted/absent in populations eating low sodium/low calorie diets, engaging in physical activity, and with low rates of obesity.
- In younger arteries, there is a dilatation of the vessel during systole that produces a lower amount of flow. When this dilation rebounds, there is an incoming diastolic flow which is absent in stiff vessels.[2]
- As people grow older, mean arterial pressure goes up. The pulse pressure goes up. The DBP goes down and the SBP goes up.[3]

V. COMPLICATIONS OF HTN

- HTN is the most frequent CV risk factor for elderly patients with:
  - Myocardial infarction
  - Stroke
- HTN is also a major risk factor in elderly patients with:
  - Chronic heart failure
  - Acute aortic syndrome
  - Atrial fibrillation
  - Diabetes mellitus

- Metabolic syndrome
- Chronic kidney disease

A. Coronary Heart Disease

- Mortality due to CHD increases as a person ages and the SBP goes up.
- If an old or very old patient has an SBP of 180 mmHg, the mortality rate from CHD is much higher than in a person whose blood pressure is lower (Figure 10–1).[4]

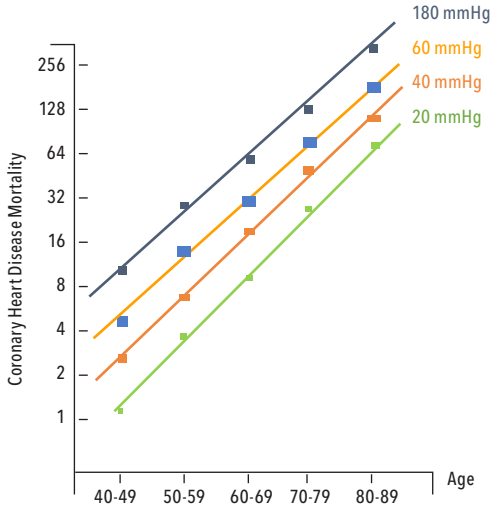

FIGURE 10–1. Coronary heart disease mortality by SBP and age

Source: Prospective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: A meta-analysis of individual data for one million adults in 61 prospective studies. *Lancet*. 2002;360:1903-1913.

- The SBP and pulse pressure jointly influence the risk of coronary heart disease.
  - The hazard ratio for coronary heart disease increases with higher pulse pressure.[5]
- The risk of adverse outcomes among elderly patients with coronary artery disease is more pronounced with abnormal diastolic blood pressure.[6]
  - There is a point where the DBP can be so low that the hazard ratio for coronary heart disease increases in much the same way as it does when the DBP is higher.
  - The hazard ratio for coronary heart disease is related to the DBP more than the SBP.
  - Thus, one should maintain the systolic and diastolic blood pressure within the optimal range, as stated in the guidelines.

B. Stroke

- Stroke mortality increases with higher systolic and diastolic blood pressure. The increase is greater with advancing age.[4]

VI. PREVENTION OF COMPLICATIONS

- By controlling HTN, many studies have shown that the risk of major CV events in elderly patients can be reduced (Table 10–1).
- A 10 mmHg reduction in SBP reduces the risk of heart failure by 28%, renal failure by 5%, and all-cause mortality by 13%.[7]

TABLE 10–1. Hypertension in the Elderly Trials – Stroke, HF, and CHD Reduction

	HYVET[8]	SHEP[9]	SYST-EUR[10]
Year	2003	1991	1997
Sample Size (N)	3,845	4,736	4,695
Age (yrs.)	Adults >80	Adults ≥60	Adults ≥60
SBP & DBP (mmHg)	SBP 160–199 DBP<110	SBP 160–219 DBP <90	SBP 160–219 DBP <95
Goals (mmHg)	150/80	SBP >180: <160 SBP 160-179: ↓20	SBP<150: ↓≥20
Median follow-up (yrs.)	1.8	4.5	2
Combined fatal and non-fatal stroke	All Stroke HR 0.70 (95% CI, 0.49, 1.01)* Stroke death HR 0.61 (95% CI 0.38, 0.99)*	↓36% (p=0.0003)*	↓42% (p=0.003)*
Combined fatal and non-fatal HF	HF HR 0.36 (95% CI, 0.22, 0.58)	↓49% (p<0.001)*	↓29% (p=0.12)
Combined fatal/non-fatal MI, CHD death, sudden death	All-cause mortality HR 0.79 (0.65, 0.95) CV death HR 0.77 (0.60, 1.01) Cardiac death HR 0.71 (0.42, 1.19)	CHD events ↓25% (95% CI 0.60, 0.94)* Non-fatal MI ↓33% (95% CI 0.47, 0.96) Non-fatal MI+CHD death ↓27% (95% CI 0.57, 0.94)*	CHD component outcomes not significant w/o HF inclusion

HYVET, HYpertension in the Very Elderly Trial; SHEP, Systolic control of Hypertension in the Elderly Program; Syst-Eur, Systolic hypertension in Europe; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; HF, Heart failure; MI, Myocardial infarction; CHD, Coronary heart disease

**Statistically significant*

Sources:

Mukhtar O, Jackson SHD. The Hypertension in the Very Elderly Trial – latest data. *Br J Clin Pharmacol*. 2012;75(4):951-954.

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VII. TREATMENT OF HYPERTENSION IN THE ELDERLY

A. Three Important Caveats

1. All clinical practice guidelines start with **lifestyle modification** as treatment for hypertension, whether in the elderly or not. Only after lifestyle modification is initiated, particularly in the lower levels of hypertension, would we go to drug treatment.

2. Nearly all antihypertensive agents will work to lower the blood pressure, but some of them are better than others when there are other **comorbidities or compelling indications**.
3. Majority of patients will require **two or more drugs** to reach their treatment goal (Figure 10–2).

B. Guidelines on Blood Pressure Goals

- In general, the goal is to bring blood pressure down below 140/90 mmHg based on several clinical practice guidelines (CPGs). However, in the very old, this can be liberalized to below 150/90 (Table 10–2).
- Guidelines on BP threshold for drug treatment are also given if lifestyle changes fail to reach BP goals (Table 10–3).

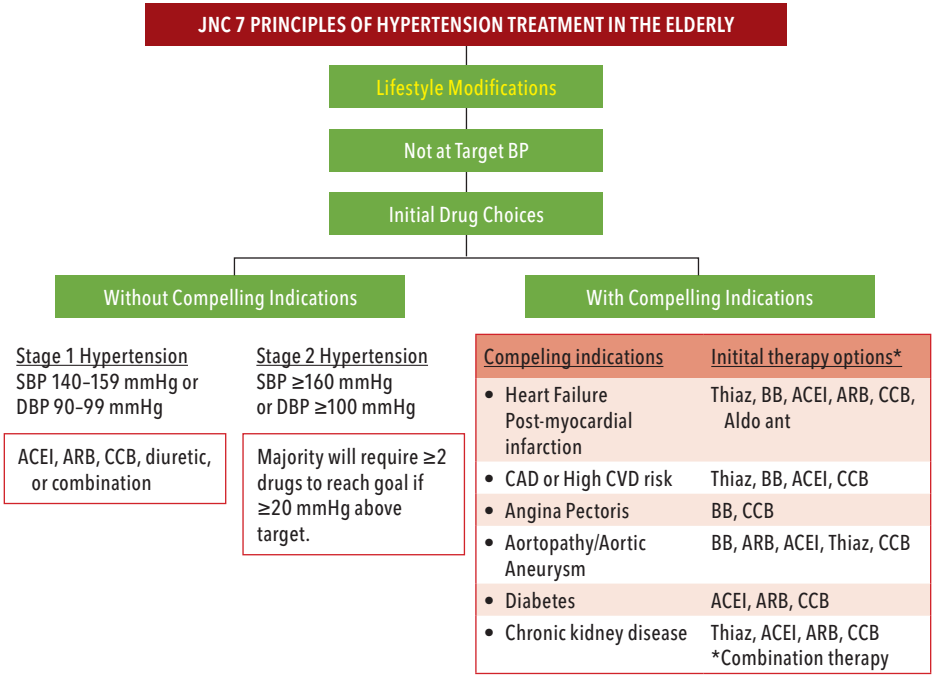

FIGURE 10–2. Principles of treatment of hypertension (JNC7)

ACEI, Angiotensin-converting-enzyme inhibitors; ARB, Angiotensin II receptor blockers; CCB, Calcium channel blockers; CAD, Coronary artery disease; CVD, Cardiovascular disease; Thiaz, Thiazide; BB, β -blockers; Aldo ant, Aldosterone antagonist

Adapted with permission from *"The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure"* by A.V. Chobanian et al. U.S. Department of Health And Human Services (2004), p 31.[11]

TABLE 10–2. BP goals (in mmHg) from different CPGs

Age (yrs.)	JNC-7[11]	JNC-8[12]	ASH/ISH[13]	CHEP[14]	ESC/ESH[15]
<60	<140/90	<140/90	<140/90	<140/90	<140/90
60–79	<140/90	<150/90	<140/90	<140/90	<140/90
≥80	<140/90	<150/90	<150/90	<150/90	<150/90

JNC, Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; ASH/ISH, American Society of Hypertension and the International Society of Hypertension; CHEP, Canadian Hypertension Education Program; ESC/ESH, European Society of Cardiology/European Society of Hypertension

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The Task Force for the the Management of Arterial Hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). 2018 ESC/ESH Guidelines for the Management of Arterial Hypertension; 2018.

TABLE 10–3. Guidelines on BP threshold (mmHg) for drug treatment if lifestyle changes fail to reach BP goals

AGE (yrs.)	JNC-7[11]	JNC-8[12]	ASH/ISH[13]	CHEP[14]	ESC/ESH[15]
<60	140/90	140/90	160/100	150/90	140/90
60–79	160/90	150/90	160/100	150/90	140/90
≥80	160/90	150/90	160/100	160/90	150/90

JNC, Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; ASH/ISH, American Society of Hypertension and the International Society of Hypertension; CHEP, Canadian Hypertension Education Program; ESC/ESH, European Society of Cardiology/European Society of Hypertension

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The Task Force for the management of arterial hypertension of the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH). 2018 ESC/ESH Guidelines for the Management of Arterial Hypertension; 2018.

C. Non-pharmacologic Treatment

Lifestyle modification measures have been shown to be beneficial in elderly patients with hypertension (Table 10–4).

TABLE 10–4. Lifestyle modification measures

Regular physical activity	Aerobic exercise, moderate intensity, ≥30 min, 5–7 days/wk.
Proper diet	Increased consumption of vegetables, fresh fruits, fish, nuts, unsaturated fatty acids, low-fat dairy products, and low consumption of red meat
Sodium restriction	<5 g/day
Weight control	Body mass index (BMI) at ~20–25 kg/m^2 Waist circumference at <94 cm in men and <80 cm in women
Smoking cessation	Support and referral to smoking cessation programs if necessary
Avoidance of excessive alcohol intake	<14 units/wk. for men and <8 units/wk. for women

D. Pharmacologic Treatment (based on Clinical Practice Guidelines on Management of Arterial Hypertension [ESC/ESH, 2018])[15]

1. Treatment Options
   - Diuretics, angiotensin-converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), calcium channel blockers (CCB), and β-blockers (BB) have all shown benefit on cardiovascular outcomes in randomized trials among cohorts of elderly patients with hypertension.
   - The choice of specific agents is dictated by efficacy, tolerability, presence of specific comorbidities, and cost.
   - More than one drug will often be required.
2. Treatment Principles
   - Initial therapy is with an ACEI or ARB combined with a CCB or diuretic; other combinations of antihypertensives can be used. Combine BB with other antihypertensives when specific clinical situations require it.
   - Initial therapy will usually be a two-drug combination: except in (a) frail older patients and (b) patients with low CV risk and with grade 1 hypertension (SBP <150 mmHg).
   - If BP is not controlled, give a three-drug combination: a renin-angiotensin system (RAS) blocker with a CCB and thiazide/thiazide-like diuretic.
   - If BP is not controlled, may add spironolactone, other diuretics, higher doses of other diuretics, a BB, or an α-blocker.
   - The combination of two RAS blockers is not recommended.
3. BP Targets

   How low should BP be lowered?
   - The evidence is strong that lowering of SBP to <140 mmHg is beneficial for all patient groups, including independent older patients.
     - Target SBP should not be <120 mmHg because of the benefit vs. harm imbalance at these levels of treated SBP.

- Treatment decisions in old and very old patients should consider independence, frailty, and comorbidities; especially in older (≥65 y/o) and very old (>80 y/o) patients.
  - The target SBP range for all patients more than 65 years of age is 130–139 mmHg. Although not achievable in all older patients, any BP lowering towards this target will likely benefit as long the treatment is well tolerated.
  - Although the specific BP at which antihypertensive drug therapy should be initiated in the elderly is unclear, a threshold SBP of 160 mmHg and a goal SBP of ≤150 mmHg seem reasonable.

4. Side Effects of Antihypertensive Treatment
   - In the elderly, antihypertensive drugs should generally be initiated at the lowest dose and gradually increased as tolerated.
   - Since there is a high prevalence of comorbidities, both CV and non-CV, among the elderly, we should be vigilant and avoid treatment-related side effects, such as:
     - Electrolyte disturbances
     - Renal dysfunction
     - Orthostatic hypotension
5. Management of Cardiovascular Disease (CVD) Risk in Patients
   - CVD risk assessment – For patients not already at high or very high CVD risk from established CV disease (CVD), renal disease, or diabetes
   - Statins – For patients at high or very high CVD risk
   - Antiplatelet therapy (in particular, low-dose aspirin) – For secondary prevention; not for primary prevention in patients without CVD
   - Routine genetic testing – Not recommended

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OPEN FORUM HIGHLIGHTS

Moderator: DR. ANNA YORK P. BONDOC

Q: *Is the approach to the elderly patients with hypertension different from younger patients, whose cut-off BP is 130/90 mmHg?*

A: The guidelines that you are talking about refer to the garden-variety patients with hypertension who are under age 60. For those over 60 years of age, the guidelines are more liberal because these patients are generally more vulnerable to the side effects of the drugs. If they get dizzy because they developed orthostatic hypotension and they fall, this is an even worse problem than hypertension. It's fine that your blood pressure is 120/80 mmHg, but my feeling is that you need to bring the BP down to approach that perfect level as long as the patient can tolerate it. Not everybody is going to tolerate 120/80, and some of them may develop undesirable side effects from the drugs. Some may also not be able to afford the cost of combination drugs.

In the geriatric population, the BP goal is less than 140/90. In the younger population, it is less than 130/90.

Q: *Is there any recent evidence on lifestyle modification as an effective management for hypertension?*

A: There is well-established data from valid studies on the benefits of lifestyle modification. For example, the data shows that if you reduce salt in the diet to less than 5 g/day, you can lower the DBP by 5 mmHg. There are also data showing that BP in obese individuals can be lowered by achieving normal body weight, and that DBP goes down by 7–10 mmHg after one stops smoking.

Q: *Are there treatment options to antihypertensive medications for 60- to 75-year-old patients?*

A: The first option is lifestyle modification – maintaining proper body weight, regular physical activity, not smoking, and avoiding drinking to excess. If you do these, they can really lower your blood pressure; and there is a possibility that you will not need medications. If your blood pressure is >160/100 mmHg you should start the medications together with lifestyle modification.

Q: *I have borderline hypertension and a family history of hypertension. Should I start medications now or wait until lifestyle modification fails to control the BP?*

A: If you have borderline hypertension, start lifestyle modification first.

Q: *How would you treat hypertension in patients with diabetes?*

A: Frequently, high blood pressure and diabetes go together. If you have them together, the risk for CV disease is even greater than if you just have one. It is very important that both blood pressure and blood sugar levels are controlled. For patients with diabetes, we generally start with CCBs or ARBs. These two classes of medicines do not have bad effects on the blood sugar. On the other hand, diuretics have hyperglycemic effects, as do β-blockers (BB) in some instances. When you're starting out, choose a CCB and/or RA blocker. If still not controlled with these, BB and diuretic may still be used. These are not absolutely contraindicated in patients with diabetes, but they are not the first choice. Only give additional medicine if blood pressure is not controlled.

Q: *Are there cases where you had to start combination pills immediately?*

A: Yes. For SBP>170 mmHg, combination pills are very good. If you need two drugs, use a combination pill instead. The advantage of using two drugs right away is you can give low doses of each drug.

Q: *Are vitamin D-deficient people more prone to health problems, such as hypertension? Are there really vitamin D-deficient people?*

A: Some small studies show that if you take vitamin D or vitamin D derivative, BP can go down. Office workers, or those who stay indoors and avoid sun exposure (to avoid getting dark and to prevent skin cancer) usually have lower vitamin D levels. Check serum vitamin D levels; and if low, prescribe supplements as needed.

Q: *Is there a limit to the duration of time that any antihypertensive drug may be continuously taken?*

A: No. Antihypertensive drug therapy is for life. However, if they are really compliant with lifestyle change and BP goes down, you can try reducing the dose of the drug, followed by a drug holiday; see what happens.

Q: *Do you encourage the elderly to take herbal medicine? If yes, which ones?*

A: For me, if you're talking of value for money, the best value for money is with medicine that have been proven to work. In the Philippines, antihypertensive drugs are cheap due to the Generics Act or even free in some health centers. Sometimes, the cost of herbal medicine is even higher than the antihypertensive medicine.

Q: *What can we do for elderly patients who come to the clinic with a SBP of 190 mmHg but are asymptomatic?*

A: Assure them that they'll be fine but they need to take their blood pressure medications because if not, they won't be fine for long.

Q: *What do we advise 80-year-old patients who say that they have survived even with an SBP of 160 mmHg?*

A: I'm an advocate of patients' rights. Therefore, they can do whatever they want to do. Our obligation is to tell them what is going to happen if they do A or if they do B and what our recommendations are. But when it comes to deciding for themselves whether they will follow it or not, that is entirely up to the patient. But we have to make sure that they are informed so that they can make informed choices.

Q: *Is there still a point to treat an elderly patient with hypertension, e.g. to lower the risk of stroke?*

A: In the case of the 80-year-old patient whose SBP did not go above 160 mmHg, advise lifestyle changes first. Later on, if the SBP still doesn't go below 160 but the patient refuses to take medications, that's still acceptable. But if it goes up to an SBP of 230, that's a different story. Explain to the patient very well what they have, what will happen to them if they don't treat their hypertension, and what our recommendations are.

Q: *Are there significant side effects to the kidney after long-term maintenance antihypertensive medications?*

A: First of all, the side effects are not exactly from the medicines themselves. None of these medicines actually cause kidney disease. With proper use, there is no harm to the kidneys. On the other hand, if you don't control the hypertension, then you will most likely go on to kidney failure. The second leading cause of dialysis in the country is uncontrolled hypertension, second to diabetes.

Q: *How do we manage a patient with diabetes who is undergoing hemodialysis and who has hypertension?*

A: Treatment of hypertension is still needed. Hemodialysis is not the treatment for hypertension.

Q: *Will you immediately treat a SBP of 160 mmHg in a patient with white coat hypertension?*

A: No. If you look at the guidelines, for those BP levels, you need to verify first by taking their blood pressure measurements at least twice on different occasions. If SBP is 150 or 160 mmHg, advise lifestyle modifications first, then follow them up. Once they come back, if the blood pressure is still high, then you may start drug treatment.

Q: *What is the best route for taking clonidine as an initial medication for chronic treatment of patients with hypertension?*

A: You don't start treatment of chronic hypertension with clonidine. Sublingual clonidine is not a mode of intake anymore, although in some places, if BP is too high, they still give it sublingual. Some studies show that whether you give it sublingually or orally, the effect on the BP is the same.

Q: *For black populations with hypertension, are there any antihypertensive medication that we should refrain from giving?*

A: Usually, the RAS blockers don't work as well in the black population as they do in the Caucasian population.

Q: *What do you recommend for patients who are extremely anxious about the side effects of antihypertensive medications?*

A: I will start by reassuring them that even as we talk of side effects and we say all drugs have side effects, the side effects that you see from antihypertensive drugs, when used properly, are nearly none. One should not be scared of giving diuretics that may lower potassium because if the proper dose is used, there's almost none of that side effect. An allergic reaction, however, cannot be predicted. It will only be discovered once a person takes a drug and reacts to it.

Q: *What drugs are cost-effective for a patient with a SBP of 180 mmHg?*

A: Generic diuretics and β-blockers have the lowest price. But now, there are also a lot of generic RAS blockers. However, if BP is not going down, then try something else.

Q: *Would you suggest to shift the class of medication or change from generic to branded for patients whose blood pressures remains high?*

A: You can do either. You can change the brand or the class of medicine.

Q: *Should the medication be changed for an elderly 80 y/o who has been taking β-blockers for 20 years?*

A: If the drug is effective and well-tolerated, even if the patient is 80 y/o, we advise to continue the medication.

Q: *Is an antihypertensive drug needed for an 80-year-old patient with a pacemaker and controlled BP?*

A: If the BP is controlled, then no. If the patient is already on blood pressure medications, then maintain.

Q: *An elderly patient is admitted into the hospital for pneumonia, and the patient's history of hypertension is not noted. The patient was cured for pneumonia but developed hypertension. How do we prevent this occurrence?*

A: Many hospitals now allow medications from home to be taken in the hospital. Just give them to the nurse so that the nurse will be the one to record and give them to you.

Q: *What is your advice for my 49-year-old previously athletic brother working in Saudi with a BP of 140–150/90 mmHg? He has no vices or other diseases and used to jog and exercise, but with family history of hypertension.*

A: If he is living a healthy lifestyle, and yet his BP is still elevated, he can get started on medications.

Q: *Is it safe to tell patients that they can look forward to stopping their antihypertensive medications if diligently combined with lifestyle modification?*

A: Yes. There is a potential. In particular, this is true for extremely obese patients who lose enough weight and follow other lifestyle modification measures.

Q: *Is it advisable for healthcare workers in public health to give antihypertensive drugs by sublingual mode in a hypertensive crisis?*

A: If you have nothing else to give and you are in the community setting, yes. If in a hypertensive crisis, the patient should be brought to the hospital.

Q: *Is it true that iron supplements increase the BP?*

A: No. It is a common misconception that if you are anemic, your blood pressure is low. Thus, it is also misunderstood that if you take something for anemia, BP increases.

Q: *For people with low BP who are not on any anti-hypertensive medications, should they be concerned?*

A: No, if that has been the BP for a long time and the patient is asymptomatic. There is no need to treat the patient.

Q: *Does the SBP need to go down to normal level? For example, if you previously had a SBP of 190 mmHg and is now at 160, is that okay already?*

A: That's better than not going to 160. Although the ideal target BP is below 130/80 mmHg, which is beneficial in reducing CV outcomes, one should be cautious in lowering the BP as to avoid adverse events.

Q: *If your normal BP is 80/60, then it increased to a SBP of 130mmHg and you already feel symptoms, is that already considered hypertension? What do you do?*

A: It's not necessarily considered as hypertension in the sense that, if you did not treat it, patient is going to get adverse events. But because the patient is not used to that SBP of 130 mmHg, he can already start to feel symptoms. With time, however, patient can tolerate it. So you don't really need to bring it down to an SBP of 80 mmHg with antihypertensive drugs, unless the patient has a highly abnormal cardiac profile.

Q: *Please comment on the use of clonidine every 15 minutes as emergency drug for a patient with SBP of 180 mmHg.*

A: An SBP of 180 mmHg is not necessarily an emergency indication, especially if the history reveals that the patient has had an SBP of 180 for a long time and is currently asymptomatic. If so, the SBP of 180 may not be an urgent concern and there is no need to treat as an emergency, unless there is an impending stroke.

Q: *When is the best time of the day to monitor your BP?*

A: You can monitor it anytime. But you should monitor it at around the same time every day.

REVIEW QUESTIONS

1. Which of the following is true?
    a. Age associated arterial stiffening results in an increase in both SBP and DBP.
    b. Flow-mediated arterial dilation increases with ageing.
    c. Older patients with hypertension have low plasma norepinephrine, low renin and low aldosterone levels.
    d. As people grow older, the systolic pressure goes up and the diastolic pressure goes down.

2. What is the mainstay treatment for hypertension?
    a. Lifestyle modification
    b. ACE inhibitors
    c. ARBs
    d. Diuretics

3. Which of the following is true regarding lifestyle interventions for hypertension?
    a. Restrict salt intake to less than 15 g/day.
    b. Keep body mass index at 30–35 kg/m^2 and waist circumference at less than 104 cm (men) or 100 cm (women)
    c. Do regular aerobic moderate exercise ≥30mins. for 5–7 days/week.
    d. Restrict alcohol to less than 21 units/wk. (men) and less than 12 units/wk. (women)

4. To which patient group is a two-drug combination not recommended as initial therapy?
    a. Young patients with hypertension
    b. Patients with high cardiovascular risk
    c. Patients with complications of hypertension
    d. Patients with low cardiovascular risk and grade 1 hypertension (SBP less than 150 mmHg)

5. Which of the following is part of the management of CVD risk in patients with hypertension?
    a. Statins
    a. Antiplatelets
    b. CVD risk assessment
    c. All of the above

ANSWERS: 1. d; 2. a; 3. c; 4. d; 5. d

10 ASTHMA AND COPD IN THE ELDERLY

Aileen S. David-Wang, MD, MSc, FPCP, FPCCP, FCCP

Delivered as a webinar on September 6, 2019
https://bit.ly/ALMW_Ch10_AsthmaCOPD

KEY POINTS

- The physiologic changes of lung function with ageing include decreased elasticity and increased air trapping.
- Asthma, although more common in younger patients, may begin in the later years.
- Ageing predisposes individuals to comorbidities, which accelerate ageing and affect management of asthma.
- In treating patients with asthma and COPD, take note that side effects are common and that physical limitations should be considered in choosing the type of inhaler. Complex medication regimens and multiple inhaler devices should be avoided.
- The updated guidelines, GINA 2019 (for asthma) and GOLD 2020 (for COPD), are available for decision-making and appropriate management.

LEARNING OBJECTIVES

To discuss the following:

➥ Physiology of the ageing lungs
➥ Asthma in the elderly
➥ Chronic obstructive pulmonary disease (COPD)

I. PHYSIOLOGY OF AGEING LUNGS

A. Ageing

- Characterized by a progressive loss of physiological integrity, which leads to loss of function and increased vulnerability to death[1]
- Considered as the single greatest risk factor for chronic noncommunicable diseases, resulting in increased morbidity and mortality[2]
  - COPD
  - Most forms of lung cancer
  - Idiopathic pulmonary fibrosis

B. Biological age differs from chronological age

- Dunedin, New Zealand study: Population-representative cohort of young adults (N = 1,037) followed from birth to age 38 years[3]

- About 25% of individuals of the same chronological age (38 years) showed different biological ages. Some individuals had a biological age of 50 years.
- Faster-ageing healthy adults showed deficits in physical/cognitive functioning compared to slower-ageing peers.
- Smoking and obesity accelerate ageing, while exercise and lifestyle modification may delay ageing.

C. Hallmarks of ageing lungs[1,2]

- Cell-intrinsic
  1. Genomic instability
  2. Telomere attrition
  3. Epigenetic alterations
  4. Loss of proteostasis
  5. Deregulated nutrient sensing
  6. Mitochondrial dysfunction
  7. Cellular senescence
- Cell-extrinsic
  1. Stem cell exhaustion
  2. Altered intercellular communication
  3. Extracellular matrix (ECM) dysregulation

D. Effects of ageing on the lungs

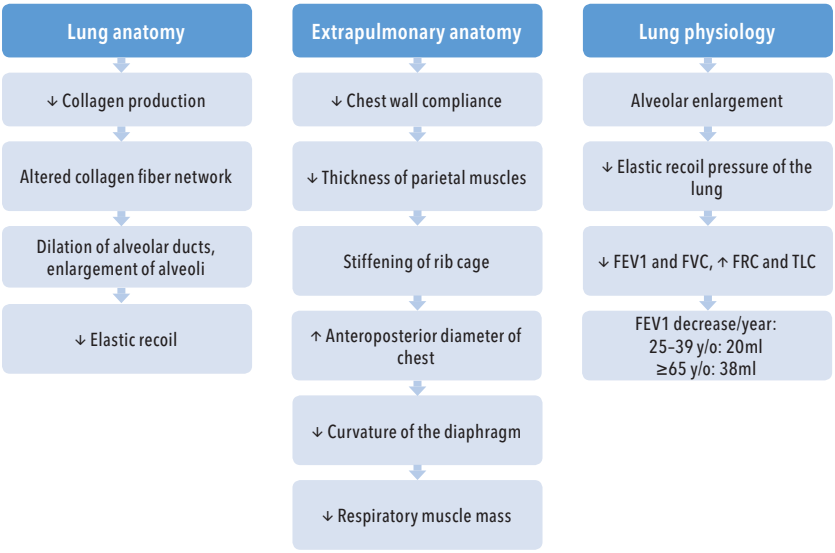

FIGURE 10–1. Changes in lung and extrapulmonary anatomy and physiology with ageing[4]

FEV, Forced expiratory volume; FVC, Forced vital capacity; FRC, Functional residual capacity; TLC, Total lung capacity

Source: Skloot GS. The effects of ageing on lung structure and function. Clin Geriatr Med. 2017;33(4):447-457.[4]

E. Comorbidity vs. multimorbidity

- Comorbidity is defined as any additional condition that has existed or has occurred in the clinical course of a patient with the index disease under study.[5]
- Multimorbidity is defined as the co-existence of two or more chronic conditions in the same individual.[6]
- The number of comorbidities increases with age.[7]
  - 50-year-old patients usually have one to four conditions while 64-year-old patients have five to eight conditions.
  - Ageing predisposes individuals to comorbidities, and comorbidities accelerate ageing. Common pathways involve oxidative stress and reduction in anti-ageing molecules such as sirtuins and Klotho.
  - Asthma and COPD patients have the worst medication adherence (33% medication possession ratios [MPR]) among the eight chronic conditions.[8]

II. EPIDEMIOLOGY OF ASTHMA

- Asthma accounts for 2.2% of total deaths in the Philippines, with an age-adjusted death rate of 21.20/100,000 population.[9]
- Asthma and COPD are among the top 10 causes of deaths in the Philippines, and rates are increasing.[10]
- The Philippines ranks second in asthma mortality in the world.[9]
- The global prevalence of asthma in adults of more than 65 years of age is 4–13%. There is higher burden of medical cost, hospitalizations, morbidity, and mortality in the older groups compared to younger groups.[11-13]

III. IMMUNOLOGY OF ASTHMA (FAHY, 2015; WOODRUFF, 2009; WENZEL, 2012)[14-16]

Asthma is a heterogeneous disorder characterized by many phenotypes and endotypes (Table 10–1).

TABLE 10–1. TH2-High vs TH2-Low Asthma

TH2-HIGH ASTHMA	TH2-LOW ASTHMA
More severe symptoms	Less severe symptoms
Presence of eosinophilia	Absence of eosinophilia
Early age of onset	Generally adult onset
Atopic/IgE component	May be linked to obesity, neutrophilia, and smoking
Responsive to inhibitors of type 2 inflammation	Poor response to inhaled corticosteroids

TH, T helper; IgE, Immunoglobulin E

IV. DIAGNOSIS OF ASTHMA

A. Compared to the symptoms of asthma in all ages outlined in GINA 2019, the following should be noted in the elderly:[13]

- Older patients may not perceive dyspnea even in the presence of significant airflow obstruction.
- Dyspnea due to asthma may be overlooked due to comorbidities (e.g., heart failure, anemia, obesity).
- Older patients may limit their activity to avoid becoming dyspneic.

B. To confirm the diagnosis of asthma, it is necessary to confirm variable airflow limitation.[13]

- Low forced expiratory volume (FEV1) and low FEV1/forced vital capacity (FVC) must be documented.
- The normal FEV1/FVC ratios are:
  - For healthy adults: >75 to 80%
  - For children: >90%
- There must be a positive bronchodilator reversibility test defined as:
  - For adults: an increase in FEV1 >12% and >200 ml from baseline 10 to 15 minutes after 200–400 mcg of salbutamol or equivalent.
  - For children: an increase in FEV1 of 12% or more.
- The same objective measures are used in the diagnosis of asthma in the elderly and in younger patients.
  - ↓ FEV1/FVC ratio decreases with ageing; thus, age-adjusted values must be used to avoid overdiagnosis of obstruction.
  - A more easily obtained surrogate for FEV1/FVC is FEV1/FEV6.
  - With ageing itself, there is **increased** bronchial hyperreactivity to methacholine; thus, provocation testing may be less accurate in the elderly.
  - Spirometry and standard bronchoprovocation tests are effort-dependent and may be difficult for those who are frail.
  - There are few studies on exhaled nitric oxide (FeNO) in the elderly.

V. MANAGEMENT OF ASTHMA

A. Principles of Asthma Pharmacotherapy (GINA 2019)

1. The control-based asthma management cycle allows us to continually assess, adjust and review response to treatment (Figure 10–2)

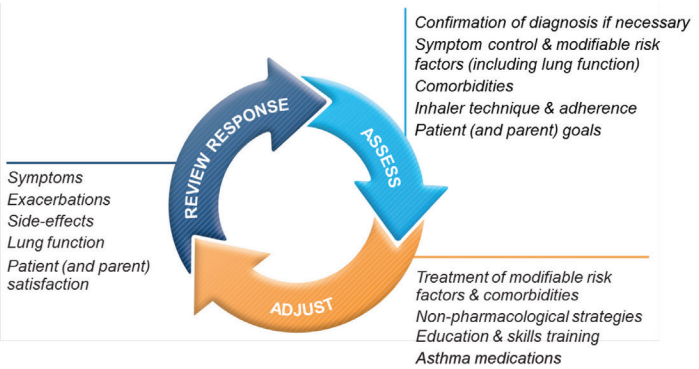

FIGURE 10–2. Control-based asthma management cycle (GINA 2019)

Reprinted with permission from "Asthma Management and Prevention for Adults and Children Older than 5 Years. A Pocket Guide for Health Professionals." by Global Initiative for Asthma (GINA). 2019. p40. Copyright © 2019 GINA[17]

2. A 5-step approach is also recommended (Figure 10–3)

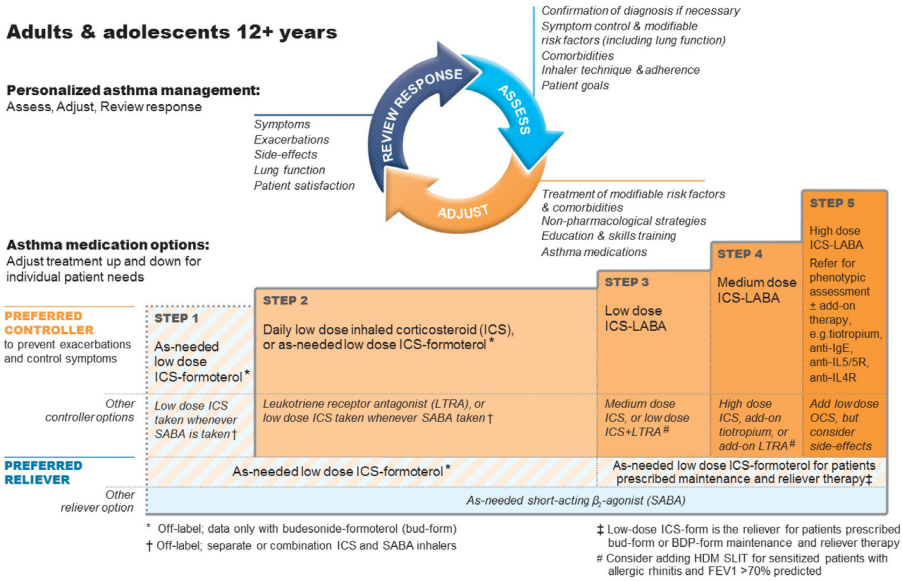

FIGURE 10–3. Ladder approach to asthma treatment

Reprinted with permission from "Asthma Management and Prevention for Adults and Children Older than 5 Years. A Pocket Guide for Health Professionals." by Global Initiative for Asthma (GINA). 2019. p46. Copyright © 2019 GINA[17]

3. Regular maintenance controllers or preventers, usually inhaled corticosteroids (ICS) and long-acting beta-2-agonist (LABA), are needed to control chronic inflammation and mucus plugging of airways.
4. A rapid-acting bronchodilator reliever is used as needed for bronchospasms due to triggers.

TABLE 10–2. Medications for asthma

CLASS	MEDICATION AND DOSAGE	NOTES
SABA	Salbutamol 2.5 mg premixed nebule OR 2.5 mg diluted in 3–4 ml saline, delivered via nebulization As needed, every 20 minutes, up to 3 doses then every 1–4 hours as needed Salbutamol metered-dose inhaler 4–8 puffs of 90 µg every 20 minutes up to 4 hours, then every 1-4 hours as needed	For symptomatic relief

TABLE 10–2. Medications for asthma (cont.)

CLASS	MEDICATION AND DOSAGE	NOTES
ICS-LABA	Budesonide/formoterol 1 puff of 160 µg/9 µg OR 2 actuation puffs of 80 µg/4.5 µg Every 12 hours	Not to exceed 320 µg/9 µg every 12 hours
	Salmeterol/fluticasone 1 actuation of 50 µg/100 µg every 12 hours	Not to exceed 1 actuation of 50 mcg/500 µg every 12 hours
ICS	Fluticasone 100–250 µg inhaled Every 12 hours	Not to exceed 500 µg every 12 hours
	Budesonide 180–360 µg inhaled Every 12 hours	Not to exceed 720 µg every 12 hours
LTRA	Montelukast 10 mg tablet per orem Once a day, in the evening	

SABA, Short-acting beta$_2$-agonist; ICS, Inhaled corticosteroids; LABA, Long-acting beta$_2$-agonist; LTRA, Leukotriene receptor antagonist
Source: Morris MJ, Pearson DJ. Asthma treatment and medication. *Medscape*. 2019. https://emedicine.medscape.com/article/296301-treatment

B. Asthma management in the elderly[13]

- The elderly is often excluded from randomized controlled trials (RCTs); thus, there is limited drug efficacy data.
- Side effects are more common in the elderly.
  - β-2-agonists have cardiotoxic effects.
  - Corticosteroids may cause skin-bruising, osteoporosis, and cataracts.
  - Concomitant use of β-blocker eyedrops may cause bronchoconstriction.
- The following conditions may affect ability to actuate an MDI device and should be considered in choosing the type of inhalers:
  - Hand arthritis
  - Muscle weakness
  - Impaired vision
  - Weak inspiratory flow
- Avoid multiple inhaler devices and complex medication regimens.

VI. EPIDEMIOLOGY OF COPD

- COPD is the 4th leading cause of death in the world.[19]
- It is projected to be the 3rd leading cause of death by 2020.[20]
- The global burden of COPD is projected to increase in the coming decades due to continued exposure to risk factors and an ageing population.
- Comorbidities (e.g., oncologic, cardiac, gastrointestinal and psychiatric) are increased in patients with COPD.[21]

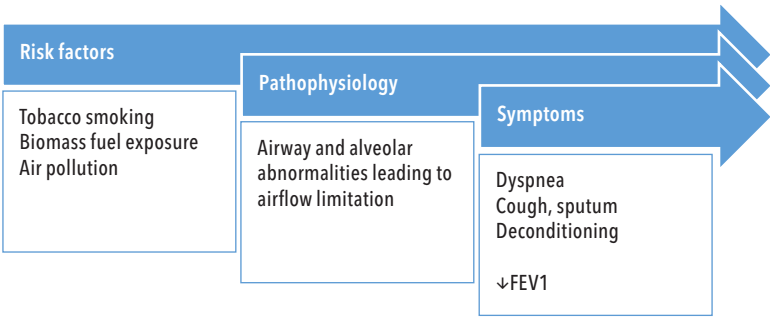

FIGURE 10–4. Key points for COPD risk factors, pathophysiology, and symptoms

Source: Global Initiative for Chronic Obstructive Lung Disease. *Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease 2020 Report.*[22]

VII. DIAGNOSIS AND CLASSIFICATION OF COPD (GOLD 2020)

The recommended COPD assessment tool includes spirometry, assessment of risk of exacerbations, assessment of symptoms (using Modified MRC dyspnea scale, and COPD Assessment Test (CAT).[22]

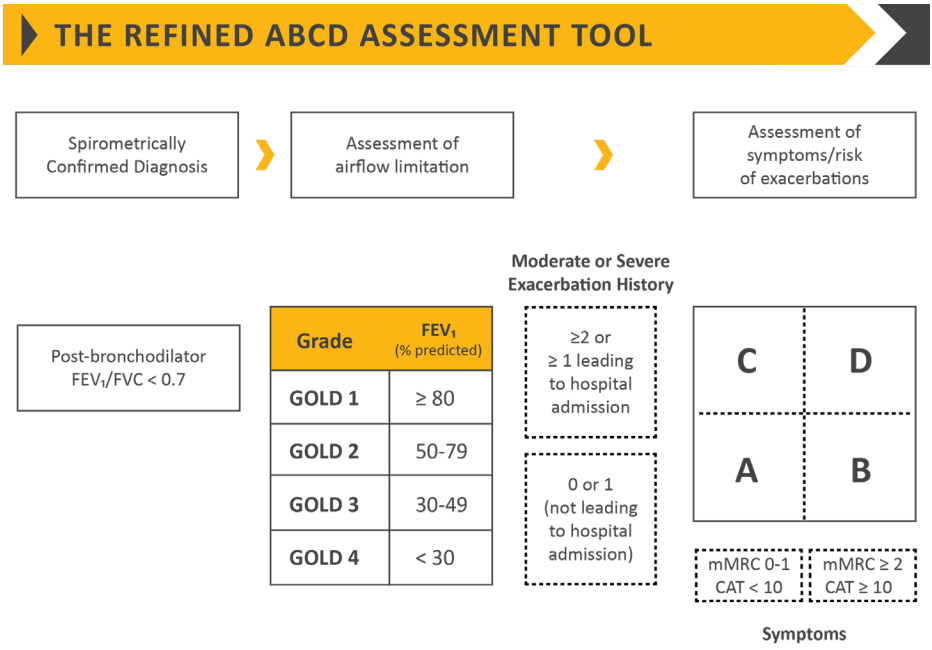

FIGURE 10–5. The Refined ABCD Assessment Tool (GOLD, 2020)

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TABLE 10–3. Modified MRC Dyspnea Scale

MODIFIED MRC DYSPNEA SCALE[a]

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

mMRC Grade 0.	I only get breathless with strenuous exercise.	☐
mMRC Grade 1.	I get short of breath when hurrying on the level or walking up a slight hill.	☐
mMRC Grade 2.	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	☐
mMRC Grade 3.	I stop for breath after walking about 100 meters or after a few minutes on the level.	☐
mMRC Grade 4.	I am too breathless to leave the house or I am breathless when dressing or undressing.	☐

[a] Fletcher CM. BMJ 1960; 2: 1662.

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CAT™ ASSESSMENT

For each item below, place a mark (x) in the box that best describes you currently. Be sure to only select one response for each question.

EXAMPLE: I am very happy	0 (X) 2 3 4 5	**I am very sad**	**SCORE**
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

TOTAL SCORE: ◯

FIGURE 10–6. CAT Assessment

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VIII. TREATMENT OF STABLE COPD

The goals of treatment for stable COPD are to reduce symptoms and risk of disease progression and mortality. The latest available guidelines are from the Philippine College of Chest Physicians (2014)[23] and GOLD 2020.[23]

TABLE 10–4. Summary of the PCCP Clinical Practice Guideline for the Diagnosis and Management of COPD

PATIENT GROUP CLASSIFICATION	A	B	C	D
1st line	prn SABA or prn SAMA	LABA or LAMA	ICS-LABA or LAMA	ICS-LABA and/or LAMA
Alternative	LABA or LAMA or SABA + SAMA	LABA + LAMA	LABA + LAMA	ICS-LABA and LAMA

PRN, "Pro re nata" or as needed; ICS, Inhaled corticosteroids; LABA, Long-acting beta$_2$-agonist; LAMA, Long-acting muscarinic antagonists; LTRA, Leukotriene receptor antagonist; SABA, Short-acting beta$_2$-agonist; SAMA, Short-acting muscarinic antagonists
Source: Philippine College of Chest Physicians. Summary of the PCCP Clinical Practice Guideline for the Diagnosis and Management of COPD.2014.[23]

TABLE 10–5. Medications for COPD

CLASS	MEDICATION	
SABA	Salbutamol 2.5 mg premixed nebule OR 2.5 mg diluted in 3–4 ml saline, delivered via nebulization As needed, every 20 minutes, up to 3 doses then every 1–4 hours as needed Salbutamol metered-dose inhaler 4–8 puffs of 90 ug every 20 minutes up to 4 hours, then every 1–4 hours as needed	For symptomatic relief
SAMA	Ipratropium 2 actuations of 34 µg Every 6 hours and as needed 2.5mL nebulization Every 6–8 hours	Not to exceed 12 actuations per day
LABA	Salmeterol 1 inhalation of 50 µg twice daily	Not to exceed twice daily administration
LAMA	Tiotropium 2 inhalations per orem of 18 µg capsule via HandiHaler device Once a day Tiotropium 2 actuations of 2.5 µg/actuation, inhaled per orem Once a day	

TABLE 10–5. Medications for COPD (cont.)

CLASS	MEDICATION	
LABA + LAMA	Salbutamol/ipratropium 1 actuation of 100 µg/20 µg Every 5 hours	Not to exceed 6 actuations/day, or 3 ml nebulization every 4 hours
	Salbutamol/ipratropium 3 ml nebulizer solution inhaled Every 6 hours	More effective than LABA or LAMA alone
ICS-LABA	Budesonide/formoterol 1 puff of 160 µg/9 µg OR 2 actuation puffs of 80 µg/4.5 µg Every 12 hours	Not to exceed 320 µg/9 µg every 12 hours
	Salmeterol/fluticasone 1 actuation of 50 µg/100 µg every 12 hours	Not to exceed 1 actuation of 50 µg/500 µg every 12 hours

ICS, Inhaled corticosteroids; LABA, Long-acting beta$_2$-agonist; LAMA, Long-acting muscarinic antagonist; LTRA, Leukotriene receptor antagonist; SABA, Short-acting beta$_2$-agonist; SAMA, Short-acting muscarinic antagonists

Source: Mosenifar Z. Chronic obstructive pulmonary disease (COPD): Treatment and management. Medscape.2019.[24]

1. **Bronchodilators**
   - Regular use of inhaled bronchodilators prevents or reduces symptoms (Evidence level A).
   - LABAs and LAMAs are generally preferred except for patients with only occasional dyspnea (Evidence level A).
   - Compared to LABAs, LAMAs have a greater effect on reducing frequency of exacerbations (Evidence level A) and hospitalizations (Evidence level B).
   - Compared to monotherapy, combination treatment with LABA+LAMA increases FEV1 and reduces symptoms (Evidence level A) and exacerbations (Evidence level B).
2. **Anti-inflammatory therapy in stable COPD**
   - An ICS combined with a LABA is more effective than the individual components in improving lung function and health status and reducing exacerbations in patients with moderate to very severe COPD (Evidence level A).[19,20,25,26]
   - Regular treatment with ICS increases the risk of pneumonia especially in those with severe disease (Evidence level A).
   - Triple inhaled therapy of ICS/LAMA/LABA improves lung function, symptoms, and health status, and reduces exacerbations compared to ICS/LABA, LABA/LAMA, or LAMA monotherapy (Evidence level A).
   - A number of recent studies have shown that blood eosinophil counts (BEC) predict the magnitude of the effect of ICS in preventing future exacerbations.
     - The threshold of a BEC is >300 cells/µL.
     - BEC can help clinicians estimate the likelihood of a beneficial preventive response to the addition of ICS to regular bronchodilator treatment.
     - BEC can be used as a biomarker in conjunction with clinical assessment when making decisions regarding ICS use.[26-30]

Note: Based on the latest GOLD 2020, asthma-COPD overlap is no longer considered a separate clinical entity. Asthma and COPD are distinct disorders that may share some common traits and clinical features.

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OPEN FORUM HIGHLIGHTS

Moderator: ANNA FRANCESCA C. MULLES, MD

Q: *Should patients with asthma undergo annual pulmonary function tests?*

A: We actually recommend regular lung function testing to diagnose asthma and to assess response to treatment.

Q: *I thought my adult-onset asthma would improve over time. Is it going to be symptom control for me forever?*

A: It's been associated with urbanization. Once an asthmatic, always an asthmatic. There is no cure for asthma. We need maintenance medications to prevent exacerbations.

Q: *Can caffeine be used as a treatment for asthma?*

A: Yes, it has bronchodilator properties, but there are systemic side effects from caffeine.

Q: *Is it true that if you had asthma when you were young, it will come back when you are old?*

A: Yes. Half of patients develop it before age 10. Asthma may disappear but tends to recur if symptoms weren't controlled to start with, and may be due to environmental factors. Once it comes back, it is unlikely to disappear.

Q: *What is the effectiveness of pulmonary rehabilitation for COPD patients?*

A: There is grade A level of evidence that it improves quality of life and reduces exacerbations, among others.

Q: *Chronic steroid intake triggers glaucoma for which beta blockers are sometimes used. How do we deal with this double-edged sword?*

A: It is a problem among the elderly. Use cardio-selective blockers. If it causes exacerbation, we have to refer back to the ophthalmologist for change in medication.

Q: *What non-pulmonary comorbidities predispose elderly patients to asthma exacerbations?*

A: Obesity; the obese female phenotype who develops it late, are more prone to exacerbation and are corticosteroid-resistant.

Q: *Are there physical exercises that can help control asthma?*

A: Yes; chest physiotherapy, breathing exercises, and upper arm exercises can all help as prescribed rehabilitation.

Q: *Is it true that obese children are prone to develop asthma?*

A: They tend to have more symptoms and more exacerbations. Obesity has been found to be a risk factor for asthma.

REVIEW QUESTIONS

1. Which of the following is not a characteristic of TH2-high asthma?
    a. More severe asthma
    b. Absence of eosinophilia
    c. Early age onset
    d. Atopic/IgE component

2. Which of following does NOT increase the probability that symptoms are due to asthma?
    a. Symptoms are often worse at night or early in the morning
    b. Symptoms vary over time and in intensity
    c. Exercise-induced dyspnea with noisy inspiration
    d. Symptoms improve with bronchodilators

3. Which of the following is true in the diagnosis of asthma in the elderly?
    a. Uses age-adjusted FEV1/FVC values to avoid overdiagnosis
    b. Normal FEV1 and low FEV1/FVC
    c. Increase in FEV1 by >12% or >200 ml from baseline 10–15 minutes after 200–400mcg Salbutamol
    d. Provocation testing may be used in the elderly population

4. Which is true for as-needed budesonide/formoterol, according to the Symbicort Given As Needed in Mild Asthma (SYGMA) trial programme?
    a. Has the same effect as terbutaline as-needed monotherapy in asthma symptom control
    b. Is similar to low-dose budesonide maintenance + terbutaline as needed in preventing severe exacerbation
    c. Has increased odds of a well-controlled asthma week than budesonide as maintenance with terbutaline as-needed
    d. Has lower odds of having a well-controlled asthma week than SABA as-needed

5. Which of the following is true regarding ICS use in stable COPD patients?
    a. Regular treatment with ICS increases the risk of pneumonia especially in those with severe disease.
    b. ICS + LABA has similar effect with the individual components in improving lung function
    c. Triple inhaled therapy of ICS+LABA+LAMA has no added benefit in improving symptoms and reducing exacerbations as compared to ICS+LABA
    d. Blood basophil counts predict the magnitude of the effect of ICS in preventing future exacerbations.

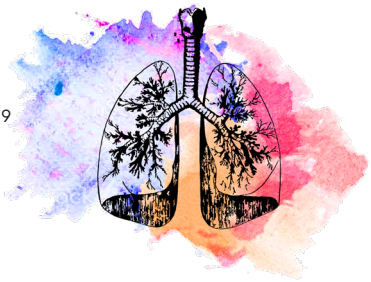
ANSWERS: 1. b; 2. c; 3. a; 4. b; 5. a

11 PNEUMONIA IN THE ELDERLY

Anna York P. Bondoc, MD

Delivered as a webinar on October 25, 2019

https://bit.ly/ALMW_Ch11_Pneumonia



KEY POINTS

- The elderly is at risk for pneumonia. Pneumonia is a common and deadly disease.
- Prevention is key. Vaccinate.
- Diagnosis is tricky. It is better to play it safe and have a high index of suspicion.
- Hospitalize when necessary. But remember that the hospital is not necessarily the best place for an elderly patient.
- Treat quickly and empirically, and tailor the treatment to the elderly individual. Choice of antibiotic should be based on etiology and diagnostic test results.
- We should always give tender loving care and be honest with the patient and family regarding prognosis.

LEARNING OBJECTIVES

- ➸ To describe the epidemiology of community-acquired pneumonia in the elderly
- ➸ To discuss why pneumonia is more dangerous in the elderly
- ➸ To outline the diagnostic and treatment approach to pneumonia in the elderly

I. EPIDEMIOLOGY

- Around 60 to 70% of patients with community-acquired pneumonia (CAP) in the United States are above 65 years of age.[1]
- Pneumonia was the 8th leading cause of death in the United States in 2013[2] and 3rd leading cause of death in the Philippines in 2018 (11.4 %).[3]

A. Why is pneumonia more dangerous in the elderly?

- CAP disproportionately affects extremes of age – the very young and the very old.
- CAP often results in hospitalization in the elderly, unlike in younger persons. This could be costly for the patient and the government, especially if admitted to the intensive care unit (ICU).
- Although most patients recover from pneumonia, it could be very debilitating and can result in significant morbidity and mortality.

B. Predisposing Factors for CAP in the Elderly

TABLE 11–1. Predisposing factors for CAP in the elderly

PREDISPOSING FACTORS	EXPLANATION
Poor nutritional status	Elderly patients may not be eating properly, losing weight and becoming malnourished; which then causes their immunity to go down. This then causes them to have a viral infection (i.e., the flu), and develop superimposed bacterial pneumonia.
Difficulty swallowing and poor mobility	• Patients who have suffered strokes are predisposed to aspiration, and even if healthy may be micro-aspirating. This leads to aspiration pneumonia. • The oropharyngeal cavity also gets colonized by bacteria, especially in patients with chronic obstructive pulmonary diseases (COPD) and other chronic lung diseases. • Being bedridden also contributes to aspiration.
Prior antibiotic therapy	Too much antibiotic therapy given to the elderly, even in situations where it is necessary, may result in resistant bugs. This makes antibiotic therapy more difficult.
Weak immune system	Poor T-cell and B-cell function

Source: Marrie TJ. Community-acquired pneumonia in the elderly. *Clin Infect Dis*. 2000;31:1066-1078.[4]

II. DIAGNOSIS

A. Diagnosing Pneumonia in the Elderly[5]

- Common manifestations of pneumonia are: cough (may be productive), fever, chills, and pleuritic chest pain.
- However, pneumonia in the elderly is very difficult to diagnose. This often leads to either overdiagnosis or underdiagnosis; therefore, a high index of suspicion is needed.
  - Less inflammatory response
  - Slight cough and expectoration
  - Nonspecific symptoms, such as loss of appetite, weakness, or could be anything
  - Most importantly, **fever may be absent**.
  - Diagnostic examinations may be normal, especially CBC and chest x-ray (Table 11–2).

TABLE 11–2. Diagnostic examinations for pneumonia in the elderly

DIAGNOSTIC EXAMINATION	REMARKS
CBC	• May be misleading since WBC might not rise due to the immunocompromised state • Normal CBC may even be a sign of sepsis
Chest x-ray	May be normal; repeat in 48 hours
Sputum culture	• Recommend to do culture prior to giving antibiotics in emergency room • Not routinely done in OPD • Often, pathogen NOT identified
Pulse oximetry	• Helpful in deciding need for oxygen therapy

CBC, Complete blood count; WBC, White blood cell; OPD, Outpatient department

- Routine arterial blood gas determination is NOT recommended. Even in septic patients, a lactate level is preferred.
- Urinary antigen testing for *S. pneumoniae* and *Legionella* are only indicated in select cases (e.g., severe CAP, history of outbreak or recent travel).
- Procalcitonin is not recommended to determine need for initial antibacterial therapy.

B. Differential Diagnosis

- **PULMONARY EMBOLISM** – low-grade fever, dyspnea, normal chest, predisposing factors to deep vein thrombosis: may be a common problem in cancer patients
- **COPD EXACERBATION** – in this case, we should treat first and withdraw antibiotics later

Viral versus bacterial pneumonia

- There is no need to determine the specific virus (respiratory syncytial virus, adenovirus, influenza, parainfluenza).
- Viral infection leads to an immunocompromised state, which may result in bacterial pneumonia.
- Most people won't really develop full blown viral pneumonia. It is the bacterial superinfection that we treat with antibiotics. If a patient does not get better with antibiotics, it may be viral pneumonia.
- Viral pneumonia is difficult to distinguish clinically from bacterial pneumonia, even with chest x-ray. WBC can go up, or it can go down, especially if sepsis sets in.
- Influenza virus may be confused with *H. influenzae*, which is a type of pneumonia-causing bacteria not common in elderly.

C. Prognostication

- It is difficult to predict who among your patients will recover and who will not survive.
- It is best to prepare the patient, the family, and yourself, as attending physician, for any eventuality.

III. TREATMENT

A. Treatment principles

- Decision support tools:
  - Pneumonia Severity Index,[6] CURB 65,[7] and CRB 65[8]
  - These help us determine a patient's risk for mortality at 30 days, and guide us in admitting patients into the ward, the ICU, or treating them as outpatients.
- When to hospitalize?[9]
  - When the patient cannot eat or drink anymore, or has severe dyspnea
  - Do not hospitalize a patient just because the relatives want easy access to nurses and doctors. The hospital may be a potentially contaminated place, and the patient may get sicker when admitted.
- American Thoracic Society (ATS) Guidelines[10] and 2017 Philippine Clinical Practice Guidelines on Community-acquired Pneumonia (Joint PSMID, PCCP, PAFP and PCR, 2017)[11] help in decision making.
- *Treat empirically* first, based on clinical scenario and common pathogens (Table 11–3). Streamline antibiotics when culture studies are available, although the pathogen is often not identified.
- Give antibiotics for 5 to 7–10 days depending on severity.

TABLE 11–3. Outpatient management of community-acquired pneumonia

PATIENT GROUP	RECOMMENDED INITIAL THERAPY
No comorbidities	• Amoxicillin 1 g three times daily • Macrolide (azithromycin 500 mg on first day then 250 mg daily) or • Doxycycline 100 mg twice daily
With comorbidities or with antibiotic use within the past three months	*Preferred*: Respiratory fluoroquinolone • Levofloxacin 750 mg daily • Gemifloxacin 320 mg daily • Moxifloxacin 400 mg daily *Alternative:* Beta-lactam • Amoxicillin/clavulanic acid 500 mg/125 mg three times daily or 875 mg/125 mg twice daily • Cefuroxime 500 mg twice daily • PLUS a macrolide

Note: Trimethoprim does not cover all organisms, but may be used as an alternative if the above antibiotics have recently been used.
Sources:
Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia: An official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med*. 2019;200(7):e45–e67.[10]
Kaysin A, Viera A. Community-acquired pneumonia in adults: Diagnosis and management. *Am Fam Physician*. 2016;94(9):698-707.[12]

TABLE 11–4. Common pathogens in community-acquired pneumonia

PREDISPOSING FACTORS	PATHOGEN
Community-acquired	*Streptococcus pneumoniae* (most common), *Haemophilus influenzae, Chlamydia pneumoniae, Mycoplasma penumoniae*
Alcoholics	Anaerobic oral flora, *Klebsiella pneumoniae, Mycobacterium tuberculosis, Streptococcus pneumoniae*
Immunocompromised (steroids, diabetes mellitus, cancer chemotherapy)	*Streptococcus pneumoniae, Mycobacterium tuberculosis*, gram-negative bacteria
Aspiration	Anaerobic oral flora
Chronic obstructive pulmonary disease Smoking	Atypical pneumonia, *Chlamydia pneumoniae, Haemophilus influenza, Legionella pneumophila, Moraxella catarrhalis, Streptococcus pneumoniae*

Note: List is not exhaustive, and one should consider other issues such as HIV status, history of travel, and exposure to animals
Source: Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults. *Clin Infect Dis*. 2007;44(Suppl 2).[13]

B. Factors affecting treatment

The elderly is more difficult to treat due to:

- Presence of many comorbid conditions
- Polypharmacy – drug interactions with antibiotics and other medications already being taken
- Kidney problems that may impair drug clearance
- Higher likelihood of being hospitalized
- Higher morbidity and mortality

C. Prevention

- Annual flu vaccine should be given to adults 50 years and older, those with pre-existing illnesses, or anyone who would like to be vaccinated.
  - Pneumococcal vaccines should be given to adults 65 years and older.
  - Pneumococcal vaccine-naïve persons or those with unknown vaccine status should be administered PCV13, followed by PPSV23 at least 8 weeks later.
  - If PPSV23 was already given without prior PCV13 administration, PCV13 must be administered at least 1 year after the last dose of PPSV23. No additional dose of PPSV23 is needed.
  - If both vaccines were administered before the age of 65, PPSV23 must be readministered after the age of 65. No additional dose of PCV13 is needed.
- Proper handwashing is essential.

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OPEN FORUM HIGHLIGHTS

Moderator: MARIA CONCEPCION C. SISON, MD

Q: *Why is pneumonia prevalent in the Philippines?*
A: A great number of the elderly are not vaccinated.
Elderly have generally poor nutritional status.
There is poor access to healthcare.

Q: *Which type of pneumonia is most common in the elderly, and what is the most serious?*
A: The worst kind of pneumonia is hospital-acquired, because gram-negative organisms are involved. Stronger intravenous (IV) antibiotics are needed when gram-negative organisms are involved, which could impair kidney function. Additionally, they are very costly.

Q: *Should an elderly person with fever of unknown origin be suspected of having pneumonia?*
A: Yes, do cultures if possible, and treat appropriately.

Q: *When should a culture and sensitivity test be done?*
A: For outpatient-based patients, sputum culture and sensitivity studies are not recommended, unless the sputum is copious.
Empiric antibiotics are started immediately.
In the emergency room or inpatient setting, if the patient requires IV antibiotics, prior culture and sensitivity with gram staining is advised. If there is no phlegm, one may nebulize prior to collection of sputum.

Q: *Is there a way to disinfect the air we breathe, especially in the hospital?*
A: Healthcare workers are advised to get flu vaccination since they are exposed to people who are ill.

Q: *What is the best way to prevent hospital-acquired pneumonia?*
A: The easiest way is proper handwashing and make sure that white coats and stethoscopes are clean. Infection control should monitor ICUs and if needed, to shut down colonized hospital units.

Q: *Is there any way to boost the immune system e.g. herbal supplements?*
A: Eat properly to boost one's own immune system. Be active since lying down does not allow you to clear your airways and may predispose you to aspiration.

Q: *Does an existing lung condition aggravate or cause pneumonia to progress faster?*
A: Patients with chronic lung problems, like chronic bronchitis or COPD, are more susceptible to have the airways colonized by bacteria. This could aggravate or worsen pneumonia. Additionally, their conditions also make diagnosing pneumonia more difficult, because their chest x-rays are already abnormal. Lastly, the presence of pneumonia on top of a chronic lung disease would most likely lead to a flare of the chronic disease.

Q: *Does pulmonary hypertension contribute to the development of pneumonia?*

A: Pulmonary hypertension could predispose patients to pneumonia if it is due to chronic lung disease or with accompanying pulmonary congestion secondary to left-sided heart failure.

Q: *Is there a prophylactic antibiotic regimen for patients who are predisposed to, but do not have pneumonia, e.g. difficulty swallowing, stroke patients?*

A: We do not recommend prophylactic antibiotics, to prevent antibiotic resistance and creating a "superbug." Prophylactic use of broad-spectrum antibiotics may lead to colonization with methicillin-resistant *S. aureus* (MRSA), diarrhea due to *Clostridium dificile* colitis or even candidemia.
We only give chronic antibiotic courses, and on a rotating basis for chronic lung diseases such as chronic bronchitis and COPD.

Q: *What is the ideal recommendation for the two anti-pneumonia vaccines?*

A: Pneumococcal vaccines should be given to adults 65 years and older.
Pneumococcal vaccine naïve persons or those with unknown vaccine status should be administered with PCV13, followed by PPSV 23 at least 8 weeks later.
If PPSV 23 was already given without prior PCV 13 administration, PCV 13 must be administered at least 1 year after the last dose of PPSV 23 was received. No additional doses of PPSV 23 needed.
If both vaccines were administered before the age of 65, PPSV 23 must be re-administered after the age of 65. No additional doses of PCV 13 needed
The vaccines are also recommended to be given earlier than age 65 if the patient has comorbidities, such as cancer or diabetes mellitus.
An annual flu vaccine is also recommended.

Q: *What is the best time to administer the flu vaccine to an elderly patient?*

A: In the USA, administration is usually in the summer. In the Philippines, there is no recommended time since there are no 'flu seasons.' However, vaccine stock availability may dictate usage.

Q: *What is the duration of immunity from the flu and pneumonia vaccines?*

A: The flu vaccine is valid for one year while the pneumococcal vaccines provide lifetime protection.

Q: *Is it advisable to give pneumococcal vaccine to an immunocompromised patient?*

A: Yes, but follow vaccine guidelines and please work closely with infectious disease specialist.

Q: *For elderly psoriatic patients who will receive biologics, is there a need for flu and pneumococcal vaccines?*

A: Yes. The flu and pneumococcal vaccines are also recommended in younger patients who will receive biologics.

Q: *What is the recommendation for patients who are unsure of vaccination history?*

A: Administration of flu and pneumococcal vaccines is recommended.

Q: *At what temperature of fever do you advise to give empiric antibiotics?*

A: We cannot decide starting antibiotics based on the fever alone. The diagnosis of pneumonia is multifactorial. We must assess the whole person, including the medical history, not just the fever. Monitoring changes from day to day in an elderly patient is important.

REVIEW QUESTIONS

1. Who among the following patients may have pneumonia?
    a. 75 y/o, previously lucid and independent, normal to low WBC, now confused, doesn't know the day, you are called by the ER, normal respiratory rate
    b. 80 y/o, stopped eating one week ago, feels weak, no fever, no cough
    c. 85 y/o, with asthma exacerbation (wheezing), sitting in your clinic, temperature 37.6°C, normal WBC
    d. All of the above

2. Which of the following statements about pneumonia in the elderly is true?
    a. Prophylactic antibiotics may be given to high-risk individuals
    b. Elderly patients with pneumonia must be admitted to the hospital
    c. Flu and pneumococcal vaccines must be given annually to prevent pneumonia
    d. Sputum culture studies are advised prior to starting intravenous antibiotics

3. Which of the following statements about prevention of CAP in the elderly is true?
    a. Individuals aged 50 and older must receive pneumococcal vaccines
    b. Proper handwashing is not part of the recommendations to prevent CAP
    c. Individuals aged 50 and older must receive an annual flu vaccine
    d. Prophylactic antibiotics are advised

4. When should an elderly suspected to have pneumonia be admitted to the hospital?
    a. If presenting with fever
    b. At onset of weakness
    c. When intolerant of oral medication
    d. If with other comorbidities

5. Which of the following statement/s about the pneumococcal vaccines is/are true?
    a. Pneumococcal vaccine naïve persons or those with unknown vaccine status should be administered with PCV13, followed by PPSV23 at least 8 weeks later
    b. If PPSV23 was already given without prior PCV13 administration, PCV13 must be administered at least 1 year after the last dose of PPSV 23 was received. No additional doses of PPSV23 are needed
    c. If both vaccines were administered before the age of 65, PPSV23 must be readministered after the age of 65. No additional doses of PCV13 are needed
    d. All of the above

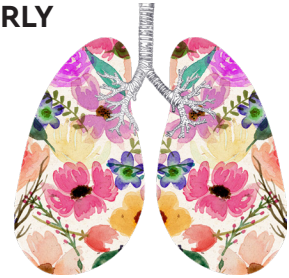
ANSWERS: 1. d; 2. d; 3. c; 4. c; 5. d

12 LUNG CANCER IN THE ELDERLY

Ma. Bella R. Siasoco, MD, FPCP, FPCCP

Delivered as a webinar on September 27, 2019

https://bit.ly/ALMW_Ch12_LungCancer



KEY POINTS

- Lung cancer is a disease of the ageing population and is the 2nd most common cancer in both sexes. The overall 5-year survival rate of 18% is the lowest among cancers and may be due to late diagnosis and lack of effective treatment even for early stages.
- Smoking cessation and annual screening with low-dose CT scan is recommended for high-risk individuals.
- Lung cancer may occur in non-smokers, often due to adenocarcinoma, and usually metastasizes early.
- Treatment for lung cancer, based on evidence-based guidelines, depends on the type and stage. Combination therapy is usually preferred and may consist of surgery, chemotherapy, radiation, and immunotherapy. However, data is limited for the elderly and those with comorbidities since they are underrepresented in clinical trials.
- Functional evaluation that assesses risk and mortality among older patients is critical for treatment planning. The Comprehensive Geriatric Assessment (CGA) is the current gold standard, while G8 is a brief screening tool.

LEARNING OBJECTIVES

- ➸ To review the epidemiology of lung cancer
- ➸ To identify the risk factors in the development of lung cancer
- ➸ To recognize why treatment strategies and prognosis differ in the elderly patient with lung cancer
- ➸ To outline current treatment options for the care of the elderly with lung cancer
- ➸ To identify tools that aid treatment prognostication of lung cancer in the elderly

I. EPIDEMIOLOGY

TABLE 12–1. Statistics on lung cancer

LUNG CANCER ACCOUNTS FOR:	
	• 13–14% of new cancer cases • 25–26% of all deaths • Top 2 cancer in both sexes • 5-year survival rate of 18% (As of 2018 Eastern Cooperative Oncology Group)[1]

TABLE 12–1. Statistics on lung cancer (cont.)

LUNG CANCER ACCOUNTS FOR:

- Increasing prevalence mortality in both sexes, despite prevalence going down worldwide[2,3]
- 11,000 deaths in 2017, making the Philippines ranked 72nd worldwide[4]

- Top 1 (men) and top 2 (women) cause of cancer deaths and disability-adjusted life years (DALYs) in 2017[5]

Sources:

[1]Siegel RL, Miller KD, Jemal A. Cancer Statistics , 2018. *Ca Cancer J Clin*. 2018;68(1):7-30.

[2]Wong MCS, Lao XQ, Ho K, Goggins WB, Tse SLA. Incidence and mortality of lung cancer: Global trends and association with socioeconomic status. *Sci Rep*. 2017;(October):1-9.

[3]Carioli G, Malvezzi M, Bertuccio P, et al. Cancer mortality and predictions for 2018 in selected Australasian countries and Russia. *Ann Oncol*. 2018:1-11.

[4]Global Life Partners. *Age-standardized Death Rate per 100,000 (Philippines).*

[5]Global Burden of Disease Cancer Collaboration. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2017: A Systematic Analysis for the Global Burden of Disease Study. *JAMA Oncol*. 2019;5(12):1749-1769.

- The median age at diagnosis is 70–75 years.
  - 68% of the patients are diagnosed after age 65.
  - 14% of lung cancers are diagnosed in patients >80 years of age.
- Longer life expectancy, not age per se, increases the number of older individuals at risk for developing lung cancer. There is no correlation between age and lung cancer.
  - Variations in lifetime chance of developing lung cancer reflect differences in baseline health, comorbidity and genetics. Those with highest life expectancy are those who may benefit most from chemotherapy (Table 12–2).
- Mortality from lung cancer in women far surpass breast cancer and may be due partly to lack of funding or social support given to lung cancer versus breast cancer.
- Mortality rates in the Philippines did not go down, compared to other countries (Australasian and Russia) (2018).[3]
- The high death rates due to lung cancer is not only because of late stage diagnosis but also due to the lack of effective treatments even for patients diagnosed with early stage I lung cancer.

TABLE 12–2. Life expectancy, lifetime chance of developing lung cancer, and median survival for untreated early stage lung cancer

	MALE	FEMALE
Life expectancy at age 75 (yrs.)	4.9 to 14.2	6.8 to 7.5
Lifetime chance of developing lung cancer	1 in 15	1 in 17
Median survival for elderly patients with untreated early stage lung cancer	14 months	

Sources: American Cancer Society. *Key Statistics on Lung Cancer.* https://www.cancer.org/cancer/lung-cancer/about/key-statistics.html. Published 2019. Accessed August 15, 2019[6]

Venuta F, Diso D, Onorati I, Anile M, Mantovani S, Rendina EA. Lung cancer in elderly patients. *J Thorac Dis*. 2016;8(I):S908-S914.[7]

II. RISK FACTORS, SCREENING AND PREVENTION

A. Risk factors

- *Cigarette smoking* is still the predominant risk factor for lung cancer.
- There are other causes such as radon and asbestos exposure or air pollution, and genetics.

B. Screening

- Elderly individuals at high risk for lung cancer can be screened, but this may be challenging (Table 12–3).[8]
- The patient's life expectancy, health, cognition, risk of disease, and preferences should guide screening decisions.
- Screening the elderly may be more effective, since they are thought to have slow-growing and more indolent bronchial cancers. In younger individuals, the disease is much more aggressive.[9] There is more time and opportunity to treat when we screen and diagnose the older population.

TABLE 12–3. Challenges in screening the elderly patient for cancer

CHALLENGES	REMARKS
Harm from screening	Older patients are frailer compared to younger, healthier individuals.
Overdiagnosis that may lead to overtreatment	Especially in elderly with comorbidities, poor health or short life expectancy
Difficulty in obtaining informed consent	Due to cognitive impairment or poor education
Distress from 'diagnostic cascade'	Especially after a positive test
May eclipse other health issues	Issues such as reducing polypharmacy, healthy behavior counseling, and fall prevention

Source: Kotwal A, Schonberg M. Cancer screening in the elderly: A review of breast, colorectal, lung, and prostate cancer screening. *Cancer J.* 2017;23(4):246-253.[10]

TABLE 12–4. Recommendations for annual screening

RECOMMENDED	NOT RECOMMENDED
Annual screening with low-dose CT scan • For smokers and former smokers • Age 55 to 74 • Have smoked for 30 pack-years or more and either continue to smoke or have quit within the past 15 years	• Screening for lung cancer with CXR once or at regular intervals • Screening for lung cancer with sputum cytology

CT, Computed tomography; CXR, Chest x-ray

C. Prevention

STOP SMOKING!

TABLE 12–5. Strategies for smoking cessation

STRATEGY	RECOMMENDATIONS
Counseling and pharmacotherapy	• Current smokers with demonstrated smoking related pulmonary disease • Lung cancer patients undergoing radiotherapy
Cessation pharmacotherapy	• Lung cancer patients undergoing surgery; if either contraindicated or refused, cessation counseling alone during the perioperative period (initiated in the pre-operative period) • Lung cancer patients with depressive symptoms (with bupropion)

TABLE 12–6. Substances NOT proven to prevent lung cancer

1. β-carotene
2. Vitamin E
3. Retinoids
4. N-acetylcysteine
5. Aspirin
6. Selenium
7. Prostacyclin analogs (iloprost)
8. Cyclooxygenase-2 inhibitors (celecoxib)
9. Anethole dithiolethione
10. Inhaled steroids
11. Pioglitazone
12. Myoinositol
13. Tea extract
14. Metformin

III. HISTOLOGIC CLASSIFICATION

- Lung cancer is classified into small cell (SCLC) (15%) and non-small cell lung cancer (NSCLC) (85%) (Figure 12–1).
- Adenocarcinoma, the most common histological type of NSCLC, comprises half of all lung cancers, and is found commonly in non-smokers.[11]
- Since there is a lack of awareness that lung cancer can occur in non-smokers, and adenocarcinoma develops in the periphery of the lung, it is often diagnosed late or in the less treatable stage of the disease.
- Genetic mutations that exist in some lung cancers can be used as biomarkers for early diagnosis, targeted treatment and prognostication.

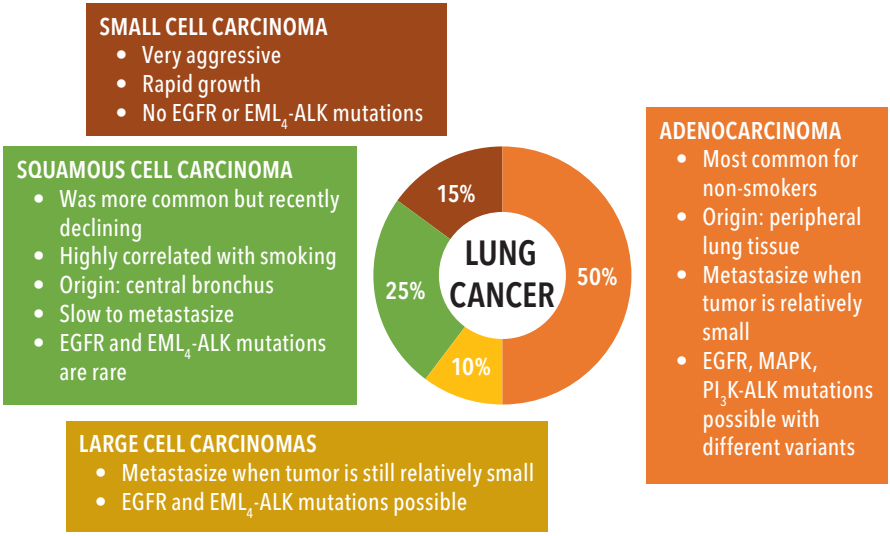


FIGURE 12–1. Prevalence and characteristics of lung cancers

ALK, Anaphylactic lymphoma kinase
eGFR, Epidermal growth factor receptor
EML_4-ALK, Echinoderm microtubule-associated protein-like 4
MAPK, Mitogen associated protein kinase
PI_3K, Phosphatidyl-inositol$_3$ kinase

IV. TREATMENT OF LUNG CANCER IN THE ELDERLY

A. Challenges in Treatment of the Elderly with Cancer:

- There are physiologic changes associated with ageing that lead to decline in organ function, affecting outcomes with treatment (Table 12–7).
- Ironically, these changes may also be the same factors that exclude patients from clinical studies that may benefit them.
- Health status and functional reserve also vary significantly in senior adults, making chronologic age alone an unreliable predictor of the risk for treatment complications.[12]
- Comorbidities may determine appropriateness of chemotherapy in individual patients.[13]
  - More than half of patients with lung cancer (57%) had comorbidities, most commonly, chronic obstructive pulmonary disease and cardiovascular disease.
  - Survival in advanced stages of lung cancer, independent of the patient's age, is negatively affected by the presence of at least two comorbidities.
- Post-treatment burden is highest in those with more comorbidities who undergo treatment.
  - Day-to-day quality of life can be greatly improved by reducing the number of visits, scheduling them on the same days, and reducing redundant laboratory tests and medications.

TABLE 12–7. Physiologic changes in older age

1. Decreased kidney function or liver function
2. Lower lean body mass – more susceptible to effects of weight loss, such as cachexia, with certain treatments
3. Lower bone marrow reserve – more prone to complications from chemotherapy-related bone marrow suppression
4. Increased body fat
5. Reduced total body water
6. Change in the gastrointestinal system
7. Comorbidities
8. Polypharmacy
9. Pharmacologic consequences – especially with drugs requiring conversion to active metabolites

B. Treatment Options

- Age-related differences should be immaterial in terms of deciding treatment options in the younger versus the senior age group.
- Treatment options depend on histologic type and stage of lung cancer.
  - Surgery
  - Radiation therapy
  - Chemotherapy
  - Targeted therapy
- Lung cancer is usually treated with a combination of therapies.
- SCLC is difficult to cure even if highly responsive to chemotherapy and radiation therapy since it is often widely disseminated by the time of diagnosis. In contrast, NSCLC is highly resistant to anticancer drugs.[14]

TABLE 12–8. Treatment of lung cancer based on type and stage

TYPE/STAGE OF LUNG CANCER	TNM STAGE 8TH ED.	% of CASES	TREATMENT	REMARKS
Non-small cell (NSCLC)				
Early disease stage	IA, IB	30%	Surgical resection *If positive margins: Re-resection OR Radiation +/- Chemotherapy	For surgery:[8] • Limited resections and omission of systematic mediastinal lymphadenectomy can be considered in the elderly on the basis of retrospective data. • Video-assisted thoracoscopic surgery (VATS) is preferred over pneumonectomy for elderly since it is associated with lower incidence of postoperative mortality and morbidity.
	IIA, IIB Operable)		Surgery + Adjuvant Chemotherapy	Platinum-based: Cisplatin + Vinorelbine
	IIA, IIB (Inoperable)		Chemotherapy + Radiation	• Cisplatin + Etoposide or Pemetrexed • Stereotactic Ablative Body Radiation (SABR) is preferred over conventional radiotherapy.

TABLE 12–8. Treatment of lung cancer based on type and stage (cont.)

TYPE/STAGE OF LUNG CANCER	TNM STAGE 8TH ED.	% of CASES	TREATMENT	REMARKS
Locally advanced	IIIA (Operable)	20%	Surgery + Chemotherapy	Chemoradiation therapy is an option for fit older patients.
	IIIA (Inoperable)		Chemotherapy + Radiation	
Regionally advanced	IIIB		Chemotherapy + Radiation Second line: Immunotherapy	Targeted immunotherapy using an anti–programmed death-1 monoclonal antibody is utilized in patients whose tumors express certain genetic mutations, such as epidermal growth factor receptor exon 19 deletions, exon 21 (L858R) substitution mutations or anaplastic lymphoma kinase–positive mutations.
With distant metastasis	IV	50%	Chemotherapy or Radiation	For palliation: Fit elderly: Carboplatin-based doublets For less fit: Single agent (gemcitabine, vinorelbine, taxanes)
Small cell (SCLC)				
Limited disease	T any, N any, M0; except T3-4 due to multiple lung nodules that do not fit in a tolerable radiation field	67%	Chemotherapy + Radiation	Etoposide + Cisplatin or Carboplatin
Extensive disease	T any, N any, M1 a/b; T3-4 due to multiple lung nodules	33%	Combination chemotherapy	For palliation: Etoposide + Cisplatin or Carboplatin

Sources:

Pallis AG, Gridelli C, Wedding U, et al. Management of elderly patients with NSCLC; updated expert's opinion paper: EORTC elderly task force, lung cancer group and international society for geriatric oncology. *Ann Oncol*. 2014;25(7):1270-1283.[9]

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V. GERIATRIC ASSESSMENT

- Age should not be the main basis for treatments that can be used for lung cancer.
- However, although the treatment benefits are not reduced due to age, older adults may not tolerate some treatments as well as younger patients can.
- A geriatric assessment is critical for individualized treatment to lessen the risk of over- or under-treatment.

TABLE 12–9. Commonly used geriatric assessment tools

TOOL	DESCRIPTION	GOALS	ADVANTAGES	DOMAINS/ITEMS
Comprehensive Geriatric Assessment (CGA)[18]	Multidisciplinary diagnostic and treatment process that identifies medical, psychosocial, and functional limitations of a frail older person	• To estimate life expectancy • To determine functional age • To identify patients at risk for functional decline or toxicity due to treatment • To catch undetected health problems • To improve outcome and patients' compliance	• Decreased overtreatment of frail older patients, and increased undertreatment of fit older patients • Uncover issues and circumstances of the older patient's life that are routinely assessed just based on their age or on ECOG or Karnofsky performance status	1. Cognitive status 2. Functional status 3. Comorbidity 4. Nutritional status 5. Mood 6. Medication review 7. Environment review 8. Social supports
Geriatric 8 (G8) Health Status Screening Tool[19]	Brief screening tool	To determine which elderly cancer patient will benefit from comprehensive geriatric assessment	• Rational use of health care resources • Spares the patient from unnecessary clinical and biological examination	1. Food intake 2. Weight loss 3. Mobility 4. Neuropsychological problems 5. Body mass index 6. Drugs 7. Health status 8. Age

ECOG, Eastern Cooperative Oncology Group

Sources:

Wildiers H, Heeren P, Puts M, et al. International society of geriatric oncology consensus on geriatric assessment in older patients with cancer. *J Clin Oncol*. 2014;32(24):2595-2603.[18]

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OPEN FORUM HIGHLIGHTS

Moderator: MITHI KALAYAAN S. ZAMORA, MD

Q: *After how many years of smoking cessation does the risk of developing lung cancer decrease?*

A: Generally, it's difficult to answer. We say years and years and decades. The arbitrary number is 15 years. But there are so many patients who develop lung cancer even beyond 15 years after smoking cessation. The sooner the patient stops smoking, the better. The younger, the better. The best intervention is to never start smoking.

Q: *Please expound on the risk of developing lung cancer in persons exposed to air pollution.*

A: Secondhand cigarette smoking undoubtedly causes it. The next most common cause is radon exposure. In the United States, radon is a byproduct of uranium which is in the soil and it creeps through the cement base of many of the infrastructures. In the Philippines, usage of biofuels is a common cause, particularly in female nonsmokers. We should emphasize that nonsmokers can develop lung cancer. Environmental exposures could predispose individuals to develop lung cancers.

Q: *What other behavioral changes can help reduce the risk of developing lung cancer?*

A: In European and American studies, they suggest testing the house for radon or uranium byproducts. We do know there are implicated environmental factors, such as air pollution. The knowledge is still developing and definite prevention measures have not yet reached maturity.

Q: *For resource-limited communities, what is the most cost-effective screening tool? What can push healthcare providers to opt for low-dose CT scan for their patients, rather than the cheaper chest x-ray?*

A: Low-dose CT scan is not for everybody but it will still be more expensive to screen patients with modalities that are not really sensitive, such as the chest x-ray and sputum cytology. Doing these on a yearly basis is going to be more costly than beneficial. The best argument to encourage the use of low-dose CT scan is that, the initial capital outlay may seem expensive but if the diagnosis is established early by low-dose CT scan, and government subsidizes treatment for early stage lung cancer, the benefits far outweigh the cost of undergoing low-dose CT scan.

One should have a high index of suspicion. A good history and physical examination should be conducted to identify those at high risk for lung cancer. Should suspicion be raised, one should get details (such as when patient stopped, how old is patient now), and then emphasize the benefit of doing a low-dose CT scan in that particular population.

Q: *Can you give us a rough idea of the financial burden of treatment of early and late-stage lung cancer in the Philippines with all modalities mentioned earlier?*

A: For early stage, surgery is still the treatment of choice, but cost depends on the institution (government or private). In the Philippines, healthcare is out-of-pocket. There are, however, clinical trials in both types of institutions that may allow the enrollment of patients.

In the advanced stage, immunotherapy using targeted therapy is available. For lung cancer, a new drug

was approved two months ago. The cost is very high but the improvement in the quality of life is immediate. I had a patient who took the drug, and there was a marked reduction in difficulty of breathing the day after therapy. The ensuing hope that it generates in the patient is, in itself, immeasurable.

Emphasis is on early detection and early diagnosis. There are survivors with advanced lung cancer who are now on their 14th year.

Q: *In what subset of population do you recommend surgery? What are the characteristics of good candidates for surgery?*

A: The tumor has to be well-localized or with a localized node metastasis that the surgeon can identify and hopefully take out completely. In stage 1 lung cancer, chemotherapy would not even be offered. Once the tumor reaches stage 2, combined modality treatment is preferred.

Q: *Which comes first–chemotherapy or surgery?*

A: If it is only localized, surgery generally comes first. If it is localized, but of significant size (for example, if it is compressing a nearby structure), neoadjuvant chemotherapy (sometimes with radiation therapy), may be needed to 'shrink' the lesion for easier excision. If diagnostic tests suggest that the lesion is localized, but it is believed that some cancer may have been left behind during surgery, adjuvant chemotherapy (chemotherapy given after surgery) is given.

Q: *Is it unethical to offer symptomatic treatment versus more aggressive management in an elderly patient with multiple comorbidities, poor quality of life and limited life expectancy?*

A: I think it is unethical to let our biases influence the information we give our patient. I think we should present to our patient the whole vista and not just what we think they should undergo. The patient is the decision-maker. Our responsibility is to help him make the decision that is right for him. I think that the ethical caregiver is one who is informed about the options, and informs the patient regarding the complications. Well-informed patients will ask questions and the caregiver should be prepared to answer them.

Q: *A breast cancer patient has bilateral pleural effusion. Is this a sign of lung metastasis? Is surgery still an option if patient has bone metastasis?*

Is this a sign of lung metastasis?

A: If the cancer is not in remission, has not been treated or has been incompletely treated, the appearance of pleural effusion in the patient MAY be suspected to be an indication of the spread to and involvement of the pleura by the cancer. Diagnostic studies (e.g., pleural fluid cell block and cytology, chest CT scan) need to be done to prove that it is indeed a spread of the breast cancer and rule out other conditions such as pneumonia or tuberculosis. Also, while it is not a frequent occurrence, the fluid may also be caused by cancer from another focus, such as the lung.

Q: *Is surgery still an option if patient has bone metastasis?*

A: The presence of metastatic foci means that the primary cancer has become bloodborne; this means that cancer cells had a chance to go all over the body. Thus, it would not be practical or beneficial to the patient to attempt to "take out" all involved areas since all areas are potentially involved already! IF surgery is to be done, it would be for palliative purposes, such as stabilization of collapsed vertebrae, removal of infected tissue, or pain control.

Q: *What is your advice for patients wanting to take traditional or alternative medicine alone or in combination with the recommended medical regimen for lung cancer?*

A: I'm not too sold on alternative medicine. In terms of chemoprevention, many of the nontherapeutic interventions have no or very limited data to support their use alone. However, as a complement to the evidence-based regimens, they can be used to control symptoms, such as vomiting or pain: but not to address the tumor or the metastasis.

Q: *What is the quality of life of older patients with lung cancer? How will the side effects and complications of these therapies affect the quality of life?*

A: Although there is some limitation in daily activities, the quality of life is mainly a function of the patient's outlook, which is influenced by the information given by the healthcare provider and the support of the family. Prior to the intervention, whether it be radiation, surgery or immunotherapy, the patient and the family have to be well prepared and informed. They should undergo therapeutic intervention knowing fully well what may happen. For those who are well prepared, some are really eager to resume their previous lifestyle rather than being depressed and just staying at home.

REVIEW QUESTIONS

1. Which is the most common type of lung cancer?
   a. Adenocarcinoma
   b. Squamous cell carcinoma
   c. Small cell carcinoma
   d. Large cell carcinoma

2. In which step in management can biomarkers for lung cancer be potentially used?
   a. Diagnosis
   b. Prognosis
   c. Prediction of outcome
   d. All of the above

3. Which is true of the Geriatric 8 (G8) Health Status Screening Tool?
   a. Identifies elderly cancer patients who would benefit from comprehensive geriatric assessment (CGA)
   b. Identifies patients who are at risk for chemotherapy toxicity
   c. Identifies risk of metastasis of lung cancer
   d. Used in staging the lung cancer

4. Which is a physiologic change in the elderly patient with lung cancer that may affect treatment response?
   a. Decreased kidney function or liver function
   b. Greater lean body mass
   c. Greater bone marrow reserve
   d. Decreased body fat

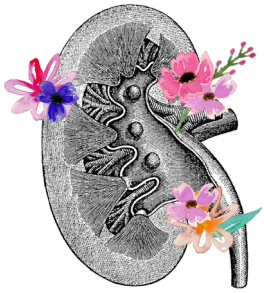
5. Which is the treatment of choice in early stage lung cancer in the elderly?
   a. No treatment
   b. Limited resection
   c. Pneumonectomy
   d. Immunotherapy

ANSWERS: 1. a; 2. d; 3. a; 4. a; 5. b

13 DIABETIC NEPHROPATHY: OPD MANAGEMENT

Agnes D. Mejia, MD, FPCP, FPSN

Delivered as a webinar on February 22, 2019
https://bit.ly/ALMW_Ch13_DiabeticNephropathy



KEY POINTS

- Diabetic nephropathy can result from longstanding uncontrolled diabetes. It must be diagnosed early to prevent its progression.
- There should be a high index of suspicion for diabetic nephropathy, especially if there is eye involvement.
- Urinalysis and serum creatinine should be used to screen patients with diabetes, followed by renal ultrasound if indicated.
- Supplements should be used with extreme caution, particularly in patients on dialysis.

LEARNING OBJECTIVES

- ➸ Discuss the natural history and clinical presentation of diabetic kidney diseases using a case-based format
- ➸ Get an overview on the different diagnostic tools used in the evaluation of the presence and progression of diabetic nephropathy
- ➸ Outline the options for clinical management for diabetic kidney diseases

I. OVERVIEW

There are five stages of diabetic nephropathy (Figure 13–1).[1]

a. In the prediabetic stage (stages 1 and 2), glomerular filtration rate (GFR) is increased and glomeruli are hypertrophied.
b. In Stage 3 (incipient) diabetic nephropathy, there is microalbuminuria, hypertension, thickened glomerular basement membrane, and mesangial expansion.
c. In Stage 4 or 5, there is overt proteinuria and decreased GFR up to the point of end-stage renal disease.

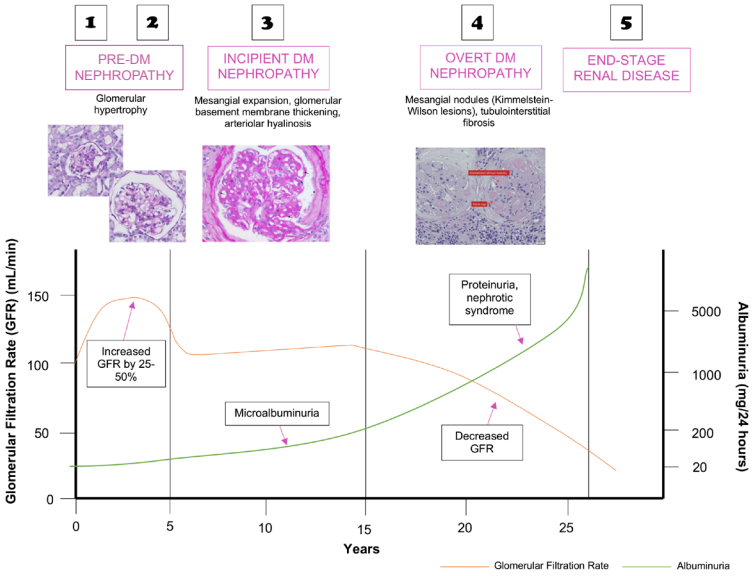


FIGURE 13–1. Stages of diabetic nephropathy

DM, Diabetes mellitus; GFR, Glomerular filtration rate

Source: Feehally J, Floege J, Johson RJ and Tonelli M. *Comprehensive Clinical Nephrology* 4th ed. 2010. Elsevier: Amsterdam, Netherlands.

Photos from:

"Diabetic nephropathy" by B. Vujičić, et al. 2012, In: Oluwafemi Oguntibeju, ed. *Pathophysiology and Complications of Diabetes Mellitus*, p.74. © 2012 Authors, licensee InTech (Attribution 3.0 Unported [CC BY 3.0]).[2]

"Comprehensive approach to diabetic nephropathy" by B. Satirapoj and S.G. Adler, 2014, *Kidney Res Clin Pract*, 33, p.124.© 2014 The Korean Society of Nephrology (CC BY-NC-ND 4.0).[3]

"Rapid decline of renal function in patients with type 2 diabetes with heavy proteinuria: A report of three cases" by C. Thiam et al, 2019, *BMC Nephrology*, 20, p.3. © 2019 Authors (CC BY 4.0).[4]

II. CASE 1: TYPE 1 DIABETIC NEPHROPATHY

- Patient X, 32 y/o, female, office employee
- Type 1 diabetes mellitus (DM) since 17 y/o, normal blood pressure (BP)
- **1st consult** in July 2015
  - (+) foamy urine
  - (+) weight gain
  - Rapid increase in serum creatinine to 287 mmol/L, from previous of 94 mmol/L taken 7 months ago
  - 24-hour total urine protein 2.68 g
  - Creatinine clearance 28 ml/min
- Based on the natural history of DM nephropathy, 7 months is too rapid to develop progressive renal failure, unless she had other events that contributed to this deterioration.

TABLE 13–1. Review of history and laboratory examination results (Patient X)	
November 2011	2D echo: 60% EF Normal KUB UTZ Normal BP (–) urine protein
December 2013	Fluorescein angiography: No microaneurysms, hemorrhages, or signs of neovascularization
March 2014	(+) 4 proteinuria Normal thyroid UTZ
July–September 2014	Minoxidil cream
August 2014	Esophagitis
November 2014	Serum creatinine 94 mmol/L
February 2015	Meniere's disease Videonystagmography test • Central vestibular disorder with concurrent peripheral positional disorder • Vestibular migraine with BPPV Cranial MRI: normal
March 2015	Sudden blurring of vision Macular edema, laser treatment Increase in serum creatinine

EF, Ejection fraction; KUB, Kidney Ureter Bladder; UTZ Ultrasound; BPVV, Benign paroxysmal positional vertigo

Clinical course:

- Her serum creatinine continued to increase, with a decrease in normalized GFR to 15.8 ml/min from a previous value of 28 ml/min. Renal scan (September 2015) was unremarkable and urinalysis showed nephrotic pattern (Table 13–2).

TABLE 13–2. Series of urinalysis results (Patient X)				
	11/17/14	**7/15**	**8/03/15**	**8/30/15**
Specific Gravity	1.040	1.016	1.020	1.017
pH	6	6	7	6.5
Protein	+4	+3	+3	+3
Glucose	+4	+1	+1	Negative
RBC	2	3–5	6–11	4–6
WBC	80	35–40	32–38	6–8

RBC, Red blood cell; WBC, White blood cell

- The plot of serum creatinine levels and GFR from November 2014 to the time of kidney transplant (May 2017) is shown in Figure 13–2.

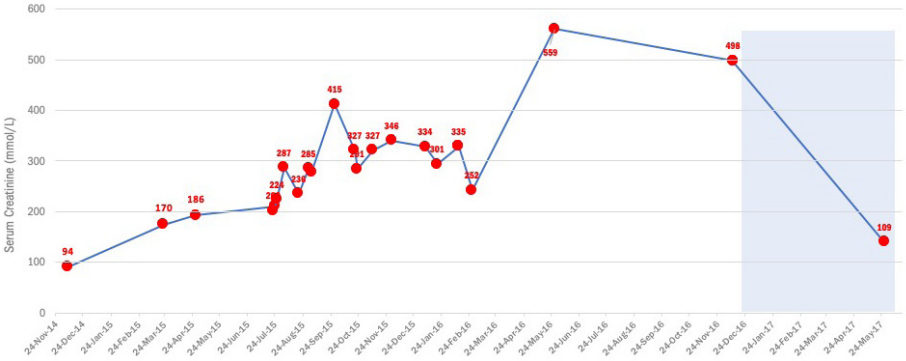


FIGURE 13–2. Plot of creatinine level and GFR until renal transplant (Patient X)

Question 1: Is this rapidly progressive glomerulonephritis (RPGN) due to non-DM glomerular disease?

- Based on the patient's urinalysis, she is not badly nephritic (RBC is not too high), but she is definitely nephrotic.
- The rapid deterioration of renal function would make one think of RPGN that may be due to non-DM glomerular disease, but the urinalysis results do not support this.

Kidney Biopsy

- No RPGN noted
- **Nodular glomerulosclerosis compatible with diabetic nephropathy** – 56% global glomerulosclerosis (19 of 34 glomeruli) and 6% segmental glomerulosclerosis (2 of 34 glomeruli)
  - Marked interstitial fibrosis and tubular atrophy
  - Moderate arteriosclerosis and moderate hyaline arteriosclerosis
  - Focal acute tubular injury

Question 2: Is this an accelerated atherosclerosis in a patient with Type 1 diabetes?

- December 2013 – Fluorescein angiography: No microaneurysms, hemorrhages or signs of neovascularization
- March 2015 – Sudden blurring of vision

TABLE 13–3. Summary of visual assessments and procedures (Patient X)

DATE (2015)	FINDINGS/ASSESSMENT	PROCEDURE	VISUAL ACUITY
February 26	Severe non-proliferative diabetic retinopathy		Right eye: 20/160 Left eye: 20/40
March 3		Both eyes: Pan retinal photocoagulation laser	
March 28		Both eyes: Intraocular bevacizumab 2.25 mg/ml (one week apart)	Right eye: 20/30 Left eye: 20/30
June 18	Right eye: Venous beading Vitreous heme Multiple intra-retinal heme Cotton wool spots Intra-retinal micro-angiopathies Left eye: Multiple intra-retinal heme Cotton wool spots		
August 11	Left eye: now with vitreous heme **Diagnosis:** Proliferative diabetic retinopathy		
September 1	Right eye: Increasing vitreous heme, fibrovascular proliferation (Figure 13–3) Left eye: increasing vitreous heme Rapid severe worsening with vitreous hemorrhage **Management:** Right eye: for surgery		Right eye: 20/100 Left eye: 20/40
September 10	Both eyes: No view of the fundus		Both eyes: 20/160
October 29	**Management:** Surgery for both eyes at NKTI		

NKTI, National Kidney and Transplant Institute

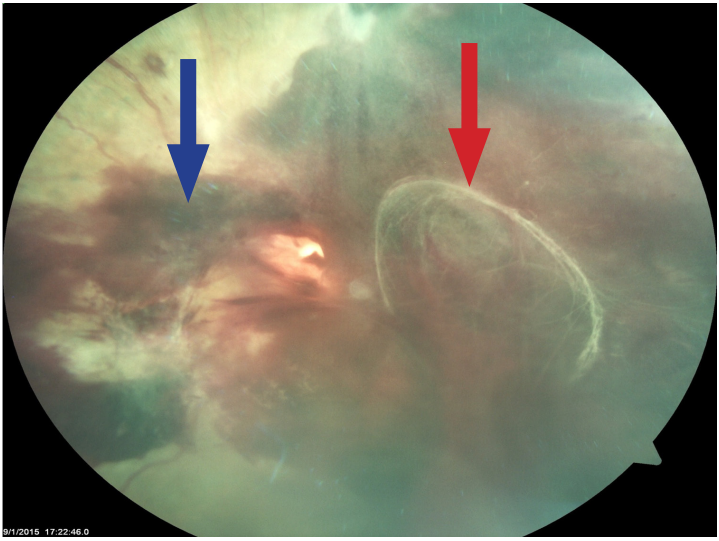


FIGURE 13–3. Retinal fundoscopy of right eye of patient X showing increasing vitreous heme (blue arrow), and fibrovascular proliferation (red arrow) (September 1, 2015). (Courtesy of Dr. Milagros Arroyo with permission)

Retinal findings: Cotton wool spots, microangiopathy, vitreous hemorrhage, and venous bleeding → Diagnosis: Proliferative diabetic retinopathy

- Accelerated Atherosclerosis in Diabetes
  - Diabetes is associated with an increased risk of arterial occlusive disease in the coronary, cerebral, and peripheral vascular beds (i.e., eyes).
  - Diabetes is associated with increased prevalence of unstable inflammatory and lipid-rich plaques.
  - Hyperglycemia directly or indirectly, has the following effects on the vascular wall:[5]
    - Macrophage lipid uptake leading to foam cell formation
    - Endothelial dysfunction
    - Increased platelet activity
    - Increased proteolytic activity
    - Glycation of extracellular matrix
    - Stimulation of smooth muscle cell proliferation
    - Increased inflammatory activity
- In summary, patient X is a case of type 1 diabetic nephropathy (stage 5) with accelerated atherosclerosis. She underwent hemodialysis and kidney transplant. Eye surgeries also enabled her to see and do computer work in the office.

III. CASE 2: TYPE 2 DIABETIC NEPHROPATHY

- Patient Y, 57 y/o, retired employee
- Type 2 DM (1996); HTN (2003); CKD with diffuse parenchymal disease (2011)
- S/P Retinal laser photocoagulation 2x (2008, 2011)

- Clue: If patient underwent therapy for DM retinopathy, it is highly likely that patient also has diabetic nephropathy (microvascular disease).
- Family history: 5 (of 7 siblings) with DM and on insulin; 1 had an acute MI

Clinical course

- Patient's serum creatinine slowly increased over 6 years. HbA1c, a marker of diabetic control, was poorly controlled (Figure 13–4).

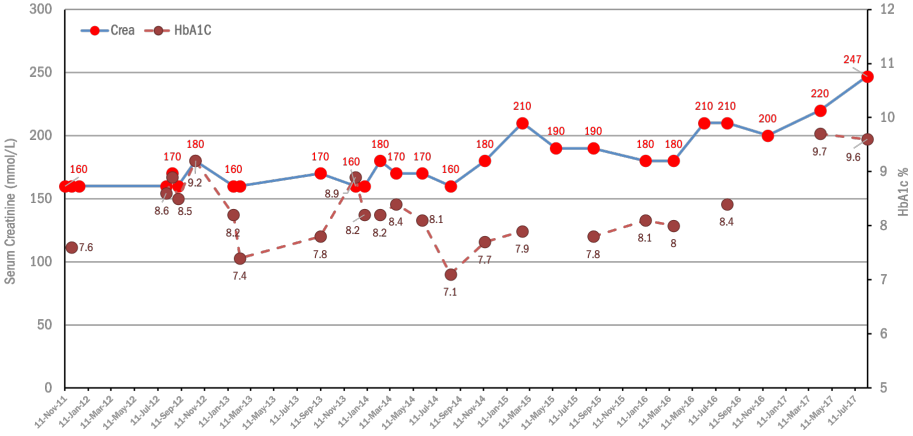


FIGURE 13–4. Progression of serum creatinine vs HbA1c (Patient Y)

- Patient's BP was poorly controlled (Figure 13–5).

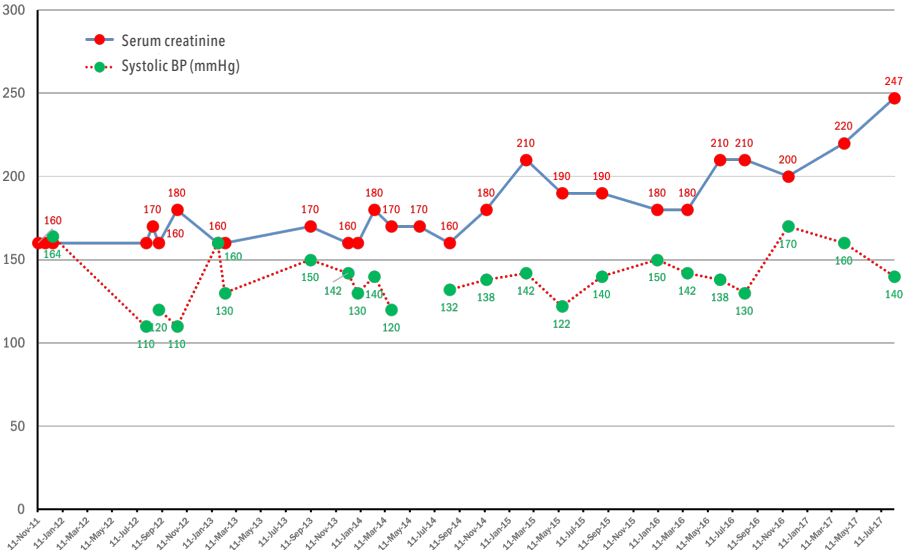


FIGURE 13–5. Serum creatinine vs Systolic BP (Patient Y)

- Due to poor control of blood sugar and blood pressure, there was onset of overt proteinuria in this patient. Patient's 24-hour total urine protein reached as high as 5.32 g (Figure 13–6)

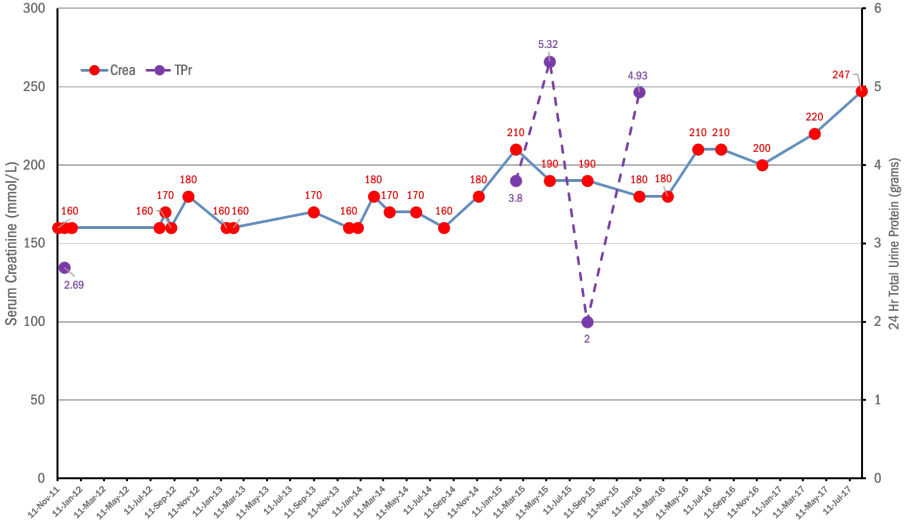


FIGURE 13–6. Serum creatinine vs 24-hour total urine protein (Patient Y)

- If protein is increased (>300 mg/g), there is a high chance of developing kidney failure (4+), based on composite ranking for relative risks by GFR and albuminuria.[6] The goal is to convert the high protein to normal or less than 1g.
- Summary on use of renin-angiotensin-aldosterone system (RAAS) blockers (Evidence-based):
  - No data supporting additional benefit on CKD outcome in patients with normo- or microalbuminuria over BP control
    - No data to support advantage on CKD outcome in elderly without proteinuria
    - Only place where there is definitive data for RAAS blockers to slow diabetic nephropathy is in advanced proteinuric disease
    - **First and foremost, blood pressure should be controlled.** Any antihypertensive drug can be used if there is no proteinuria.
  - A multifactorial intervention strategy is recommended in diabetic kidney disease (DKD)
    - HbA1c target individualized, but generally ~7%[7]
      - Intensive glucose control reduces risk of micro- and macro-albuminuria.[8]
      - Ten years after pancreatic transplant in a 33 y/o woman with type 1 DM for 17 years, normal sugar improved the diabetic nephropathy and showed a normal kidney biopsy.[9]
    - BP target of <130/80 mmHg[10]
      - Lower blood pressure is associated with lower frequency of renal events in type 2 DM[11]
    - Use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) when albumin excretion exceeds 30 mg/g

- ACE inhibitors slow the progression of albuminuria and renal function decline in patients with type 2 DM.[12]
- ARBs have demonstrated beneficial impact on markers of kidney disease.[13,14]

- Statins are recommended to reduce risk of atherosclerotic events in patients with CKD but not in patients on hemodialysis.[7]
- Attaining multiple treatment targets is associated with lower risk of end-stage renal disease (ESRD) and related death in type 2 DM by as much as 60%.[15]
  - HbA1c <7%
  - BP <130/80 mmHg
  - LDL-C <2.6 mmol/L (100 mg/dL)
  - Triglyceride <2 mmol/L (177 mg/dL)
  - Use of RAS inhibitors

- In summary: Patient Y, who has type 2 diabetes and stage 4 diabetic nephropathy, requires good blood pressure and blood sugar management, use of dual RAAS blockade to control proteinuria if necessary, and proper patient education.

IV. CASE 3: ATHEROSCLEROTIC RENAL ARTERY SCLEROSIS

- Patient Z, 67 y/o, male, lawyer
- With DM and hypertension >10 years
- S/P Retinal laser photocoagulation, 3 sessions, 2017
- On insulin >10 years
- ARB >2 years
- 24-hour urine total protein = 4.8 g (September 2016)
- Referred for clearance for cataract surgery
- High serum creatinine of 600 unit (mmol/L) (from previous of 117 a year ago) (Figure 13–7) (Table 13–4)

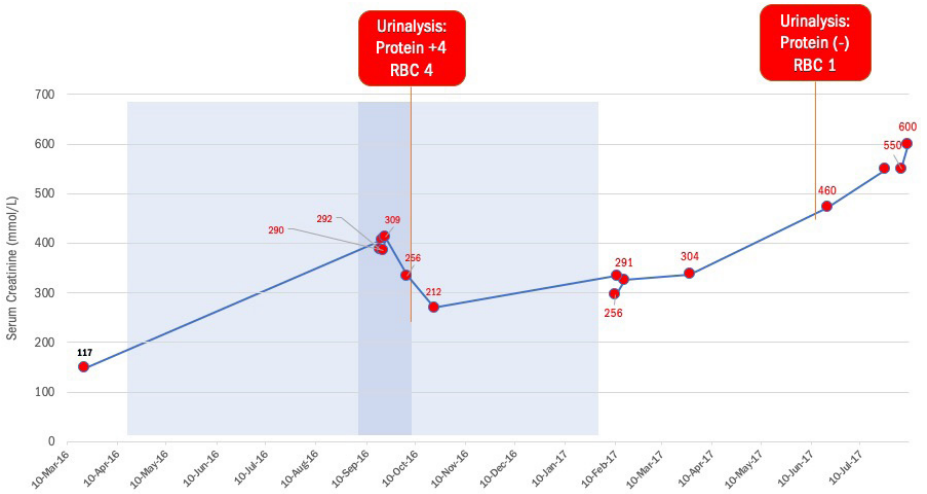


FIGURE 13–7. Trend for serum creatinine levels and urine protein/RBC (Patient Z)

TABLE 13–4. Summary of diagnostics (Patient Z)

LABORATORY EXAM	RESULT
Serum creatinine	600 mmol/L
Urinalysis	No RBC, No protein
GFR scan	
Left	8.3 ml/min
Right	5.7 ml/min
Normalized	13.7 ml/min
CT stonogram	Normal kidney size, no lithiasis
2D echo with Doppler	EF 46% with some hypokinesia (by Simpson's)

- On physical exam of the feet, there was mottling, which was assessed as cholesterol embolization. Its clinical outcome is similar to atherosclerotic renal artery disease (Figure 13–8).

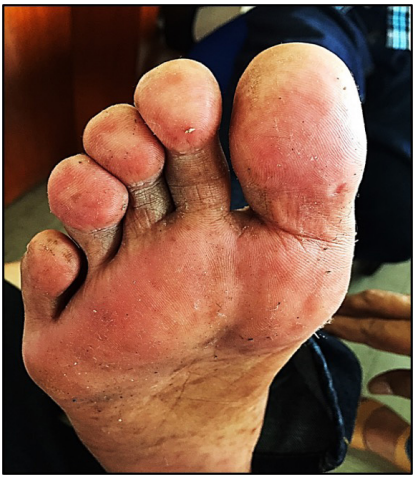


FIGURE 13–8. Photo of mottling on right foot of Patient Z

- The prevalence of renal artery narrowing (50% or greater) is 16.4% over the age of 60 years (Table 13–5).

TABLE 13–5. Prevalence of atherosclerotic renal artery stenosis

STUDY POPULATION	PREVALENCE OF NARROWING OF 50% OR GREATER (%)
Autopsy	11-42
Under age 60	5.5
Over age 60	16.4
During cardiac catheterization	
(+) coronary stenosis	29
(–) coronary stenosis	10
During aortic angiography	
Aortic aneurysm	38
Aortic occlusive disease	33
Lower limb occlusive disease	39

** Populations at risk are shown in red font*

Source: Chonchol M, Linas S. Diagnosis and management of ischemic nephropathy. *Clin J Am Soc Nephrol*. 2006;(1):172-181.[16]

- For the patient, there was no imaging proof that there was renal artery stenosis; but the kidneys were not of equal size. The patient most likely had atheroembolism.
- Risk of atrophy in kidneys with atherosclerotic renal artery stenosis[17]
    - "Atrophy" = loss of 1 cm in length
    - N = 204 kidneys in 122 patients followed 33 months
    - Risk factors: SBP >180 mmHg, renal artery peak SV >400 cm/s, reduced renal cortical end-diastolic velocity
    - Rise in creatinine infrequent
- In summary, patient Z had an acute injury secondary to cholesterol embolization and was started on dialysis.

V. CLINICAL MANAGEMENT OF DKD

A. Best understanding of DKD

- Getting detailed history is important. Look at the patients' records.
- Do proper physical examination.
- Do not rely on diagnostics alone.

B. Histopathology of DKD

- Includes:
    - Diabetic nephropathy
    - Atheroembolic disease
    - Ischemic nephropathy
    - Interstitial fibrosis
- In type 2 DM, the histopathologic changes in DKD are not just due to microangiopathy.
    - Ageing
    - Atherosclerosis
    - Hypertension
    - Episode of Acute Kidney Injury (AKI)

C. Burden of DKD

- Metabolic syndrome prevalence in the Philippines increased from 18.6% to 27.4% from 2003 to 2008.[18]
- Overall prevalence of hypertension in the Philippines is 25.4% and as high as 57.2% above age of 70.[18]
- Overall prevalence of diabetes is 7.1%.[18]
- The national incidence and prevalence of dialysis patients are rising from 2001 to 2015.[19]
    - Among the causes of dialysis from 2001 to 2013 are diabetes, hypertension, and inflammation, in order of decreasing prevalence.
- In the U.S., diabetes is the leading cause of end-stage renal disease,[20] similar to that of the Philippine situation.

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OPEN FORUM HIGHLIGHTS

Moderator: ANNA YORK P. BONDOC, MD

Q: *When you encounter a patient with diabetes in your clinic for the first time, what is the first thing that you would suggest and how would you make the patient feel less overwhelmed?*

A: Patients are so afraid of dialysis. First, educate patients on how to take blood pressure and suggest blood pressure monitoring. For the diet, adjust to what they like because we tend to be so restrictive. Advise small frequent feedings to reduce weight. Food should not be too salty; just salt to taste. Ask about their jobs and adjust their medications to their budget accordingly, since some may be taking expensive vitamins and supplements. Do a thorough physical exam, and listen to all the vessels (Figure 13–9). For kidney evaluation, initially request for urinalysis and creatinine, and work from there, if an ultrasound is needed. There is no need to order renal scan right away. Always refer to an ophthalmologist once you diagnose type 2 DM.

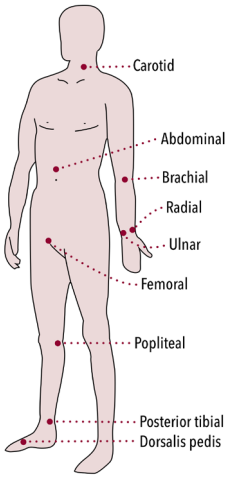

FIGURE 13–9. Arterial pulses and bruits

Q: *Can you comment on the Philippine diet being too salty? How about junk food?*

A: Salt sensitivity is not 100%. However, salt intake can increase blood pressure. Low salt intake is equivalent to 12.5 mg hydrochlorothiazide diuretic.
Junk food is very high in salt and calories. Even soft drinks are high in sodium. Beer is high in uric acid.

Q: *What is your advice on alcohol intake?*

A: Red wine is better than beer, but should still be taken in moderation.

Q: *Do you advise a routine urinalysis be done to patients with hypertension and/or diabetes?*

A: As a rule, if you have a young patient with hypertension (<30 years old), you need to do extra workup (i.e., urinalysis, creatinine, uric acid, abdominal ultrasound) even if the patient has a family history of hypertension. The most common cause of secondary hypertension is kidney disease.
For a newly diagnosed patient with hypertension, regardless of age, baseline screening workup is done, including CBC, FBS, uric acid, and lipid profile. Those with gout usually have hypertension.
For patients with recurrent urinary tract infection based on urinalysis and are asymptomatic, it should be called "abnormal urinalysis," then worked up for kidney disease.

Q: *How do we screen for diabetes and atherosclerosis in the age group 50 years and above?*

A: I request for FBS, HbA1c and urinalysis.

Q: *For a patient with prediabetes whose mother had diabetic kidney disease, when do you request for 24-hour total urinary protein?*

A: If a patient has a sibling with diabetic kidney disease (DKD) and is diabetic but with no DKD, the patient has a 40% chance of eventually developing DKD. Hence, early on, the patient should be screened by making sure DM is controlled and urine microalbuminuria-to-creatinine ratio is normal. There is a strong genetic component if diabetes runs in the family. In some studies, DKD can be reversed if caught early and sugar is controlled.

Q: *When should we refer patients with diabetes to a nephrologist?*

A: There is no need to refer right away if patients have normal urinalysis and creatinine. But if there is already an eye problem, patient must already be screened for urine microalbuminuria. Always compute for the GFR.

Q: *Most of my patients in the hemodialysis center are asking about the efficacy of insulin plants, are they really useful or just a form of traditional medicine?*

A: I discourage herbal treatment among my patients undergoing dialysis because we don't know the potassium and sodium content.

Q: *My endocrinologist advised against taking any food supplements together with antidiabetic and antihypertensive drugs. My cardiologist, however, recommended that I take fish oil. Is this okay?*

A: The intake of fish oil depends on your cardiovascular status.

REVIEW QUESTIONS

1. At what stage of type 1 diabetic nephropathy can overt proteinuria be observed clinically?
   a. Stage 2
   b. Stage 3
   c. Stage 4
   d. Stage 5

2. What are the two most important parameters in preventing progression in type 2 DM?
   a. Good blood sugar control, normal cholesterol levels
   b. Good BP and blood sugar control
   c. Good BP and normal cholesterol levels
   d. Low salt diet and good BP control

3. Who is at risk for developing atherosclerotic renal artery stenosis?
   a. A 29-year-old woman with hypertension
   b. A 47-year-old man with peripheral arterial occlusive disease
   c. A 59-year-old man with HbA1c of 9%
   d. A 33-year-old woman with low HDL

4. What is the most common indication for dialysis?
   a. Chronic glomerulonephritis
   b. Diabetic kidney disease
   c. Hypertensive kidney disease
   d. Acute kidney injury

5. What happens to the affected kidney with renal artery stenosis?
   a. Ruptures
   b. Enlarges
   c. Easily infects
   d. Atrophies

ANSWERS: 1. c; 2. b; 3. b; 4. b; 5. d

14 TYPE 2 DIABETES IN OLDER ADULTS

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https://bit.ly/ALMW_Ch14_Type2Diabetes

KEY POINTS

- There are special considerations in the management of diabetes in older adults due to the presence of comorbidities, complications, cognitive impairment and frailty.
- We should refer to an endocrinologist when a patient has a complicated diabetes condition. This includes hypoglycemia, which is common in the older adult.
- Treatment should be individualized and consider the patient's overall health status and cognition.
- Medications should always be reviewed; particularly those that need dose adjustments and can cause detrimental side effects in older patients.

LEARNING OBJECTIVES

- ➸ To define diabetes in older adults
- ➸ To outline the recommendations for screening and prevention for diabetes in older adults
- ➸ To determine the need for specialist referral in an older patient with diabetes
- ➸ To understand importance of proper assessment and individualized treatment in the older adult with diabetes
- ➸ To discuss treatment options (i.e., lifestyle modification, medications) for both diabetes and its complications

I. EPIDEMIOLOGY

Why a separate guideline for older adults?

- A separate clinical guideline for older adults was issued by the Endocrine Society (cosponsored by European Society of Endocrinology, The Gerontological Society of America, and The Obesity Society) in 2019.[1]
- Type 2 diabetes is an age-related disease, with more than 90% of older adults having type 2 diabetes.[2]
- The prevalence of increased fasting blood sugar (FBS) is higher with age, and is highest in the sixth decade, based on surveys in 2013, and even more so in 2018 (Philippine DOST-FNRI).[3]
  - In this age group, majority had diabetes for more than 10 years and a significant number will have several complications and comorbidities.

- In the U.S., 60% of diabetics aged 60 or older have had diabetes for more than 10 years[4] with a dramatic rise in complication rate with age.[5]
- Locally, the highest prevalence rate of diabetes complications for all age groups (DiabCare 2008 study)[6] is for microvascular complications.
  - Microvascular complications – 68.1%
  - Macrovascular complications – 14.8%
  - Severe late complications – 9.4%
- In addition, the prevalence rates of complications in newly-diagnosed persons with diabetes in Manila are:[7]
  - 20% peripheral neuropathy
  - 42% proteinuria
  - 2% diabetic retinopathy
  - 11% had some form of ECG abnormality (ischemia, left ventricular hypertrophy)
- Overall prevalence rate of complications is quite high for both US and Philippines (Figure 14–1).

FIGURE 14–1. Comparison of prevalence rates of diabetes complications in persons with ≥10-year duration of type 2 diabetes, U.S. versus Philippines

	PREVALENCE RATE (%)	
COMPLICATION	U.S.* (2007-2010)[4]	PHILIPPINES† (2008)[6]
Macrovascular		
Angina	10	13
Myocardial infarction	15	5
Microvascular		
Non-proliferative retinopathy	32	23
Microalbuminuria	30	34

**Adults ≥65 y/o; †mean age 61 yrs.*

Sources:

Laiteerapong N, Huang ES. Diabetes in older adults. In: Barrett-Connor E, Becker DJ, Boyko EJ, et al., eds. *Diabetes in America*. 3rd ed. Bethesda, MD: NIH Pub; 2017:16-1 to 16-26.

Jimeno C, Sobrepeña L, Mirasol R. DiabCare 2008: Survey on glycaemic control and the status of diabetes care and complications among patients with type 2 diabetes mellitus in the Philippines. *Phil J Intern Med*. 2012;50(1):15-22.

- Thus, care in this group is quite challenging and requires particular attention.
- Type 2 diabetes in the older population occurs as a result of complex interaction between genetic, lifestyle, and ageing influences. This complexity means there is substantial heterogeneity in the pathophysiology, clinical features, and rate of disease progression among older people.[8]
  - Ageing decreases glucose tolerance and insulin secretion.
  - These impairments limit the response to lifestyle-induced insulin resistance, resulting in progression to prediabetes and type 2 diabetes.
  - Glucose toxicity from persistent hyperglycemia can worsen insulin resistance and further impair pancreatic B-cell function.
  - Lipotoxicity may also contribute to this vicious cycle.[8]

II. SCREENING AND PREVENTION OF DIABETES IN THE ELDERLY

A. How do we screen?

TABLE 14–1. Screening indications and tests

WHO TO SCREEN?	HOW TO SCREEN?
1. 65 years and older 2. At an *earlier age* if: Prediabetes Overweight/ obese First degree relative with diabetes Hypertension, cardiovascular disease HDL<35 mg/dl TG>250 mg/dl Inactivity Sleep apnea*	Any of the following: 1. FBS or HBA1c (if not anemic) every 2 years 2. OGTT

FBS, Fasting blood sugar; HBA1c, Glycosylated hemoglobin; OGTT, Oral glucose tolerance test; HDL, High-density lipoprotein; TG, Triglyceride

**Sleep apnea is an emerging health issue and is associated with the development and exacerbation of DM and its complications.*

TABLE 14–2. Diagnostic criteria for prediabetes and diabetes

DIAGNOSTIC TEST	PREDIABETES*	DIABETES†
a. FPG	100 to 125 mg/dL (=IFG)	≥126 mg/dL
b. 2-h PG (during 75-g OGTT)	140 to 199 mg/dL (=IGT)	≥200 mg/dL
c. HBA1c	5.7–6.4%	>6.5%
d. RPG		≥200 mg/dL in a patient with classic symptoms of hyperglycemia or hyperglycemic crisis

**Any of 3 criteria (a to c), for prediabetes; †Any of 4 criteria (a to d), for diabetes)*

FPG, Fasting plasma glucose; IFG, Impaired fasting glucose; IGT, Impaired glucose tolerance; OGTT, Oral glucose tolerance test; HBA1c, glycosylated hemoglobin; RPG, Resting plasma glucose

Source: American Diabetes Association. 2. Classification and diagnosis of diabetes: Standards of medical care in diabetes - 2019. *Diabetes Care*. 2019;42(Suppl 1):13-28[9]

B. How do we prevent the disease?

- ***Metformin and lifestyle*** were more effective compared to placebo in preventing diabetes over four (4) years and even at follow up many years later (multicenter trial; N>3000) (Diabetes Prevention Program Research Group).[10]
- Lifestyle modification performed better and was more cost-effective than metformin. The lifestyle group was more active and maintained their weight better.

III. ASSESSMENT OF OLDER PATIENTS WITH DIABETES

A. Need for Specialist Referral

Does everybody need an endocrinologist?

1. Newly diagnosed patients with diabetes should work with their primary provider to set treatment goals.
2. Refer to endocrinologist if:
   - Type 1 diabetes
   - Complex regimen – three (3) or more agents; use of insulin
   - Recurrent hypoglycemia - defined as blood sugar less than 70 mg/dL usually with symptoms of shakiness, irritability, confusion, tachycardia, hunger and loss of consciousness

- Multiple diabetes complications

B. General Health Assessment

Aside from general health tests and diabetes-specific tests, we need to further assess the elderly with diabetes so we can individualize their treatment (Table 14–3).

TABLE 14–3. General health assessment for older patients with diabetes

DOMAIN	PURPOSE/TOOL	IMPLICATIONS FOR TREATMENT
1. Functional status (ADL; IADL)	Helps in advising the family on their need for additional supervision or care. ADL • Eating • Bathing • Dressing • Toileting • Transferring IADL • Preparing meals • Shopping • Managing money • Using the phone • Managing medications	• Inability to do IADLs may lead to malnutrition and poor compliance to medications. • May trigger a detailed assessment on cognition, presence of hypo- or hyperglycemia, micro- and macrovascular complications, so that these can be addressed to improve the functional status.
2. Cognition	Montreal Cognitive Assessment (MOCA)[11] • It is a 30-point test that has been validated in Filipino population. • A score of 20 indicates cognitive impairment.	• Diabetes increases the risk for dementia due to increased vascular pathology. • The harm from unrecognized cognitive impairment can thus be avoided. • Test yearly if borderline and every 2–3 years if normal. • If there is cognitive impairment, treatment needs to be simplified and goals need to be tailored to improve compliance and prevent complications of hypoglycemia.
3. Fall risk	Simple SARC-F Sarcopenia questionnaire (0–10 points)[12] • **S**trength • **A**ssistance in walking • **R**ise from a chair • **C**limbs stairs • **F**alls	• Provide nutrition and advise on modifying their environment to prevent falls.[13]
4. Frailty	• Frailty is a pre-disability condition. • We should identify if our patients are 'frail' in order to guide treatment.[14] • FRAIL questionnaire[15] ○ **F**atigue ○ **R**esistance ○ **A**mbulation ○ **I**llnesses ○ **L**oss of weight	• Intervention can prevent or delay functional decline and disability. • For more frail patients, we should be less aggressive and have less rigid glucose control.

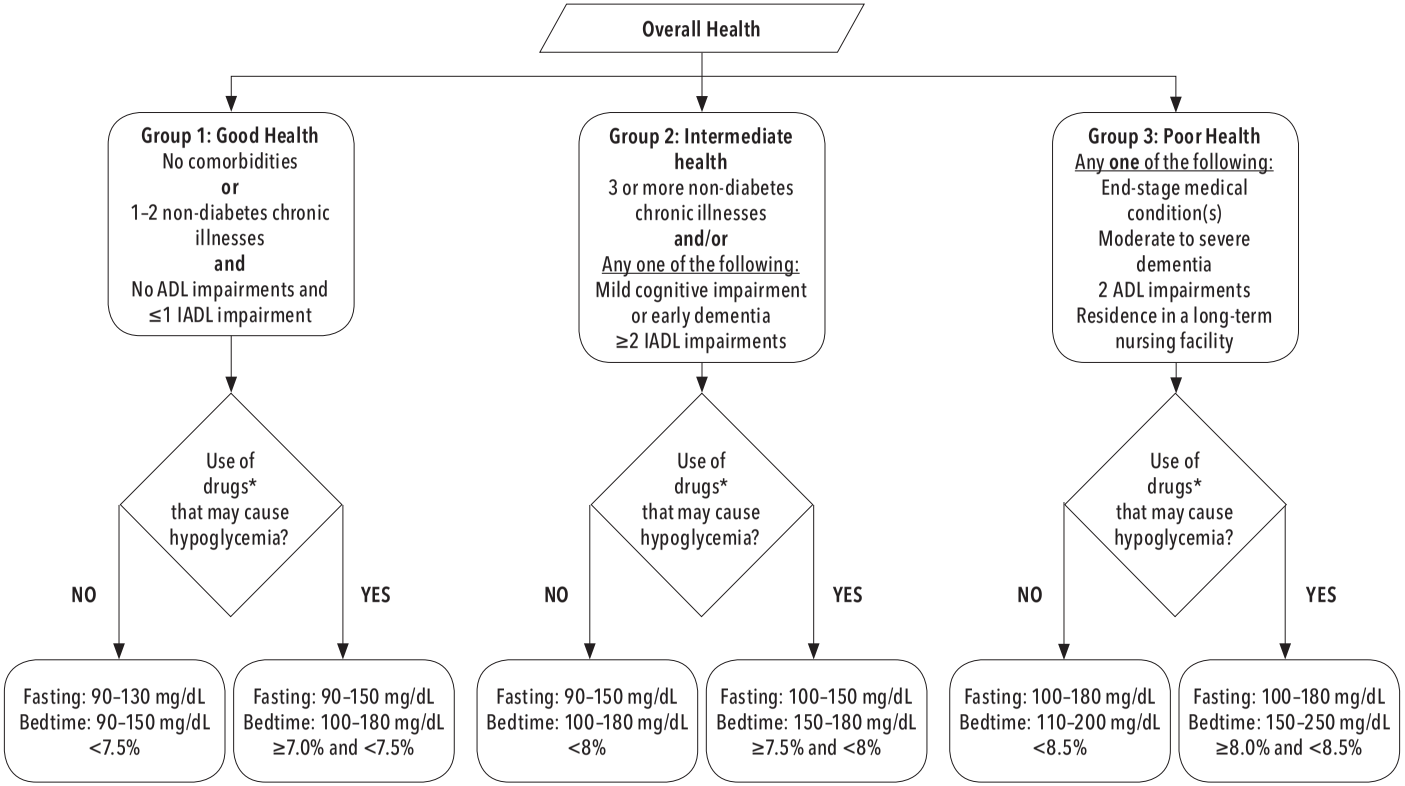

FIGURE 14–1. Overall health category and target goals for FBS and HBA1c

**e.g., insulin, sulfonylureas, glinides.*
Note. There should be shared decision-making and individualized goal may be adjusted lower or higher.

TABLE 14–3. General health assessment for older patients with diabetes (cont.)

DOMAIN	PURPOSE/TOOL	IMPLICATIONS FOR TREATMENT
5. Overall health category	• Patients can be grouped into group 1 (good health), 2 (intermediate health), or 3 (poor health) based on patient comorbidities and use of drugs that may induce hypoglycemia[16,17] (Figure 14–1).	• Once ADLs and cognitive function have been assessed, HBA1c goals can be set between 7 to 8.5% based on overall health category (Table 14–3).

ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living

IV. TREATMENT GOALS

A. Individualized goals

- Maintain HBA1c at around 7.5%
  - There is a U-shaped relationship between mortality and HBA1c, that is, higher mortality at the extremes, and lowest between 7 and 8.5% (ACCORD, 2010;[18] VADT, 2009;[19] ADVANCE, 2008;[20] Currie, 2010[21]).
  - Avoid hypoglycemia to prevent serious consequences such as myocardial infarction or stroke.
  - Avoid hyperglycemia. If HBA1c is above 8.5% or FBS >200 mg/dL, symptoms include frequent urination, dehydration, dizziness, falls, urinary infections, electrolyte abnormalities, and poor wound healing.
- Use HBA1c or fingerstick monitoring to assess glycemia.
- Stringent vs less stringent glucose control (Figure 14–2)
  - If low-risk patient (long life expectancy, absence of comorbidities), go for stringent glucose control.
  - If high-risk patient (longstanding DM, short life expectancy, severe comorbidities), go for less stringent glucose control.

		Glucose Control	
		HBA1c target	
		7% (Strict) ← 7.5% → 8% (Lenient)	
	Patient/disease features		
Usually not modifiable	Adverse drug event risk (especially hypoglycemia)	Low	High
	Disease duration	Newly diagnosed	Long-standing
	Life expectancy	Long	Short
	Pertinent comorbidities	Absent	Present
	Cardiovascular disease or complications	Absent	Present
Potentially modifiable	Capacity for treatment adherence	Excellent capacity	Poor capacity
	Family and community resources	Readily available	Limited

FIGURE 14–2. Approach to Glucose Control

Sources:

Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: A patient-centered approach: Update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2015;38(1):140-149.[22]

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B. Treatment options

TABLE 14–4. Treatment options for diabetes mellitus in older adults

Lifestyle modification	1.	Physical activity	Stay active with at least 150 minutes per week of moderate-intensity aerobic exercise.
	2.	Proper nutrition	• Diet should be nutrient-dense and non-restrictive and non-restrictive, and instead, it should limit simple sugars and control portions. • Adequate amounts of protein must always be included in the diet, especially for those with muscle wasting (sarcopenia). • Vitamin D supplementation should be given to those with deficiencies. • Fiber should be increased by favoring vegetables, legumes, whole grain and high fiber breakfast cereals.
Medications for Type 2 Diabetes	3.	Metformin	• Metformin is the drug of choice of most treatment algorithms as long as GFR >30 ml/min in the absence of gastrointestinal intolerance. • Discontinue metformin temporarily for patients receiving radiocontrast dye, nephrotoxic drugs, with heart failure, undergoing prolonged surgery with possibility of large volume losses, and hypotension, which may precipitate acute kidney injury. • Metformin may increase vitamin B metabolism. Thus, there may be a need to prescribe vitamin B12 to patients taking metformin.
	4.	SGLT-2 inhibitors and GLP-1 receptor agonists	• These reduce the progression of CKD and decrease CV events and are thus preferred for patients with chronic kidney disease or established atherosclerotic CV disease provided the creatinine clearance is greater than 30–60 ml/min, depending on the agent. • Side effects include dehydration, weight loss, fungal infections, and fractures.
	5.	DPP-4 inhibitors or gliptins	• They are weight-neutral, do not cause hypoglycemia, and can be used in patients with low GFRs. • Certain DPP-4 inhibitors may cause water retention that can exacerbate congestive heart failure or cause bipedal edema.
	6.	Thiazolidinediones	• They can reduce CV mortality and strokes but may worsen heart failure and cause fractures.[24,25]
	7.	SU, glinides and insulin	• Use sparingly due to their potent hypoglycemic effects.

GFR, Glomerular filtration rate; CKD, Chronic kidney disease; CV, Cardiovascular; MI, Myocardial infarction; SGLT-2, Sodium-glucose co-transporter-2; GLP-1, Glucagon-like peptide 1; DPP-4, Dipeptidyl peptidase 4; SU, Sulfonylureas

Sources:

Zhu Z-N, Jiang Y-F, Ding T. Risk of fracture with thiazolidinediones: An updated meta-analysis of randomized clinical trials. *Bone*. 2014;68:115-123.[24]

Watts NB, Bilezikian JP, Usiskin K, et al. Effects of canagliflozin on fracture risk in patients with type 2 diabetes mellitus. *J Clin Endocrinol Metab*. 2016;101(1):157-166.[25]

TABLE 14–5. Treatment of diabetes comorbidities

1. Hypertension	• Treatment of hypertension is associated with lower all-cause mortality, myocardial infarction, stroke and CKD. • The goal is a blood pressure of 140/90; but may be lower if with previous CV disease, CKD (GFR<60 ml/min) or albuminuria; or higher if in group 3 (poor health). • Antihypertensive medications ○ ACE inhibitors are as effective as ARB for kidney protection and are better for patients with heart complications. ○ Calcium-blocker ○ Diuretic (thiazide/loop) or β-blocker, depending on comorbidities
2. Dyslipidemia	• Do annual lipid profile. • Treat patient if LDL>70 mg/dL or TG >500 mg/dL. • In secondary prevention trials, statins have been shown to lower MIs, revascularization stroke and all-cause mortality. • In primary prevention trials, statins lowered MI but not stroke, CV mortality nor all-cause mortality. • Statins are the first-line modality. • Ezetimibe may also be used. PCSK9 inhibitors are still unavailable in Philippines. • For high TGs, fibrate or fish oil may be used. • Targeting TG <200 results in even lower CV mortality based on newer guidelines.[26]
3. Congestive heart failure	• It occurs four times more often in diabetics due to accelerated atherosclerosis and diabetic cardiomyopathy. • Use the following hypoglycemic agents with caution due to side effect of increased fluid retention: glinides, saxagliptin, and thiazolidinediones. • SGLT-2 inhibitors may be beneficial due to osmotic diuresis from glucose excretion in the urine.
4. Atherosclerosis	• Diabetes increases risk for stroke and peripheral arterial disease. • For secondary prevention, start aspirin.[27] • For primary prevention, risk versus benefit must be weighed. • Any serious CV event is reduced with aspirin but there is risk of major bleeding.[28] ○ Low dose aspirin (80–162 mg) should be used.

CKD, Chronic kidney disease; GFR, Glomerular filtration rate; CV, Cardiovascular; ACE, Angiotensin-converting enzyme; ARB, Angiotensin II receptor blocker; LDL, Low density lipoprotein: TG, Triglyceride; PCSK9, Proprotein convertase subtilisin/kexin type 9; SGLT-2, Sodium-glucose co-transporter-2

Sources:

Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk. *Eur Heart J*. 2019;00:1-78. doi:10.1093/eurheartj/ehz455[26]

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The ASCEND Study Collaborative Group. Effects of aspirin for primary prevention in persons with diabetes mellitus. *N Engl J Med*. 2018;379(16):1529-1539.[28]

TABLE 14–6. Treatment of diabetes complications		
1.	**Eyes**	• Check yearly for retinopathy, maculopathy, glaucoma and cataracts.
2.	**Kidneys**	• Test the following: ○ Urinary albumin-to-creatinine ratio ○ GFR – testing may be more frequent if less than 60 ml/min • Note that doses of hypoglycemic agents need to be adjusted based on kidney evaluation: ○ Metformin: The dose should be decreased to 1000 mg if GFR is less than 45 ml/min. ○ SU: Older SU should be discontinued if GFR is less than 60 ml/min while newer-generation SU should be stopped if GFR is less than 30 ml/min. ○ DPP-4 inhibitors: Saxagliptin, sitagliptin and alogliptin need appropriate dose adjustments. ○ SGLT-2 inhibitors: They may need dose adjustment depending on GFR. ○ GLP-1 agonists: Exenatide and lixisenatide need adjustment.
3.	**Nerves**	• Pain, motor strength loss, contractures, deformities, weakness, proprioceptive deficits, and balance and gait problems can ensue. • Avoid sedatives and drugs which cause orthostatic hypotension. • Patients may benefit from physical therapy or fall management program. • Neurologist, podiatrist or vascular surgeon referrals may be required.

GFR, Glomerular filtration rate; SU, Sulfonylureas; DPP-4, Dipeptidyl peptidase 4; SGLT-2, Sodium-glucose co-transporter-2; GLP-1, Glucagon-like peptide 1

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OPEN FORUM HIGHLIGHTS

Moderator: MONICA THERESE CATING-CABRAL, MD

Q: *What is the goal for HBA1c for the older population?*

A: The HBA1c goal is 7–7.5%. If they have more comorbidities, I'd be happy with 8%.

Q: *What is the drug of choice for the older population with diabetes?*

A: The drug of choice is still metformin because it has been shown to be cost-effective and can decrease cardiovascular mortality and weight.

Q: *What do you do for a patient who is already on glibenclamide or glimepiride?*

A: In a financially challenged environment like ours, I would then switch to or add metformin. After that, I drift over to the other agents. If they cannot afford the DPP-4 and SGLT-2 inhibitors, I put them on thiazolidinediones, especially if they are men.

Q: *How do we know if it's a problem of insulin resistance or insulin secretion/production by the pancreas?*

A: We look at the phenotype for that. We also look at the history – if the patient has had diabetes for a while, she might already have a problem with insulin secretion. But if they are obese and it's only for a short duration, they probably have insulin resistance. We can also look at the insulin levels.

Q: *Is prediabetes the same as impaired glucose tolerance? Do you treat patients with prediabetes?*

A: Yes, sometimes we also use the term "borderline" because that is what the patients understand. Definitely we treat patients with prediabetes. If they are motivated, I start them on lifestyle modification. If not, I give them metformin.

Q: *Does metformin damage the kidneys?*

A: This is a misconception. The dose needs to be adjusted, however, if GFR falls below 45 ml/min, and metformin should be discontinued in patients with a GFR less than 30 ml/min.

REVIEW QUESTIONS

1. All the following patients need to be referred to the endocrinologist, EXCEPT:
    a. Patient with type 1 diabetes
    b. Patient using triple therapy or insulin
    c. Patients with recurrent hypoglycemia
    d. Patient newly-diagnosed with Type 2 diabetes, whose mother is undergoing dialysis

2. Which of the following should be routinely assessed in an elderly patient with diabetes?
    a. Activities of daily living
    b. Frailty
    c. Cognitive function
    d. All of the above

3. Which agent decreases both cardiovascular and renal complications of diabetes?
    a. Metformin
    b. Thiazolidinediones
    c. SGLT-2 inhibitors
    d. Sulfonylureas

4. For which GFR level should we adjust the dose for metformin?
    a. Less than 45 ml/min
    b. Less than 60 ml/min
    c. Less than 90 ml/min
    d. None since the dose is the same regardless of GFR

5. In treating patients with diabetes who have comorbidities, which of the following is true?
    a. ACE inhibitors are safer than ARBs for patients with cardiac complications.
    b. Lipid profile testing should be done every 3 months and medications adjusted accordingly.
    c. Primary prevention of atherosclerosis using antiplatelet therapy is recommended routinely.
    d. Dyslipidemia treatment is initiated when LDL >50 mg/dL and TG>500 mg/dL.

ANSWERS: 1. d; 2. d; 3. c; 4. a; 5. a

15 OSTEOPOROSIS AND BONE HEALTH

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https://bit.ly/ALMW_Ch15_Osteoporosis

KEY POINTS

- Osteoporosis is not part of normal ageing. It causes significant morbidity, mortality, and decreased quality of life.
- At 50 years of age, 1 in 3 women and 1 in 5 men will suffer a fracture in their remaining lifetime.
- Osteoporosis is a silent disease and pain is not felt unless a fracture has already occurred.
- Screen for osteoporosis in women older than 65 years old and men older than 70 years old; earlier if with risk factors, or in any adult who sustains a fragility fracture.
- Lifestyle measures to help prevent osteoporosis include adequate intake of calcium and vitamin D, maintenance of a healthy weight, regular exercise, smoking cessation, avoidance of excessive alcohol intake and fall prevention.
- For patients, talk to your doctor about your bone health and ask about:
    1. Your risk factors for osteoporosis
    2. The right amount of calcium and vitamin D to take
    3. If a bone mineral density scan is recommended for you
        - Succeeding bone mineral density scans should be done on the same machine at the same facility.
        - If you are diagnosed with osteoporosis, discuss your treatment options with your doctor and take any prescribed medications regularly.

LEARNING OBJECTIVES

- ➥ To review bone physiology
- ➥ To discuss the epidemiology and pathogenesis of osteoporosis
- ➥ To identify screening and diagnostic tools for osteoporosis
- ➥ To outline the management of osteoporosis

I. BONE PHYSIOLOGY

- Bone is living tissue.
- Old bone is constantly broken down and replaced by new bone.

A. Bone Remodeling[1]

- It is the process of breakdown and repair of all normal adult human bones.

- Functions:
  i. To repair microdamage within the skeleton - to maintain skeletal strength
  ii. To supply calcium from the skeleton - to maintain serum calcium
- Process of Bone Remodeling (Figure 15–1)

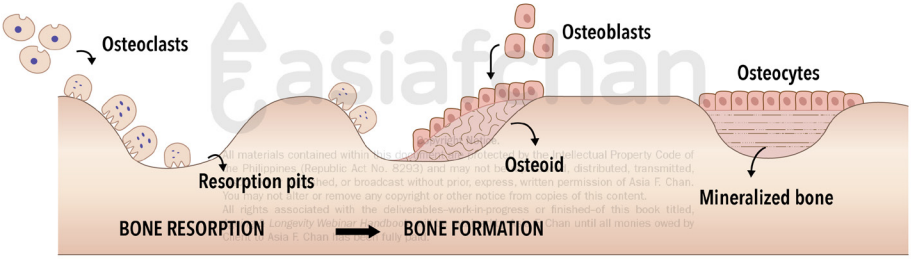
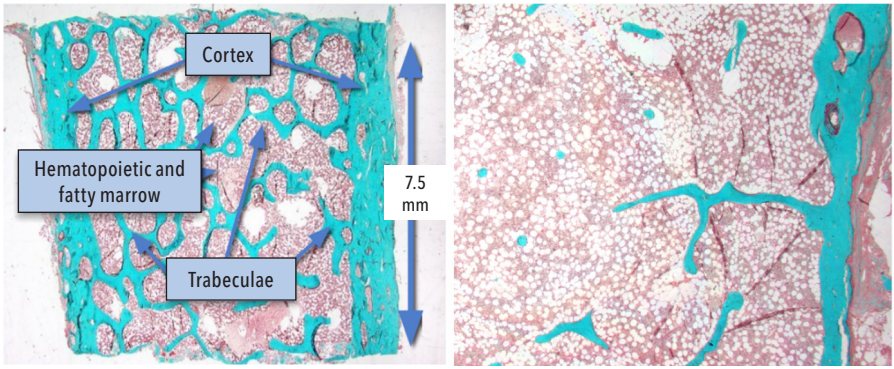


FIGURE 15–1. Bone remodeling. Osteoclasts, found in resorption pits, are primarily responsible for bone resorption. Osteoblasts, on the other hand, are primarily responsible for bone formation. These produce the osteoid, a gelatinous substance composed of fibers, collagen and ground substance. The osteoid will then undergo mineralization, producing mature bone.

B. Anatomic Bone Structure



(a) Normal Bone (b) Osteoporotic bone

FIGURE 15–2. Anatomic structure of bone (trans-iliac crest biopsy specimens). (a) Normal bone. The image shows the normal cortical thickness (teal) and a trabeculae form network of trusses (support system) filled with hematopoietic and fatty marrow. (b) Osteoporotic bone. The image shows a thinned-out cortex and a loss of trabeculae (making bones weak).

Courtesy of Dr. Stephen Hodgson, Mayo Clinic

TABLE 15–1. Normal versus Osteoporotic bone

NORMAL BONE	OSTEOPOROTIC BONE
Normal cortex thickness	Thin cortex
Trabeculae form network of trusses (support system), filled with hemopoietic and fatty marrow	Loss of trabeculae (making bone weak)

II. DEFINITION OF OSTEOPOROSIS

Osteoporosis is defined as: "A disease characterized by low bone mass and microarchitectural deterioration of bone tissue, leading to enhanced bone fragility and a consequent increase in fracture risk." (Consensus Development Committee, 1993), and "A skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture (NIH Consensus Statement: Osteoporosis Prevention, Diagnosis, and Therapy, 2000).[2]

III. EPIDEMIOLOGY OF OSTEOPOROSIS

- Why is osteoporosis a global health problem?
  - The number of fractures in Asia is expected to increase exponentially (2.28-fold) in the next 30 years, from 1.12 M (2018) to 2.56 M in 2050.[3]
- The burden of suffering is related to the increased incidence of fractures.
  - 1 osteoporotic fracture occurs every 3 seconds
  - At 50 years of age, 1 in 3 women and 1 in 5 men will suffer a fracture in their remaining lifetime
  - For women, the risk of hip fracture >the risk of breast, ovarian and uterine cancer combined
  - For men, the risk of hip fracture >the risk for prostate cancer
  - 50% of people with 1 osteoporotic fracture will have another, with the risk of new fractures rising exponentially with each fracture
- There is increased risk with age.
  - The risk of sustaining a fracture increases exponentially with age.
  - There is an increased rate of falls among the elderly.
  - The elderly represent the fastest growing segment of the population.
  - There are increased financial and human costs with decreased life expectancy.

IV. PATHOGENESIS OF OSTEOPOROSIS[4]

- Multifactorial
  - Ageing, menopause and other risk of fracture factors → bone resorption exceeds bone formation → BONE LOSS
  - Low peak bone mass
  - Poor bone quality
  - Falls leading to fractures
- Osteoporosis occurs more as we age but it is NOT a natural part of ageing.
- There is gain and loss of bone throughout the life span (Table 15–2).[5]

TABLE 15–2. Changes in bone metabolism with age

Age group	Changes in bone metabolism
Teens	Pubertal growth spurt where bone formation exceeds bone resorption
20s to 30s	Peak bone mass, where old bone is continually being replaced by new bone to maintain its integrity
Old age	Old bone is not being replaced by new bone, with a decline in bone density

- Menopause – the process wherein ovaries stop the production of estrogen naturally (marked by the absence of menstruation for 12 consecutive months) or from any other cause

V. SCREENING AND RISK FACTORS FOR OSTEOPOROSIS[6]

- Why should we screen for osteoporosis?
  - It is a silent disease.
    - Bone loss may occur without any symptoms, and you may only feel something when you have already broken a bone.
  - There are crippling consequences of osteoporosis-related hip fracture.[7]
    - 5% to 20% die within a year
    - 30% retain permanent disability
    - 40% are unable to walk independently
    - 80% are unable to carry out at least 1 independent activity of daily living
  - Fragility fractures have a significantly negative long-term impact on health-related quality of life of people aged 50 years and older.[8]
    - Hip and spine fractures negatively affect mobility, self-care, and ambulation.
    - After a fracture, women never recover to their pre-fracture status.
  - Complications of fractures
    - Hip fractures - Deep vein thrombosis and pulmonary embolism (20–50%)
    - Vertebral fractures - Restrictive lung disease
    - Lumbar fractures - Abdominal distention, early satiety, and constipation
- Who should be screened for osteoporosis?[9]
  1. Women aged >65 and men >70
  2. Postmenopausal women 50–64 years old and men 50–69 years old with risk factors
  3. Adults with a disease or condition associated with low bone mass or bone loss
  4. Adults taking medications associated with low bone mass or bone loss
  5. Adults with a fragility fracture AT ANY AGE
  6. A FRAGILITY FRACTURE is any fracture that:
     - Is due to a fall from a standing height or less
     - Can happen easily, by tripping, coughing or bending over, with low trauma and low force
     - Can occur anywhere but are most common in the vertebrae, femur and distal forearm

TABLE 15–3. Causes of secondary osteoporosis

1.	Anorexia nervosa
2.	GI malabsorption (e.g., celiac disease, postoperative states)
3.	Vitamin D and/or calcium deficiency
4.	Hyperthyroidism
5.	Hyperparathyroidism
6.	Cushing's syndrome
7.	Hypogonadism
8.	Rheumatoid arthritis
9.	Renal disease
10.	Liver disease
11.	Osteogenesis imperfecta
12.	Marfan's/Ehlers-Danlos syndrome
13.	Gaucher disease
14.	HIV infection and/or medications
15.	Diabetes mellitus (Type 1 and 2)
16.	Drug-induced

GI, Gastrointestinal

FIGURE 15–3. Risk factors for osteoporosis

TABLE 15–4. Drugs that cause osteoporosis

1. Glucocorticoids – most common
2. Immunosuppressants (e.g. cyclosporine)
3. Antiseizure medications (particularly phenobarbital and phenytoin)
4. GnRH agonists (when used to suppress ovulation)
5. HIV medications
6. Heparin
7. Chemotherapy, leading to amenorrhea
8. Thiazolidinedione
9. Depot medroxyprogesterone acetate
10. Excess thyroid hormone
11. SSRIs
12. Proton pump inhibitors

HIV, human immunodeficiency virus; SSRI, Selective serotonin reuptake inhibitor

VI. DIAGNOSIS OF OSTEOPOROSIS

How is osteoporosis diagnosed?

1. Signs and symptoms only after a fracture
   - Back pain, caused by a fractured or collapsed vertebra
   - Loss of height over time
   - A stooped posture
   - A bone fracture that occurs much more easily than expected
2. Testing
   - Central Bone Mineral Density (BMD) Testing – gold standard
     - Dual-energy X-ray absorptiometry (DXA)
   - It should be done in a facility with accepted quality assurance measures.
   - The relative risk of having a fracture increases as bone mineral density (BMD) decreases.
     - Areas measured:
       - Lumbar spine (L1–L4)
       - Total proximal femur
       - Femoral neck
       - 1/3 of the proximal radius (non-dominant hand)
   - Perform repeat testing (every 1–2 years) using the same machine.
   - If peripheral bone density testing is abnormal, get a central BMD.
3. Defining Osteoporosis by BMD (Table 15–5)
   a. T-score
      - Compares BMD to that of a normal 30-year-old adult population
   b. Z-Score
      - Age-matched comparison of BMD
      - Used for premenopausal women or men younger than 50 years old
        - Consider secondary osteoporosis if Z-score is lower than the T-score

TABLE 15–5. Defining osteoporosis using T-score and Z-score

	T-score*	Z-score†
Normal	–1.0 SD and above	Above –2.0 SD
Low bone mass/Osteopenia	Between –1.0 and –2.5 SD	Below –2.0 SD
Osteoporosis	At or below –2.5 SD	
Severe osteoporosis	At or below –2.5 SD with 1 or more fractures	

BMD, Bone mineral density; SD, Standard deviation
**Compared to the mean bone mineral density (BMD) of a young adult reference population*
†Age-matched comparison

4. Osteoporosis Self-Assessment Tool for Asians (OSTA) (Figure 15–4)[10-12]
   - Used to identify an individual's risk for osteoporosis in areas where DXA is unavailable
   - 91% sensitivity and 45% specificity to detect a femoral neck BMD (equivalent to a femoral neck BMD T-score <–2.5)
   - Uses a patient's age and weight
     - e.g., a 67-year old woman who weighs 42 kg is at high risk for osteoporosis

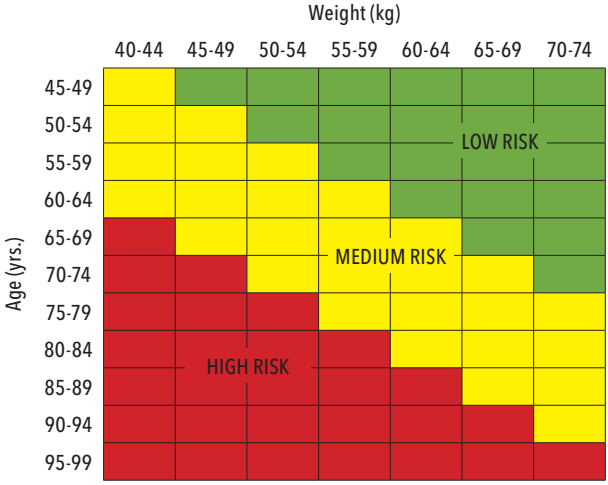


FIGURE 15–4. Risk of osteoporosis based on Osteoporosis Self-Assessment Tool for Asians

Source: Koh L, Ben Sedrine W, Torralba T, et al. A simple tool to identify Asian women at increased risk of osteoporosis. *Osteoporos Int*. 2001;12:699-705.[11]

5. Vertebral Imaging/Vertebral Fracture Assessment[13]
    a. All women >70 y/o and all men >80 y/o if T-score is <1.0
    b. Women 65–69 y/o and men 75–79 y/o if T-score is <1.5
    c. Postmenopausal women aged 50 to 64 yrs. and men aged 50 to 69 yrs. with specific risk factors:
        i. Low trauma fracture
        ii. Historical height loss of >1.5 in (4 cm)
        iii. Prospective height loss of >0.8 in (2 cm)
        iv. Recent/ongoing long-term glucocorticoid treatment

VII. MANAGEMENT OF OSTEOPOROSIS[14-16]

A. Prevention of Osteoporosis

How is the risk for osteoporosis reduced?

1. Get enough calcium and vitamin D.
   - 1200 mg of elemental calcium
     - Combined sources from diet PLUS supplement

TABLE 15–6. Dietary sources of calcium

SERVING/FOOD ITEM	AMOUNT OF CALCIUM (MG)
8 sardines	370
1 cup cooked leafy greens	200-350
2 tbsps. chia seeds	200
1 cup beans	120-180
1 tbsp. sesame seeds	90
1 orange	70
20 almonds	60
6 Brazil nuts	40

     - Calcium carbonate needs stomach acid to be dissolved, so it should be taken with food and should be limited to 500 mg per dose.
   - 800 IU of vitamin D
     - Vitamin D is similar to a key that unlocks the door to let calcium into the body.
     - Vitamin D is manufactured in our skin following direct exposure to sun.
       - Advise 10–15 minutes midday sun exposure of hands, arms and face face; 2 to 3 times per week depending on skin sensitivity
       - The amount produced is reduced with clothing, sunscreen, window glass and pollution
     - Sources of Vitamin D
       a. Fatty fish (e.g., tuna, mackerel, and salmon)
       b. Foods fortified with vitamin D (e.g., dairy products, orange juice, soy milk, and cereals)
       c. Mushrooms
       d. Beef liver
       e. Cheese
       f. Egg yolks
2. Exercise
   - Weight-bearing
   - Use weights lighter than 15 lbs., if with osteopenia
3. Avoid excessive alcohol
   - One should limit to no more than 1 drink per day for women and 2 for men.
     Note: 1 alcoholic drink is equivalent to:[17]
     - 12 ounces of regular beer, which usually contains 5% alcohol
     - 5 ounces of wine, which typically contains about 12% alcohol
     - 1.5 ounces of distilled spirits, which contains about 40% alcohol

4. Stop smoking
   - Smokers reach menopause, on average, 2 years earlier than non-smokers.
5. Avoid falls
   - In older adults, falls occur while walking slowly, with the tendency to collapse sideways or backwards and land directly on a hip. Thus, osteoporotic fractures commonly affect the hip joint. Younger and more agile persons tend to move faster and fall forward, land on the outstretched wrist, thus fracturing the distal radius.

B. Pharmacologic Treatment of Osteoporosis

TABLE 15–7. Pharmacologic treatment of osteoporosis

CLASS OF MEDICATION/ EXAMPLE	MECHANISM OF ACTION	ADVERSE EFFECTS
Bisphosphonates a. Alendronate b. Zoledronic acid	• Inhibits osteoclast-mediated bone resorption by binding preferentially to active sites of bone resorption, thereby inhibiting osteoclast action without inhibiting osteoblast action • Decreases bone turnover, resulting in progressive increase in bone mass • May lead to significant decreases in serum calcium and phosphate levels	Most common GI symptoms; acute flu-like illness Rare Renal complications Osteonecrosis of the jaw Atypical fragility fractures
Raloxifene	• Selective estrogen receptor modulator • Selective agonist on bone metabolism, preventing bone loss • decreases total and LDL cholesterol levels	Most common Hot flushes, flu-like syndrome, leg cramps, peripheral edema, sweating, arthralgia Rare GI disturbances, rashes, thrombocytopenia, increased BP, headache, mild breast symptoms (e.g. tenderness, pain, enlargement)
Hormone replacement therapy	• Estrogen receptor modulator • Anti-resorptive role on bones	Significant Increased risk of breast, endometrial, and ovarian cancers, CV disorders (e.g., DVT, pulmonary embolism, stroke, MI), dementia, gallbladder disease General disorders GI disturbances, palpitation, back or pelvic pain Potentially fatal Anaphylaxis
Tibolone	• Steroid that acts as a selective estrogen activity regulator • Estrogen receptor activator, resulting in decrease in bone resorption • Does not stimulate estrogen receptors in the breast and endometrium	Weight gain, dizziness, rash, pruritus, headache, migraine, visual disturbances, GI symptoms, facial hair growth, altered liver function, ankle edema, depression, arthralgia or myalgia, irregular vaginal bleeding

TABLE 15–7. **Pharmacologic treatment of osteoporosis (cont.)**

CLASS OF MEDICATION/ EXAMPLE	MECHANISM OF ACTION	ADVERSE EFFECTS
Calcitonin	• Polypeptide hormone that inhibits osteoclastic bone resorption and reduces bone turnover • Decreased tubular reabsorption and promotes renal excretion on Ca, Cl, Na, Mg, K, and phosphate	Diabetogenic effect, GI disturbances, abdominal pain, injection site inflammation, dizziness, tingling of hands, tremors, urinary frequency, skin rash, flushing
Estrogen therapy/ Hormone therapy	• Modulates pituitary secretion of gonadotropins, LH, and FSH through negative feedback • Anti-resorptive role on bones	Significant Endometriosis, retinal vascular thrombosis, increased HDL and triglycerides, decreased LDL, increased risk of gallbladder disease
Parathyroid hormone 1-34 (teriparatide)	• Biosynthetic peptide fragment of the parathyroid hormone, which preferentially stimulates osteoblastic over osteoclastic activity • Stimulates bone formation on trabecular and cortical bone surfaces, increasing skeletal mass and bone strength	Nausea, pain in the limbs, headache, dizziness, muscle cramps, injection site reactions, depression, increased uric acid concentrations
Denosumab	• Monoclonal antibody • Binds to receptor activator of nuclear factor kappa-B (RANKL), preventing it to bind to its receptor, RANK, thus inhibiting osteoclast formation	Significant Back pain, musculoskeletal pain, hypercholesterolemia, hypercalcemia, cystitis, dermatitis, rash, eczema, hypersensitivity reactions (anaphylaxis) Rare Osteonecrosis of the jaw, atypical femoral fractures

GI, Gastrointestinal; LDL, Low-density lipoprotein; CV, Cardiovascular; DVT, Deep vein thrombosis; MI, Myocardial infarction; LH, Luteinizing hormone; FSH, Follicle-stimulating hormone; HDL, High-density lipoprotein

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OPEN FORUM HIGHLIGHTS

Moderator: JULIE ANNE GABAT-TAN, MD

Q: *Can you screen for osteoporosis earlier if your patient has pituitary insufficiency or surgical menopause?*

A: Anybody who is at risk, at any age, must be screened and treated to avoid that first fracture. (Note: Both conditions cause hypogonadism, which is a secondary cause of osteoporosis. Pituitary insufficiency results in secondary hypogonadism due loss of FSH and LH signals to the ovary to produce estrogen. Surgical menopause is the removal of ovaries [primary producers of estrogen] causing primary hypogonadism)

Q: *Can we replace cow's milk with soya milk?*

A: Yes, as long as it contains as much calcium as the cow's milk, so check the labels. A glass of cow's milk contains around 200 mg. The recommended daily allowance is 1200 mg.

Q: *Should we take calcium carbonate, or calcium with vitamin D?*

A: If you are lacking in the diet, you should take calcium. The recommended daily allowance of calcium is 1200 mg. For vitamin D, I recommend you check the baseline levels of vitamin D in your blood to see how insufficient you are and how much you need. Regular supplement contains 400–600 IU which is the recommended daily allowance if you have sufficient Vitamin D. If you have vitamin D insufficiency, we want to increase the level above 30 ng/dL, which can range from 1000–5000 IU per day. It usually takes one month to increase the level by 10 ng/dL, but overweight and obese patients need more since vitamin D is fat-soluble. There are really a lot of vitamin D-deficient Filipinos because we don't go out in the sun. [Some] Filipinos also may also have a vitamin D receptor mutation.

Q: *Are there any side effects when we take excess vitamin D and calcium?*

A: It is hard to overdose with vitamin D because the excess is converted into something water-soluble and easy to excrete. But there's a risk if one takes too much calcium since it can be deposited in the blood vessels and soft tissues (e.g., kidney stones, atherosclerosis). It is better to take calcium sources from the diet, but if you cannot, just take 1 supplement a day. I wouldn't advise taking more than what your doctor recommends.

Q: *Can carrying heavy loads predispose to osteoporosis or pathologic fractures?*

A: If your bone is normal, lifting heavy loads will not make your bone weaker or predispose you to fractures. Since it is a weight-bearing exercise, the load makes the normal bone stronger. However, if your bones are already weak and you carry heavy loads the wrong way, then you may develop a fracture.

Q: *Do you recommend nutrition drink supplements (e.g., Ensure milk) for a bedridden patient who is 80 years of age?*

A: It depends on the nutritional needs of the patient. Nutrition drink supplements are very high in calories and can help if the patient doesn't eat enough. Being bedridden is also a risk factor for osteoporosis. Since bedridden patients are not bearing any weight, the osteoclasts are more active, and predispose them to osteoporosis. You should have the patient screened. If a bedridden patient is moved the wrong way, they may get fractures. Vitamin D deficiency due to lack of sun exposure should also be treated.

Q: *How effective is denosumab in increasing bone density?*

A: Denosumab is given once every 6 months as an injection. It is an antibody against receptor activator of nuclear factor kappa-B ligand (RANKL), which activates osteoclasts. The data shows that you can increase your bone density with denosumab. However, unlike bisphosphonates which should be given drug holidays due to cumulative deposition that predisposes to fractures, one should not miss any doses or do drug holidays with denosumab. The theory is that, because the bone density decreases back to its original level or lower once you do, and since the patient is older, there is an increased risk for vertebral fractures. It's good for patients who can't tolerate or remember taking tablets. It can be taken for 10 years.

Q: *What is the maximum dose of Vitamin D for patients with a fracture already?*

A: The dose of cholecalciferol (Vitamin D3) depends on your levels and response to the supplement. So you should get tested. Vitamin D2 is plant-derived (10,000 to 50,000 IU) and can be taken once a week.

Q: *Do you treat osteopenia?*

A: Osteopenia is not usually treated unless a patient has risk factors that can predispose one to fracture, such as steroid or hormone use, malignancy or a previous fracture. There is a country-specific assessment scale that can serve as a guide to whether we should treat or not, called FRAX or the Fracture Risk Assessment Tool (https://www.sheffield.ac.uk/FRAX/tool.aspx?country=33)[20]. FRAX is not all encompassing for all possible risk factors, and all the other conditions of the patient and the characteristics of the various treatments available should be considered before making a decision to treat a patient with osteopenia. Patients should talk to their doctor and discuss if treatment is indicated.

Q: *If a patient does not respond to intravenous zoledronic acid or any biphosphonate after a year, what is next treatment to give?*

A: Reassess why the drugs are not working and identify underlying conditions. Another possible reason is non-compliance. It's less likely that the patient is non-compliant with intravenous zoledronic acid since it is only given once a year. However, for oral bisphosphonates, it is possible that they are non-compliant. But if you've ruled out the above reasons, depending on the bone density, two other options are denosumab, every 6 months, or teriparatide, a daily injectable anabolic drug. Teriparatide can only be given for two years, after which when you have built up the bone, you should immediately follow with oral bisphosphonate or denosumab. FDA approval for teriparatide is only up to two years because there is an increased risk for sarcoma as shown in animal studies.

Q: *Are scoliosis and multiple sclerosis considered risk factors for osteoporosis?*

A: Diseases like this become risk factors when patients are unable to exercise and bear weight.

Q: *Is it still recommended for adults to go under the sun to get vitamin D? How does climate change affect this recommendation?*

A: The recommendation is still 10 am–3 p.m. for 10–15 minutes. There's only a certain wavelength of light at which there is UVB light.

Q: *Have you encountered jaw osteonecrosis in your patients treated with bisphosphonates?*

A: Not in my own practice fortunately, but it's common enough. But the benefits outweigh the risks. It can be a problem for patients who need dental work. So before starting bisphosphonates, ask your patients about needing any dental work and get this done before starting the bisphosphonates.

Q: *Can you give hormonal therapy?*

A: Yes, to patients who just started menopause, for as long as they have symptoms of menopause. Check for contraindications such as history of cancer or current smoking. Give it at the lowest dose possible and reassess regularly if it is still needed to control symptoms of menopause.

Q: *When do you suspect atypical fractures?*

A: In a patient on bisphosphonates for 3 years or more who develops inguinal pain, or on the sides of the hips. On x-ray: "beaking" on the femoral shaft → transverse fracture.

Q: *How do we ensure adequate Vitamin D levels without an increase in skin cancer from sun exposure?*

A: Take supplements instead of going out in the sun.

REVIEW QUESTIONS

1. Who should be screened for osteoporosis?
    a. Adults with a fragility fracture at any age
    b. Men starting at 50 years of age
    c. Women starting at 40 years of age
    d. Postmenopausal women at any age

2. Which is a normal Z-score result? (compared to the mean BMD of a young adult)
    a. Below –2.0 SD
    b. Above –2.0 SD
    c. Below 2.0 SD
    d. Above 2.0 SD

3. Which of the following is the gold standard screening test for osteoporosis?
    a. Osteoporosis Screening Tool for Asians (OSTA)
    b. Central Bone Mineral Density (BMD) Testing
    c. Peripheral Bone Density Test
    d. Vertebral Imaging

4. Which of the following medications is associated with secondary osteoporosis?
    a. Calcium
    b. Glucocorticoids
    c. Paracetamol
    d. Penicillin

5. Which of the following is a risk factor for osteoporosis?
    a. Intake of sugar-sweetened beverages
    b. Obesity
    c. Parental history of hip fracture
    d. Sedentary lifestyle

ANSWERS: 1. a; 2. b; 3. b; 4. b; 5. c

16 TAKING CARE OF THE AGEING KIDNEYS

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Delivered as a webinar on September 13, 2019

https://bit.ly/ALMW_Ch16_AgeingKidneys

KEY POINTS

- Our kidneys get older. The ageing kidneys of healthy elderly share two characteristics in common with chronic kidney patients: decreased GFR and decreased urinary concentrating ability. However, for the healthy elderly, kidney function, including erythropoietin and electrolyte levels, remain normal.
- The elderly are prone to drastic changes in fluid and nutritional intake and should be closely monitored.
- We should maintain a healthy lifestyle to prevent comorbidities, such as hypertension and obesity, and take proper care of our kidneys.
- We should follow the 8 golden rules for kidney health:
    1. Keep fit and active.
    2. Keep regular control of your blood sugar.
    3. Monitor your blood pressure.
    4. Eat healthy and keep your weight in check.
    5. Maintain a healthy fluid intake.
    6. Do not smoke.
    7. Do not take over the counter pills on a regular basis.
    8. Get your kidney function checked if you have one or more of the 'high risk' factors.

LEARNING OBJECTIVES

- ➸ Describe the structural and functional changes in the kidneys with ageing
- ➸ Discuss the effects of ageing on pre-existing kidney disease
- ➸ Discuss ways of taking care of our kidneys to mitigate the effect of ageing

I. PHYSIOLOGY IN HEALTHY AGEING KIDNEYS

A. Serum Creatinine Levels in Ageing

- In the healthy ageing population, serum creatinine levels remain within the normal range through the years (Figure 16–1).

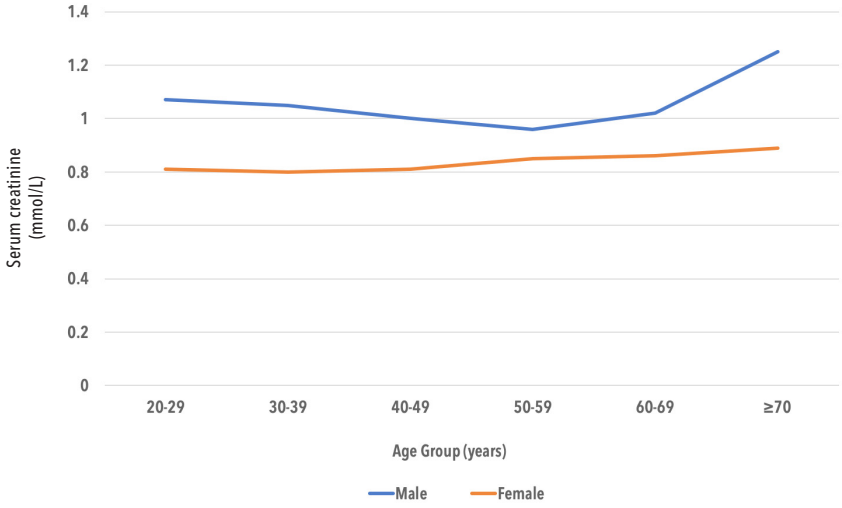

FIGURE 16–1. Serum creatinine levels across various age groups with healthy individuals with normal blood pressure and body mass index, and not on medications (N=180)

Source: Czarkowska-Paczek, B., Wyczalkowska-Tomasik, A., & Paczek, L. (2018). Laboratory blood test results beyond normal ranges could not be attributed to healthy aging. *Medicine*, 97(28), e11414.[1]

- There is a decline in estimated glomerular filtration rate (eGFR) to around 70 to 80 ml/min for both sexes with age as shown in these studies of Filipino (Table 16–1) and Japanese populations (Figure 16–2).

TABLE 16–1. Estimated GFR across age group and sex (Philippine National Nutrition Survey 2003–2004)

AGE (YRS.)	eGFR (ml/min)		
	BOTH SEXES	MALE	FEMALE
20–29	**119** (113–125)	**124** (112–135)	**114** (113–117)
30–39	**109** (103–114)	**113** (104–123)	**104** (102–106)
40–49	**103** (96–110)	**106** (95–117)	**100** (92–108)
50–59	**100** (90–109)	**104** (86–92)	**96** (88–105)
60–69	**86** (84–92)	**89** (76–88.9)	**83** (81–84)
≥70	**77** (75–80)	**82** (76–89)	**74** (72–76)
Mean	**107** (106–110)	**112** (106–117)	**102** (100–104)

eGFR, Estimated glomerular filtration rate

Source: Food and Nutrition Research Institute (Department of Science and Technology). *Philippine Facts and Figures*. 2003–2004.[2]

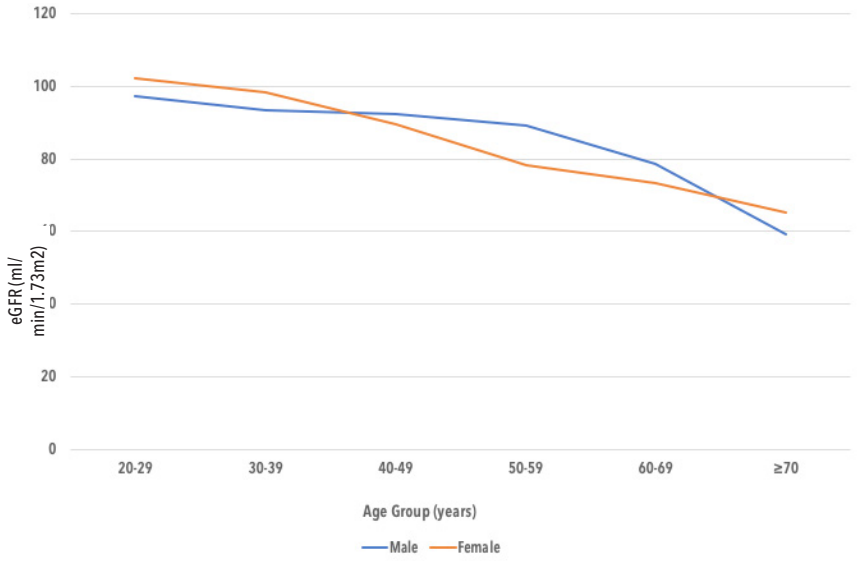

FIGURE 16–2. eGFR across various age groups (N=72,521 healthy Japanese subjects visiting a preventive medicine clinic)

eGFR, Estimated glomerular filtration rate

Source: Baba M, Shimbo T, Horio M, Ando M, Yasuda Y. Longitudinal study of the decline in renal function in healthy subjects. *PLoS One.* 2015:1-1[3]

B. Creatinine as a Marker of GFR

- Creatinine is endogenously produced from metabolism of muscle creatine.
- Serum creatinine levels reflect total body supply of creatinine and correlate with muscle mass.
- Several factors may affect serum creatinine levels (Table 16–2).
- The amount of excretion which reflects creatinine production varies according to body weight, gender and age.
  - Female: 15 to 20 mg/kg/day
  - Male: 20 to 25 mg/kg/day

TABLE 16–2. Factors affecting serum creatinine level

FACTOR	EFFECT ON SERUM CREATININE	MECHANISM
Kidney disease	Increase	Decreased filtration rate *However, increase is blunted by increased tubular secretion and reduced generation of creatinine.
Reduced muscle mass	Decrease	Reduced creatinine concentration
Ingestion of cooked meat	Increase	Transient increase in creatinine generation
Malnutrition	Decrease	Reduced creatinine generation
Trimethoprim, Cimetidine	Increase	Inhibition of tubular creatinine secretion
Ketoacidosis	Increase	Positive interference with picric acid assay method for creatinine

Source: Manjunath G, Sarnak MJ, Levey AS. Prediction equations to estimate glomerular filtration rate: An update. *Curr Opin Nephrol Hypertens*. 2001;10:785-792[4]

C. Cystatin C as a Marker of GFR

- Cystatin C is a protease inhibitor that is produced by all nucleated cells, and found in virtually all tissues and fluids.
- It is freely filtered by the glomeruli, reabsorbed and degraded by the proximal tubules.

II. STRUCTURAL CHANGES IN THE AGEING KIDNEY[6]

- The main histologic change (=nephrosclerosis), based on renal biopsy findings of healthy living kidney transplant donors, is due to arteriosclerosis that leads to glomerulosclerosis, tubular atrophy, and interstitial fibrosis.
- The gross anatomical findings (based on CT scan imaging studies) have two components.
  1. Reduced kidney volume
     - The smaller number of intact functioning nephrons excrete practically the same amount of solutes as in the normal kidney. Thus the solute excreted per surviving nephron is increased.
  2. Renal cyst
     - On ultrasound, it is seen as thin-walled, with anechoic content and absent septa, calcification or solid components.
     - The number of simple renal cysts increases with age, but is compatible with life and does not affect kidney function.[6]

TABLE 16–3. Histological and gross anatomical changes in kidneys with ageing

HISTOLOGICAL CHANGES (RENAL BIOPSY)	GROSS ANATOMICAL CHANGES (CT SCAN)
Glomerular changes • Pericapsular fibrosis • Wrinkling of capillary tufts • Progressive thickening of basement membrane • Collapse of glomerular tufts, leading to global sclerosis	Reduced kidney volume ○ *Age 40s* → Cortex becomes thinner and medullary volume increases ○ *Age 50s* → Atrophy of tubules and reduced medullary volume lead to shrinkage of kidneys
Bowman's space • Deposition of matrix-like hyaline material	Renal cyst ○ Typically cortical ○ Distinct, sharp defined outline ○ Thin cyst wall, with characteristically smooth, transparent, avascular, yellowish/bluish white in color

Source: Denic A, Glassock RJ, Rule AD. Structural and functional changes with the aging kidney. *Adv Chronic Kidney Dis*. 2016;23(1):19-28.[5]

III. EFFECTS OF AGEING ON PRE-EXISTING KIDNEY DISEASE

A. Loss of urinary diluting/concentrating capacity of ageing kidneys[7]

- The elderly are predisposed to hypoosmolality and hyponatremia due to loss of diluting capacity. They are also predisposed to dehydration, hyperosmolarity, and hypovolemia due to loss of concentrating ability (Figure 16–3).

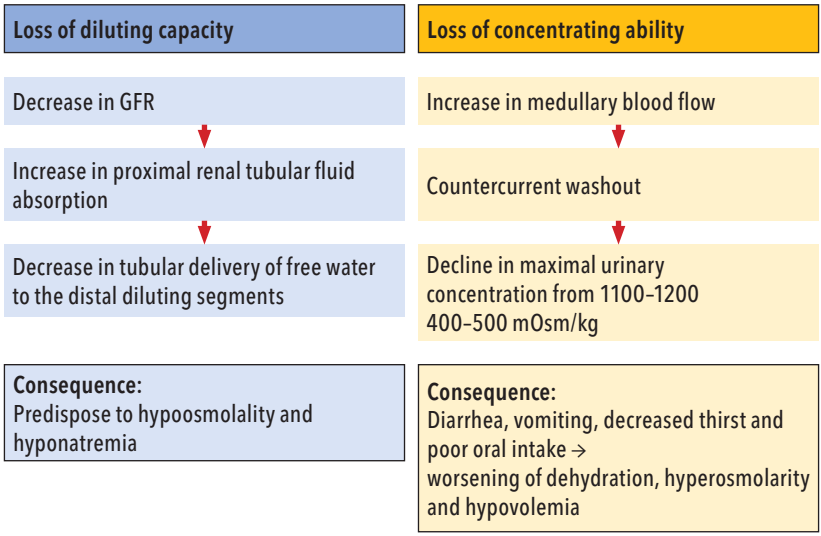

FIGURE 16–3. Mechanisms of loss of urine diluting and concentrating capacity of ageing kidneys

- In both healthy ageing kidneys and CKD, there is decrease in GFR and dysfunction in urine dilution and loss of concentrating ability.
- However, healthy ageing kidneys have normal erythropoietin, hemoglobin, serum urea calcium, magnesium, phosphate, vitamin D, parathyroid hormone, and urinalysis while abnormalities are present in CKD (Table 16–4).

TABLE 16–4. Healthy ageing kidneys versus chronic kidney disease

LABORATORY PARAMETER	HEALTHY AGEING KIDNEY	CHRONIC KIDNEY DISEASE
Erythropoietin	Normal	Low
Hemoglobin	Normal	Low
Serum urea	Normal	Increased
Serum Ca, Mg, Phosphate	Normal	↑Phosphate, ↓Ca++, ≈Mg++
Vitamin D, PTH	Normal	↓Vitamin D, ↑PTH
Fractional excretion of K	Decreased	Increased
Urinalysis	Normal	Presence of hematuria, proteinuria

Ca, Calcium; Mg, Magnesium; PTH, Parathyroid hormone; K, Potassium

Source: Musso CG, Oreopoulos G. Aging and physiological changes of the kidneys including changes in glomerular filtration rate. *Nephron Physiol*. 2011;119(suppl 1):1-5.[8]

B. Clinical Implications of Ageing Kidneys

- Age-related functional decline in the kidney has very little effect on life expectancy, but ageing kidneys are more susceptible to acute kidney injury.
- Older people are prone to dehydration and overhydration and have increased sensitivity to salt restriction and increased salt intake.
- Protective actions include caution in using NSAIDs and contrast agents in the elderly especially those with preexisting kidney disease and dose adjustment of some medications.

C. Impact on Kidney Donation

Motivated older individuals may be accepted for kidney donation.

- There is lower mortality rate in a cohort of 219 healthy living donors older than 70 years of age compared to healthy age-matched controls.[9]
- In contrast, there was increased long-term risk for ESRD, cardiovascular and overall mortality in kidney donors (mean age: 46 y.o.) compared to a control group in a Norwegian case-control study.[10]

IV. 8 GOLDEN RULES FOR TAKING CARE OF THE KIDNEYS

#1: Keep fit and active.	Regular physical activity helps to maintain an ideal body weight, reduce your blood pressure and the risk of CKD.	"Move Your Feet" campaign (World Kidney Day, 2018)
#2: Keep regular control of your blood sugar.	• The criteria for the diagnosis of diabetes mellitus are[12]: 1. Fasting plasma glucose FPG ≥126 mg/dL 2. 2-hour plasma glucose PG ≥200mg/dL during oral glucose tolerance test OGTT 3. HbA1C ≥6.5% 4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random PG ≥200 mg/dL • Diabetic nephropathy is the top 1 cause of ESRD (Philippine Renal Disease Registry [2000-2016])[13]	• "Protect Your Kidneys: Control Diabetes" campaign (World Kidney Day, 2010) • Fasting PG diagnosis Diabetes risk test (Figure 16–4)
#3: Monitor your BP.	• Hypertensive nephrosclerosis is the top 2 cause of ESRD (Philippine Renal Disease Registry [2000-2016]).[13]	• "Protect your kidneys: Keep your pressure down" (World Kidney Day, 2009) • For the nonproteinuric patients (Urine albumin excretion ≤30mg/24 hrs.): ○ Maintain a BP that is consistently ≤140 mmHg systolic and ≤90 mmHg diastolic.[14] • For urine albumin excretion of >30 mg/24 hrs.: ○ Maintain a BP that is consistently ≤130 mmHg systolic and ≤80 mmHg diastolic

#4: Eat healthy and keep your weight in check.	• Obesity-related glomerulopathy[15] 1. Physiologic response: increases in GFR, renal plasma flow, and filtration fraction, increases in renal tubular reabsorption of sodium 2. Glomerulomegaly 3. Focal segmental glomerulosclerosis[16] 4. Sub-nephrotic proteinuria 5. Absence of nephrotic syndrome even in patients with massive proteinuria • There is increased risk of incident CKD in a cohort of metabolically healthy BUT obese group without CKD (multivariate-adjusted hazard ratio of 1.38; 95% CI, 1.01–1.87) compared with the metabolically healthy non-obese group.[17] • The incidence of ESRD increased as the BMI increased in a large community-based screening (Okinawa Dialysis Registry), especially important among males since risk is higher.[18]	• "Healthy lifestyle and healthy kidney" (World Kidney Day, 2017) • WHO recommendations:[19] ○ Limit energy intake from total fats and sugars ○ Increase consumption of fruits and vegetables, as well as legumes, whole grains and nuts ○ Engage in regular physical activity (60 minutes a day for children and 150 minutes spread through the week for adults).
#5: Maintain a healthy fluid intake.	• Age-associated abnormalities of water homeostasis (changes in body water and osmolality):[7] ○ 5 to10% increase in total body fat and a decrease in total body water of an equal magnitude ○ Plasma volume has been shown to decrease by as much as 20% relative to body weight and surface area. ○ Consequence: Loss or gain of body fluids will cause clinically significant shifts in the concentration of body solutes particularly sodium (hypo/hypernatremia). ○ Elderly subjects appear to have a higher osmolar set point for thirst. ○ The loss of an appropriate thirst response compromises the critical compensatory mechanisms responsible for the drive to replace lost body fluid, and the only true physiological means of correcting a hyperosmolar state. • Elderly are prone to dehydration/congestion, due to: ○ Concentrating/diluting problems ○ Compromised homeostatic mechanisms, e.g., loss of thirst ○ Variable fluid needs in healthy older people that is greatly influenced by level of physical activity, ambient temperature, and medication use	• Healthy water intake should be part of the food pyramid.[20] ○ The adequate intake (U.S. population) for total water (beverages and food) for ≥50-year-old adults is 2.7 L/d for women and 3.7 L/d for men.
#6: Do not smoke.	Heavy cigarette smoking may increase the overall risk of CKD, and particularly for those due to hypertension and diabetes.[21]	Encourage smokers to quit smoking.

#7: Do not take over-the-counter pills on a regular basis.	• Types of kidney injury as adverse effects of non-steroidal anti-inflammatory drugs[22] ○ Acute kidney injury (AKI) may occur due to reduced renal plasma flow caused by a decrease in prostaglandins that regulate vasodilation at the glomerular level. ○ Acute interstitial nephritis (AIN), characterized by the presence of an inflammatory cell infiltrate in the interstitium of the kidney, may be caused by an immunological reaction after NSAID exposure for around a week. ○ Chronic kidney disease may occur after long term use of NSAIDs. • The odds for AKI are even higher in the elderly taking non-COX-2-selective NSAIDs (OR, 1.74, 95% CI, 1.32, 2.29) compared to the general population using NSAID (1.62, 95% CI, 1.43, 1.84).[23]	
#8: Get your kidney function checked if you have one or more of the 'high risk' factors.	• **Risk factors** 1. Diabetes 2. Hypertension 3. Obesity 4. Family history of kidney disease 5. African, Asian, or Aboriginal origin 6. There is a need to differentiate between age- and disease- related changes in the kidneys.	• When to see a nephrologist? ○ When there is deterioration of kidney function that is faster than what is normally expected due to ageing, consider the presence of comorbidities or chronic kidney disease, and refer accordingly.[24] • It is imperative that elderly population get routine serum creatinine examinations so one can compute the decline in kidney function.

Source: World Kidney Day. *8 Golden rules: What can you do for your kidneys?* https://www.worldkidneyday.org/facts/take-care-of-your-kidneys/8-golden-rules/. Accessed March 6, 2020.[11]

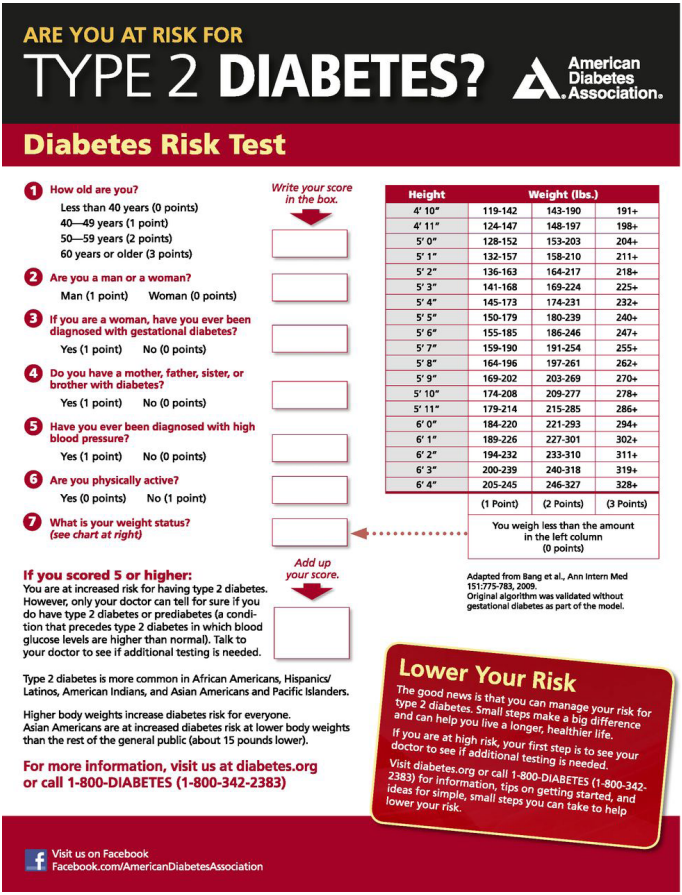

FIGURE 16–4. Diabetes Risk Test

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OPEN FORUM HIGHLIGHTS

Moderator: JULIE ANN GABAT-TAN, MD

Q: *Is it normal for a 95-year-old patient, who has normal urinalysis results, to urinate 50 to 60 ml every hour?*

A: The elderly may have problems in the voluntary control of urination. Because of the weakness of the external sphincter muscles, they are unable to voluntarily control micturition, which is why they urinate more frequently.

Q: *What causes the formation of renal cysts? If an elderly patient comes with a simple renal cyst on CT scan or ultrasound, do we have to monitor it? And if so, how frequently do we monitor? Are there instances when it can affect kidney function and needs to be removed?*

A: Renal cyst is a diverticulum of the renal tubule, which is commonly due to an obstruction of the distal tubule. Renal cysts are part of ageing and we don't monitor it very frequently. They should get evaluated for renal function, which includes ultrasound, every year. However, they should be assured that these are simple renal cysts and will not significantly affect their kidney function. We usually leave renal cysts alone. The most important thing is to differentiate between simple and complicated renal cysts.

Q: *Why is there a high risk of kidney disease among Asians and Aboriginals? Does this mean that our kidneys age faster compared to our Caucasian counterparts? What is special about the African American population that they are included in the CKD-EPI equation?*

A: There are many theories: genetic, such as being born with lesser nephrons, a phenomenon called 'nephron endowment', or being smaller in built; and environmental. If we are going to compare studies, the rate of deterioration is similar among races, around 1ml/min/year. African Americans were found to have a faster rate of deterioration in kidney function. I cannot say with certainty as to why this is so.

Q: *How does alcohol intake affect kidney function?*

A: Alcohol does not greatly affect kidney function. However, extra-renal consequences of alcohol intake, such as dehydration, liver injury, rhabdomyolysis, and acidosis, may indirectly affect the kidney.

Q: *Does long-term intake of whey protein for weight gain or muscle building destroy the kidneys or hasten the progression of kidney decline? Are body builders more at risk for faster kidney decline? Is it not compensated by increased water intake? How do we advise patients who are keen on building muscle?*

A: A high-protein diet causes glomerular hyperfiltration, and hyperfiltration leads to glomerulosclerosis. If you are taking a very high-protein diet, glomerulosclerosis will be accelerated. There are some body builders with elevated creatinine levels who are on a high-protein diet. Increasing water intake is not going to cure the kidney problem. The recommended amount for normal protein intake is about 0.8 g/kg body weight. More than 1.3 g of protein per kg body weight is associated with a faster rate of progression of renal failure among patients with CKD because the kidneys work harder. A lot of waste matter will be generated from a high-protein diet, which the kidneys have to handle.

Q: *Will the intake of prednisone and other anti-lupus medications for three or more years in a patient with lupus, without diabetes and with healthy kidney function, who takes in 2 to 3 glasses of water per day and extra salty food, eventually lead to kidney injury?*

A: There are very distinct pathologic lesions in lupus nephritis, for which prednisone and other medications are indicated. However, changes such as fibrosis and sclerosis are irreversible changes and will not respond to steroids anymore.

Q: *Is voluntary restraint of urination a risk factor for kidney disease if habitually done among elderly patients?*

A: As the urinary bladder fills up to a certain volume, one starts to feel the urge to void. Normally, we can consciously suppress urination by contracting the urinary sphincter muscle. Eventually this desire to urinate disappears. However, as the bladder continues to fill up, the urge to void appears again becoming more frequent and stronger. Soon urination becomes compelling. Normally, we can hold our bladder only to a certain degree. The complete emptying of the urinary bladder is our strongest defense against urinary tract infection. It flushes out the bacteria that may have entered the urinary bladder. Most of the time, the elderly have weak urinary sphincter muscle. They urinate more often and sometimes there is urinary leak. The muscles of the urinary bladder may become weak with ageing so the bladder does not completely empty when they contract. The retention of urine in the bladder allows the bacteria to multiply.

Q: *What can you advise a 65-year-old patient with nephrolithiasis of the left kidney, a serum creatinine of 265 mg/dL, who is also an alcoholic and smoker? Is this patient a likely candidate for dialysis? How can we control and prevent further kidney damage?*

A: The nephrolithiasis on the left may just be an incidental finding. The creatinine level will not go up if you have one healthy kidney. This healthy other kidney will take over the function of the diseased kidney. If you have a creatinine of 200 mg/dL and above, this means that both kidneys are probably damaged. Since both kidneys are damaged, and one kidney has a nephrolithiasis that might not even be obstructing, there may be other reasons. Go through the history to explain the elevated creatinine level and involvement of both kidneys. Smoking is a risk factor. The patient may also have hypertension or diabetes, or maybe taking NSAIDS.

Q: *Are fish oil supplements helpful for the ageing kidneys and are they safe for kids who are aged 5 years and older?*

A: We don't have definite studies on fish oil supplements. They have been studied on a certain type of glomerulonephritis, for which they are given as treatment. However, we do not generally recommend them.

Q: *Chronic and repetitive UTI is a common complaint among the elderly. How do we manage these repeated bouts of UTI?*

A: First, determine if it is symptomatic or asymptomatic. Second, determine if there are structural changes in the bladder, such as neurogenic bladder, that need to be corrected. In addition, there is a guideline on recurrent UTI among the elderly. If there is no fever, no leukocytosis and some pus cells in the urine, then we can just observe. Treat accordingly and as necessary, such as when the patients present with fever or general body malaise and other systemic symptoms.

Q: *How long is the validity of a creatinine result, particularly for contrast studies? What time interval is acceptable?*

A: If it is just because of the ageing process, one year is still acceptable within which time the creatinine level should be stable. But we have to understand that many things can happen to the kidneys, such as NSAID use that can cause acute kidney injury. Thus, it is best to get creatinine levels right before contrast studies.

Q: *Would it be more cost effective to use cystatin C than creatinine for our patients? Is it available in most laboratories?*

A: It is available in some centers but is still more expensive compared to serum creatinine. If it becomes widely used, maybe the cost will go down. As of now, creatinine level is still the measure ffor assessing kidney function because it is available in almost all laboratories and the cost is not that prohibitive. If the cost of cystatin will go down maybe it can be the standard measure together with creatinine because the equation uses both cystatin and creatinine.

Q: *In relation to AKI, particularly in the elderly patients taking NSAIDs, how soon do we repeat the creatinine to say that the injury has resolved?*

A: In the elderly individuals, it is difficult to say when the kidney function has recovered after an acute kidney injury, because the recovery period is not predictable for them. We should monitor creatinine every week to pick up further improvement or deterioration of kidney function. We might miss out on the chance to intervene if there's a progressive increase in creatinine level. There are two presentations: 1. Acute kidney injury due to decreased renal blood flow, which happens fast, and 2. Acute interstitial nephritis, which occurs in a week.

Q: *When are keto-analogues recommended for chronic kidney disease patients and how effective are they?*

A: First, we have to start with the diet. For patients with CKD stage 3 with a GFR of 30 to 60 ml/min, they should be started on a low-protein diet (less than 0.6g/kg) to prevent hyperfiltration of the kidneys. The protein should be of high biologic value. If with a GFR below 30 ml/min, patients should be place on a very low protein diet (0.3 g/kg), which is the time to give supplements. Keto-analogues provide the necessary amino acids that are converted to protein in the setting of a very low protein diet. There are many studies that showed a delay in the onset of dialysis among patients who were placed on a very low protein diet with ketoanalogue/essential amino acid supplements. Our aim is to delay dialysis because it is inevitable once the kidney function is very low. It is cost effective.

Q: *What is your opinion on the use of statins for patients with high blood cholesterol level, since the latter is responsible for atherosclerosis? Do its beneficial effects (i.e., preventing atrophy and collapse of the glomeruli and kidney disease) outweigh its adverse effects?*

A: The use of statins in the pre-dialytic patients is beneficial. We need to lower down lipid levels. For the dialytic patients, there is no benefit in giving statins versus placebo. The KDIGO guidelines state that, if the patient is on statins pre-dialysis, continue its use when patient goes into dialysis. If patient is not on statins pre-dialysis, do not start statins when patient begins dialysis.

Q: *How is nephrolithiasis managed in the elderly patients since we cannot over or underhydrate the patient? Does calcium intake or calcium supplements predispose to stone formation in the elderly?*

A: Around 3.7 L is adequate intake for women aged 19 to older than 70 years and 2.7 L for men in the same age group. Water intake is similar in the young. Elderly patients have to drink on a regular basis and not binge on water intake. Hydration is still one of the measures to prevent stone formation but medical management is available for stone dissolution. The usual calcium intake does not cause stones. In fact, withdrawing calcium is not good. Calcium binds the oxalates, which is one of the culprits of stone formation. Among patients with kidney stones, the usual intake of calcium as a supplement is not contraindicated.

Q: *Will elderly patients with renal calcinosis eventually require dialysis?*

A: No. Renal calcinosis is the deposition of calcium in the renal parenchyma. It is non-obstructing. It is not usually a cause of end-stage renal disease. For these particular patients, there may be comorbidities, such as diabetes and hypertension, that lead to the development of ESRD. These are more important causes of ESRD than calcinosis.

Q: *Is there a possibility of nephrogenesis as a form of kidney remodeling in humans?*

A: I don't know. We don't have anything yet in the pipeline for regeneration of kidneys. We still consider the kidney endowment theory, which states that you have the same number of nephrons at birth; but there will be attrition due to glomerulosclerosis as you age.

Q: *What medication is advised for a patient with hypertension who has microalbuminuria?*

A: For patients with microalbuminuria, we would recommend an ACE inhibitor or an angiotensin receptor blocker because these have been shown to reduce proteinuria and better protect the kidneys compared to other antihypertensive medicines.

Q: *Can you give us a maximum age at which one can still benefit from a renal transplant, knowing that the elderly are not routinely placed in the kidney transplant waiting list?*

A: I really don't have a cap on the age of the patients, for as long as the patient is healthy; healthy means, still with good blood vessels, a good heart and good cerebral function. In fact we have previously mentioned that even the elderly can donate their kidneys, provided that they are healthy.

Q: *If you have a patient with congestive heart failure on fluid restriction, what is the acceptable or maximum creatinine level for the patient to proceed to dialysis?*

A: Patients who fail to respond to the standard management of congestive heart failure can start dialysis to remove the fluid.

REVIEW QUESTIONS

1. Which of the following markers of GFR is produced by all nucleated cells, found virtually in all tissues and fluids, freely filtered by the glomeruli, reabsorbed and degraded by the proximal tubules, and is NOT affected by age or muscle mass?
   a. Creatinine
   b. Blood urea nitrogen
   c. Cystatin C
   d. EDTA

2. Which of the following is decreased in chronic kidney disease?
   a. Parathyroid hormone
   b. Vitamin D
   c. Fractional excretion of potassium
   d. Phosphate

3. Which of the following factors increase serum creatinine?
   a. Reduced muscle mass
   b. Low protein diet
   c. Malnutrition
   d. Ketoacidosis

4. Which of the following statements is correct?
   a. Ageing kidneys are generally less susceptible to acute kidney injury
   b. Features of nephrosclerosis are arteriosclerosis, glomerulosclerosis, tubular atrophy and interstitial fibrosis
   c. Age-related kidney functional decline has a very large effect on life expectancy
   d. None of the above

5. What is the normal range of excretion rate of creatinine among adult females?
   a. 10–15 mg/kg/day
   b. 15–20 mg/kg/day
   c. 20–25 mg/kg/day
   d. 15–25 mg/kg/day

ANSWERS: 1. c; 2. b; 3. d; 4. b; 5. b

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SECTION 3

SPECIAL TOPICS

Lilibeth S. Genuino, MD, FPOGS (Editor)

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17 ANEMIA IN THE ELDERLY

Cecilia C. Santos-Acuin, MD, PhD

Delivered as a webinar on April 26, 2019
https://bit.ly/ALMW_Ch17_Anemia

KEY POINTS

- Anemia is a common problem among elderly Filipinos (occurring in 19–23%), lowering quality of life and increasing mortality risk.
- Nutritional deficiency causes around 1/3 of cases, with iron supplementation given initially as a therapeutic trial
- Further diagnostic workup for non-nutritional causes of anemia is guided by mean corpuscular volume and serum ferritin levels.
- Management requires consideration of non-nutritional causes and close follow up.

LEARNING OBJECTIVES

- ➸ Give the definition and epidemiology of anemia in the elderly
- ➸ Discuss the causes and consequences of anemia in the elderly
- ➸ Outline the diagnosis and management of anemia in the elderly

I. DEFINITION AND EPIDEMIOLOGY

Anemia in the elderly is more common and more dangerous than we think.

A. Definition of anemia

- Anemia is a condition where the body has fewer than normal functioning red blood cells.
- The definition of anemia and 'low hemoglobin' in the elderly is not straightforward. There are also gender and racial differences.[1]
- In the Philippines, we follow the WHO lower limit of normal blood hemoglobin concentration for those older than 15 y/o: 12 g/dL (non-pregnant women) and 13 g/dL (men).
- The suggested optimal hemoglobin levels to avoid hospitalization and mortality are:[3]
  - 13 to 15 g/dL (women)
  - 14 to 17 g/dL (men)

B. Prevalence and Causes of Anemia in the Elderly

- Most anemia in the elderly is of moderate public health importance, defined as a prevalence of 20.0% to 39.9%, based on estimated hemoglobin or hematocrit blood levels.[2]
- The prevalence of anemia increases with age, affecting almost half of the individuals in their 80s and 90s, especially men.[4,5]
- In the Philippines, its prevalence among elderly patients (≥60 y/o) has decreased from 2008 to 2013, from 33.4% to 23% in men and 32.8% to 19.1% in women (Figure 17–1),[6,7] The global prevalence of anemia is 23.9% (WHO, 1993–2005).[8]

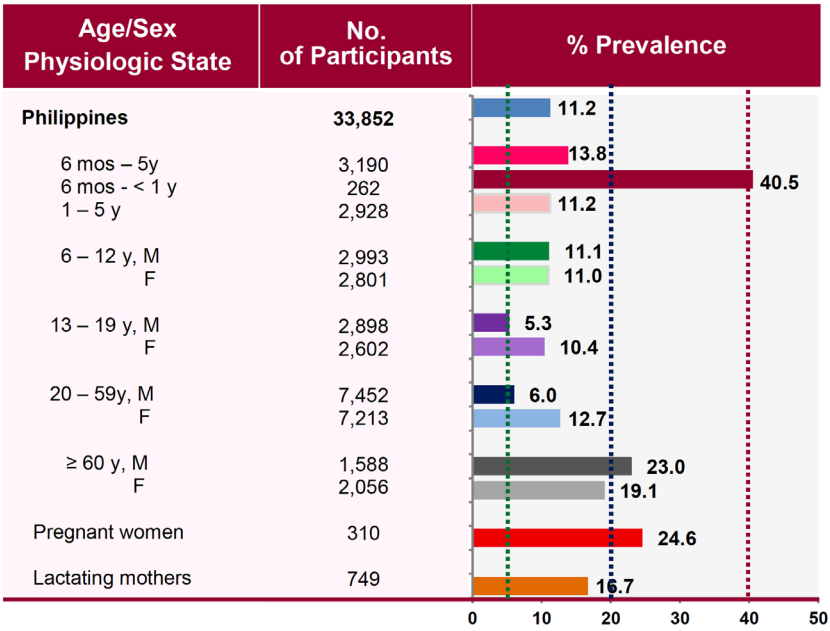

FIGURE 17–1. Anemia prevalence by age, sex and physiologic state: Philippines, 2013

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- Not all anemia is due to nutritional deficiency. A small study in the Philippines on adults <60 y/o showed that the causes of anemia are nutritional (37.6%), hemoglobinopathies (27.8%) and non-nutritional (34.7%).[10] The distribution of causes for older adults >60 y/o may be different.
- Severe anemia is most prevalent in nutritional causes (18.8%), as compared to hemoglobinopathies (3.6%) or other causes (5.7%) (Table 17–1).[10] Since nutritional anemia is easily treatable, those working in resource-constrained settings should always initially consider this diagnosis in the elderly and give a therapeutic trial of iron supplements.

TABLE 17–1. Diseases frequently associated with anemia in the elderly

PREDOMINANT MECHANISM	CATEGORY	SUBTYPES	SPECIFIC EXAMPLES
Decreased production or maturation of red blood cells	Chronic Inflammatory Diseases	Rheumatologic diseases	Rheumatoid arthritis, polymyalgia rheumatica
		Chronic infectious diseases	Chronic hepatitis, osteomyelitis
		Inflammageing	Frailty, cachexia, geriatric syndromes
		Miscellaneous	Chronic leg ulcers
	Endocrinologic and metabolic causes	Low production of EPO	Anemia of chronic kidney disease* or pure EPO deficiency
		Thyroid dysfunction	Hypothyroidism or hyperthyroidism
		Insulin deficiency	Diabetes mellitus
	Nutritional	Vitamin deficiency	Vitamin B12 and/or folate deficiency
		Trace element deficiency	Copper deficiency
		Iron-deficiency	Blood loss
Increased loss or destruction of red blood cells	Blood loss	Gastrointestinal tract bleeding	Peptic ulcer, ulcerative colitis, etc.
		Diffuse gastrointestinal tract bleeding	Anticoagulant-mediated bleeding
		Surgical procedures	Multiple abdominal surgeries
		Different locations	Epistaxis, hematuria
	Hemolysis/ destruction	Chronic nonmechanical hemolysis	Autoimmune hemolytic anemia
		Mechanical destruction of red cells	Heart valve-mediated red cell lysis
		Hypersplenism	Hepatosplenomegaly
Both	Drug-induced anemia	Chemotherapy	Chemotherapy-induced pancytopenia
		Antimetabolites, anticonvulsants	Folate deficiency
		Toxic drug reactions	Drug-induced hemolysis
	Nonhematopoietic neoplasms	Gastrointestinal tumors	Colorectal cancer, gastric cancer, etc.
		Multiorgan metastases	End-stage carcinomas
		BM metastasis	Various cancer types including breast and prostate

EPO, Erythropoietin

Source: Stauder R, Valent P, Theurl I. Anemia at older age: etiologies, clinical implications, and management. *Blood*. 2018;131(5):505-514.[5]

1. Nutritional Anemia
   - Aside from iron deficiency, deficiency in folic acid (from excessive alcohol use and malnutrition) and vitamin B12 (primarily related to atrophic gastritis) may also be responsible for anemia.
   - It is important to assess life history, including chewing, swallowing, and food intake issues.
   - Dentition must be evaluated as part of the physical examination.
   - There is a need to increase intake of food rich in certain nutrients after age 50. Aside from iron, folate, and vitamin B12, micronutrients, such as selenium and magnesium, should be taken (Table 17–2 and Table 17–3).
   - A healthy diet in sufficient amount should be taken by the elderly at regular intervals.
   - Absorption of these nutrients may also pose a problem in the presence of other illnesses, especially in the presence of other illnesses.

TABLE 17–2. Recommended vitamin intake in elderly

Life stage/ age group	Weight (kg)		Vitamin A[a] (µgRE)		Vitamin D[b] (µg)		Vitamin E[c] (mg α-TE)		Vitamin K (µg)		Thiamin (mg)		Riboflavin (mg)		Niacin[d] (mgNE)		Vitamin B_6 (mg)		Vitamin B_{12} (µg)		Folate[e] (µgDFE)		Vitamin C (mg)	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Adults, yr																								
19-29	60.5	52.5	**700**	**600**	*5*	*5*	*10*	*10*	**61**	**53**	**1.2**	**1.1**	**1.3**	**1.1**	**16**	**14**	**1.3**	**1.3**	**2.4**	**2.4**	**400**	**400**	**70**	**60**
30-49	60.5	52.5	**700**	**600**	*5*	*5*	*10*	*10*	**61**	**53**	**1.2**	**1.1**	**1.3**	**1.1**	**16**	**14**	**1.3**	**1.3**	**2.4**	**2.4**	**400**	**400**	**70**	**60**
50-59	60.5	52.5	**700**	**600**	*10*	*10*	*10*	*10*	**61**	**53**	**1.2**	**1.1**	**1.3**	**1.1**	**16**	**14**	**1.7**	**1.6**	**2.4**	**2.4**	**400**	**400**	**70**	**60**
60-69	60.5	52.5	**700**	**600**	*15*	*15*	*10*	*10*	**61**	**53**	**1.2**	**1.1**	**1.3**	**1.1**	**16**	**14**	**1.7**	**1.6**	**2.4**	**2.4**	**400**	**400**	**70**	**60**
>70	60.5	52.5	**700**	**600**	*15*	*15*	*10*	*10*	**61**	**53**	**1.2**	**1.1**	**1.3**	**1.1**	**16**	**14**	**1.7**	**1.6**	**2.4**	**2.4**	**400**	**400**	**70**	**60**

NOTE: Recommended Nutrient Intakes (RNI) are in bold font, while Adequate Intakes (AI) are in italics.

[a]1 retinol equivalent (RE) = 1µg retinol = 12 µg β-carotene or 24 µ other provitamin A carotenoids; 1 µg RE = 3.33 IU vitamin A

bIn the absence of adequate exposure to sunlight, as calciferol; 1 µg calciferol = 40 IU vitamin D

[c]1 mg alpha-tocopherol equivalent (α-TE) = 1.49 IU natural form or 2.22 IU synthetic form

[d]As niacin equivalent (NE)

[e]1 dietary folate equivalent (DFE) = 1 µg food folate = 0.6 µg folic acid from fortified foods or as supplement = 0.5 µg taken on an empty stomach

Adapted with permission from *"Philippine Dietary Reference Intake 2015 Summary Tables (Revised September 2018)"* by Food and Nutrition Research Institute, Department of Science and Technology. p 3. Copyright @2015 FNRI, DOST.[11]

TABLE 17–3. Recommended mineral intake in elderly

Life stage/ age group	Weight (kg)		Iron (mg)		Zinc (mg)		Selenium (µg)		Iodine (µg)		Calcium (mg)		Magnesium (mg)		Phosphorus (mg)		Fluoride (mg)		Electrolytes		
	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	Sodium (mg)	Chloride (mg)	Potassium (mg)
Adults, yr																					
19-29	60.5	52.5	**12**	**(28)**	**6.5**	**4.6**	**38**	**33**	**150**	**150**	**750**	**750**	**240**	**210**	**700**	**700**	*3.0*	*2.6*	*500*	*750*	*2000*
30-49	60.5	52.5	**12**	**(28)**	**6.5**	**4.6**	**38**	**33**	**150**	**150**	**750**	**750**	**240**	**210**	**700**	**700**	*3.0*	*2.6*	*500*	*750*	*2000*
50-59	60.5	52.5	**12**	**10**	**6.5**	**4.6**	**38**	**33**	**150**	**150**	**750**	**800**	**240**	**210**	**700**	**700**	*3.0*	*2.6*	*500*	*750*	*2000*
60-69	60.5	52.5	**12**	**10**	**6.5**	**4.6**	**38**	**33**	**150**	**150**	**800**	**800**	**240**	**210**	**700**	**700**	*3.0*	*2.6*	*500*	*750*	*2000*
>70	60.5	52.5	**12**	**10**	**6.5**	**4.6**	**38**	**33**	**150**	**150**	**800**	**800**	**240**	**210**	**700**	**700**	*3.0*	*2.6*	*500*	*750*	*2000*

NOTE: Recommended Nutrient Intakes (RNI) are in bold font, while Adequate Intakes (AI) are in italics.

( ) Requirements cannot be met by usual diet alone. Intake of iron-rich and iron-fortified foods and the use of supplements are recommended, if necessary.

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2. Anemia of Renal Insufficiency or Chronic Inflammation
    - Renal insufficiency may lead to a reduction in erythropoietin, the hormone that regulates red blood cell production.
    - Anemia of chronic inflammation may result from an autoimmune disorder, where the body's immune system attacks the joints and/or body organs, resulting in lower red blood cell production.
3. Myelodysplastic Syndrome (MDS)
    - MDS is a primary disorder of hematopoiesis that is more common among people aged 65 y/o and older.
    - It can be associated with normocytic or macrocytic anemia.
4. Other Causes
    - Medication and ethanol use are important contributors to anemia in the elderly.
    - Sarcopenia, or decreased skeletal muscle mass, may contribute to and is closely associated with anemia.
    - Many cases of anemia in the elderly remain unexplained.

C. Consequences of Anemia in the Elderly

- Consequences of anemia or low-normal hemoglobin are more marked in the elderly. The risk for all-cause mortality is higher in those with hemoglobin below 14 g/dL (women) and 15 g/dL (men)
- On the other hand, levels above 15 g/dl (men) increases the risk for thrombosis.[12]
- Poorer health outcomes are observed in the elderly with anemia, even those with mild form.[1]
    - Patients with heart failure and low hemoglobin levels have more symptoms, poorer hemodynamics and greater mortality than those with higher hemoglobin levels.
- Those above 65 y/o have increased frailty, poorer exercise performance, diminished cognitive function, risk of developing dementia, decreased mobility, increased risk of recurrent falls, and lower bone and skeletal muscle density.

II. DIAGNOSIS AND MANAGEMENT

A. Steps in the diagnosis of anemia (Figure 17–2)

STEP 1.

1. Mean corpuscular volume (MCV) is one of the most useful diagnostic tests for anemia. It is used to narrow the differential diagnoses and determine initial tests in both young and old patients.
    - A low MCV is strongly suggestive of iron-deficiency anemia, especially if it is an acquired abnormality.
    - A low MCV in newborns suggests thalassemia.
2. Serum ferritin measurement is recommended an elderly patient with microcytic or normocytic anemia, although it may not be widely available.
3. Serum ferritin is helpful in determining iron stores. A serum ferritin of less than 15 μg/L in those 5 y/o or older is indicative of depleted iron stores. Low levels of both serum ferritin and hemoglobin support a diagnosis of anemia (WHO, 2011).[13]
4. Other tests may be ordered if there is chronic bleeding (e.g., fecal occult blood) or chronic inflammation (e.g., soluble transferrin receptor assay).

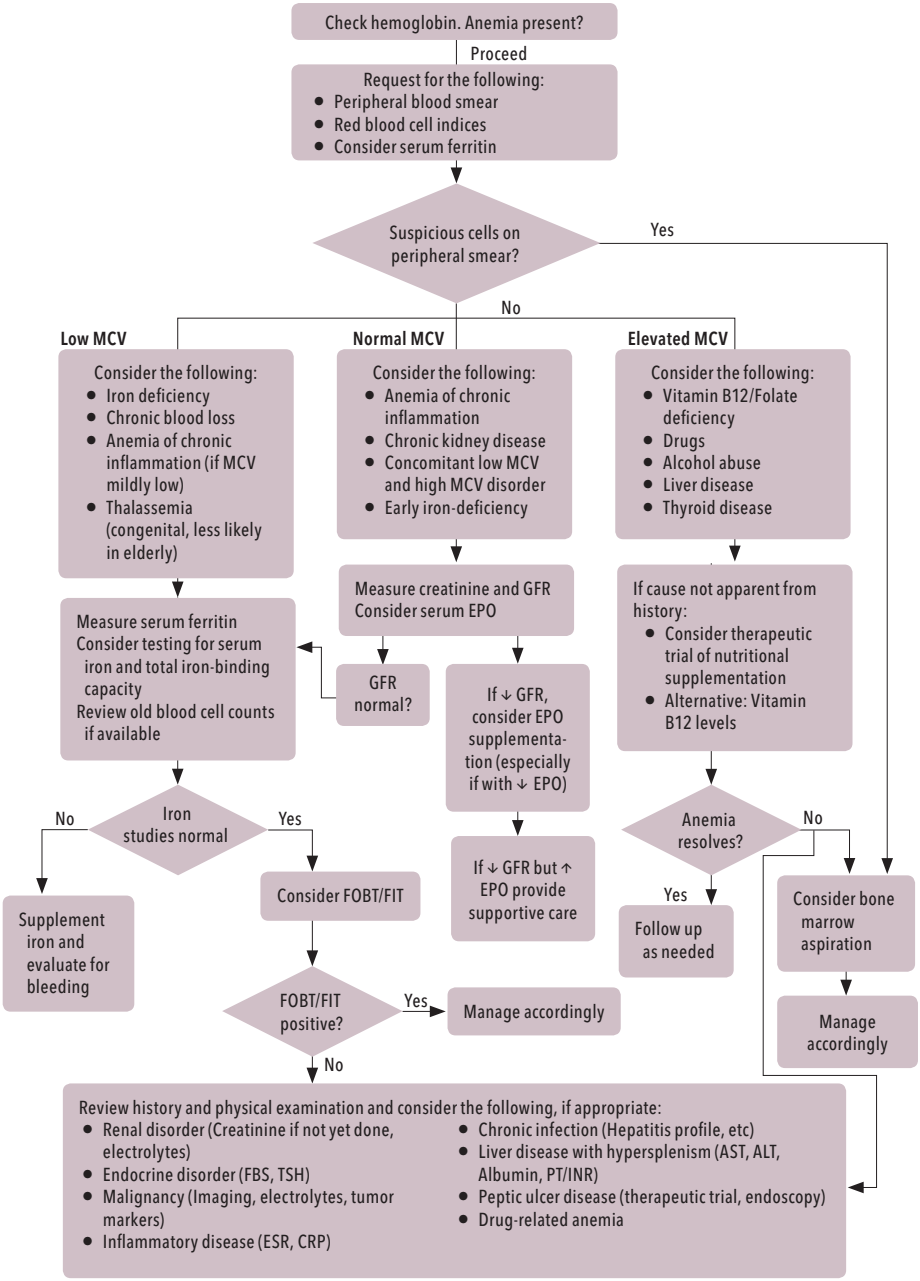

FIGURE 17–2. Diagnostic and therapeutic algorithm for anemia

MCV, Mean corpuscular volume; GFR, Glomerular filtration rate; EPO, Eyrthropoietin; FOBT, Fecal occult blood test; FIT, Fecal immunohistochemistry test; FBS, Fasting blood sugar; TSH, Thyroid-stimulating hormone; ESR, Erythrocyte sedimentation

rate; CRP, C-reactive protein; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; PT, Protime; INR, International normalized ratio

Source: Steensma DP, Tefferi A. Anemia in the elderly: How should we define it, when does it matter, and what can be done? *Mayo Clin Proc*. 2007;82(8):958-966.[1]

Bargman JM, Skorecki KL. Chronic Kidney Disease. In Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. *Harrison's Principles of Internal Medicine 20th ed*. USA: McGraw-Hill; 2018.[13]

STEP 2.

- Treat the nutritional cause first by giving a therapeutic trial with iron supplements. If the patient does not respond, consider a bone marrow exam for unexplained or intractable anemia.

STEP 3.

- Nutritional deficiency anemia (iron, folate, vitamin B12) can be addressed with supplementation, while severe anemia due to renal failure may require erythropoietin treatment.
- There are currently no clinical guidelines for the appropriate use of erythropoietin for the treatment of mild anemia in the elderly.
- There should be close follow-up especially if patient is frail and has poor appetite and comorbidities. Always consider functional status.

B. Treatment of Anemia

The target hemoglobin level is 9 to 11.5 g/dL. Thromboembolism risk should be considered.

1. ***Supplements***
    a. Iron
        - Consider gastrointestinal absorption and side effects in selecting iron preparations.
        - Give ferrous sulfate 325 mg/tab (65 mg elemental iron) or ferrous gluconate 325 mg (38 mg elemental iron) once daily.
        - If patient is unable to take oral iron, you may give slow infusion of IV ferric carboxy maltose, iron polymaltose or iron sucrose.
            - Infuse very slowly because this can be very painful.
    b. Oral vitamin B12 therapy
        - Give high-dose oral cyanocobalamin, 1 to 2 mg per day
    c. Folic acid at 1 mg/day
    d. Vitamin C, vitamin D, vitamin E, magnesium, selenium
        - These co-nutrients are important in different pathways for the absorption and processing of iron.
2. ***Diet and physical activity***
    a. Consider lifestyle, comorbidities, and access to caregivers.
    b. Give them food that they like over dietary supplements.
        - Food beliefs and misinformation must be addressed.
        - Fresh food is better than processed food since nutrients are at their peak.
        - Seasonality and nutrient retention during preparation must be considered.
        - Factors that may affect food intake include taste, texture, hydration, and frequency of bowel.

- A balanced diet with proper amount of needed macronutrients (carbohydrates, proteins at 1.5g/kg/day, and fats) should be provided.

c. Socialization must be encouraged among elderly patients since they eat and exercise better when with others.
   - Sarcopenia can be prevented or retarded through aerobic and progressive resistance exercise.

d. If weight loss is warranted, it should be tailored to patient's capacity.

3. ***Other therapeutic options***

a. ***Erythropoietin (EPO)***
   - EPO is a glycosylated protein hormone produced principally by the kidney, and is the principal regulator of erythropoiesis.
   - Recombinant erythropoietin, developed in the 1980s and considered a biologic equivalent of EPO, has become the treatment of choice for anemia associated with chronic kidney disease.

b. ***Erythropoiesis-stimulating agents (ESAs)***
   - Non-human and recombinant isoforms with differing glycosylation (glycoforms) evolved to improve sports performance (now banned) and to mimic erythropoietin's biologic function.
   - May be used in CKD but with precaution since high doses of epoetin alpha are associated with myocardial infarction, stroke, and even death.

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OPEN FORUM HIGHLIGHTS

Moderator: MARIA SONIA S. SALAMAT, MD

Q: *At what level of hemoglobin do we advise transfusion for our elderly patients?*

A: Below 7 or 8 g/dL. But look at the patient. Look at the comorbidities. The patient may have heart problems, kidney disease, or other illness that might not allow them to accommodate the additional volume.

Q: *What is the most common side effect of iron supplements, especially for the elderly? Is it recommended to give proton pump inhibitors in combination with the iron supplement to reduce gastric irritation?*

A: Please avoid giving too many medications since elderly patients are already on polypharmacy and are at risk for drug-drug interactions. Instead, give less-irritating iron, such as iron gluconate, or give the iron immediately after meals to reduce irritation

Q: *What is the preferred oral iron supplement for patients with gastroesophageal reflux?*

A: Avoid ferrous sulfate or elemental iron since it is the most irritating. Use coated forms of iron.

Q: *Do you recommend giving multivitamins to elderly patients?*

A: Yes, if not eating regularly (i.e., skipping meals), not eating properly or not eating enough. You may give multivitamins with iron since you need the other micronutrients to improve iron absorption.

Q: *How long do we need to give iron supplementation? What laboratory examinations do we need to request in order to check response to therapy, especially in resource-constrained areas?*

A: If you can, do a peripheral smear. If not available, at the very least, check the patient's hemoglobin. The lifespan of red blood cells is 120 days (4 months). Therefore, give supplementation up to four months. Then allow another 2 to 3 months to replenish iron stores.

REVIEW QUESTIONS

1. What is the most common cause of anemia in the elderly?
   a. Medications and ethanol use
   b. Nutritional anemia
   c. Anemia of renal insufficiency
   d. Myelodysplastic syndrome

2. What can be determined from the mean corpuscular volume?
   a. It can differentiate between nutritional and non-nutritional causes of anemia
   b. It can classify macrocytic anemias as hemolytic or non-hemolytic
   c. It can classify microcytic anemias as megaloblastic or non-megaloblastic
   d. It can classify normocytic anemias as intravascular or extravascular

3. In patients with anemia and normal mean corpuscular volume, which test should be ordered next?
   a. Serum ferritin
   b. Serum total iron binding capacity
   c. Homocysteine
   d. Serum erythropoietin

4. Which elderly patients should be given supplements ?
   a. With hemoglobin level that is less than normal
   b. Unable to eat regularly and sufficiently
   c. With chronic diseases
   d. Underweight

5. Which is the preferred iron supplement for patients with gastroesophageal reflux disease?
   a. Coated forms of iron
   b. Ferrous sulfate
   c. IV ferric carboxy maltose given as slow infusion
   d. Red meat

ANSWERS: 1. b; 2. d; 3. d; 4. b; 5. a

18 ARTHRITIS IN THE ELDERLY

Evelyn S. Osio-Salido, MD, MSc, FPCP, FPRA

Delivered as a webinar on May 31, 2019
https://bit.ly/ALMW_Ch18_Arthritis

KEY POINTS

- Arthritis is found in 35% of Filipinos aged 50 y/o.
- The most common forms of arthritis are osteoarthritis, gouty arthritis, and rheumatoid arthritis.
- It is possible to have healthy joints and be free of arthritis while ageing.
- Prevention of arthritis in the elderly begins during youth. Modifiable risk factors should be corrected.
- Arthritis can and should be treated appropriately, with definitive treatment and adequate control of pain.

LEARNING OBJECTIVES

- ➟ To differentiate articular from periarticular conditions in the elderly
- ➟ To understand the epidemiology of arthritis in the elderly
- ➟ To enumerate the causes of arthritis in the elderly
- ➟ To understand the treatment modalities and preventive measures in the management of arthritis in the elderly
- ➟ To recognize key points on keeping the joints healthy while ageing

IS THE PROBLEM REALLY ARTHRITIS?

Articular or Periarticular?

- It is **arthritis** if it is a problem within the joint, such as those which arise from the cartilage and subchondral bone.
- It is a **periarticular** problem or soft tissue rheumatism when the problem is outside the joint, such as those involving the tendons, muscles, or ligaments.
- Physical examination helps differentiate these two conditions. In arthritis, pain and tenderness is diffuse in the joint and present during both active and passive range of motion. In soft tissue rheumatism, tenderness is localized and pain is present only during active range of motion.

I. EPIDEMIOLOGY OF ARTHRITIS

A. Prevalence of Arthritis in the Philippines[1]

- The overall prevalence is 6.5%.
  - Having 6 million adults with arthritis is a problem if these adults have productivity losses due to their disease.
- There is increasing prevalence of arthritis with age (15.4% for 60 to 69 y/o, and 19.6% for those above 70 y/o) (Table 18–1).

TABLE 18–1. Prevalence of arthritis in 2003 vs 2008 (via questionnaire, self-report), NNHeS, Philippines

	PREVALENCE OF ARTHRITIS, % (95% CI) useholds)	
AGE (YEARS)	**2003 N=4,753 adults (2626 households)**	**2008 N=7,202 adults (3744 households)**
20-29	1.1 (0.16-1.98)	0.6 (0.2-0.92)
30-39	3.8 (2.28-5.24)	2.8 (2.02-3.64)
40-49	6.4 (4.12-8.78)	5.8 (4.45-7.21)
50-59	12.2 (8.71-15.75)	9.9 (8.08-11.78)
60-69	**17.1 (14.79-19.43)**	**15.4 (12.59-18.16)**
>70	**23.8 (20.68-26.96)**	**19.6 (15.74-23.52)**
Over-all Prevalence	**6.5 (5.56-7.53)**	**6.3 (5.67-6.87)**

Sources:

Food and Nutrition Research Institute (Department of Science and Technology). *6th National Nutrition and Health Survey: Biochemical Facts and Figures*; 2004.[2]

Food and Nutrition Research Institute (Department of Science and Technology). *Philippine Nutrition: Facts and Figures 2008 (7th National Nutrition Survey);* 2010. http://enutrition.fnri.dost.gov.ph/site/preview.php?xx= uploads/2008_FaF.pdf.[3]

B. Types and Causes of Arthritis

TABLE 18–2. Types and causes of arthritis

TYPE	CAUSE
Infectious arthritis	Microbes
Traumatic arthritis	Trauma
Gouty arthritis* Pseudogout Basic calcium phosphate	Metabolic disease (crystal deposition)
Rheumatoid arthritis* Seronegative spondyloarthritis	Immunologic dysfunction
Hemophiliac arthropathy	Clotting dysfunction
Charcot arthropathy	Nerve dysfunction
Osteoarthritis*	Failure of joint protective mechanisms

**Most common arthritides among Filipinos*

II. PATHOGENESIS OF ARTHRITIS IN THE ELDERLY

Why is there a higher prevalence of arthritis in the elderly?

TABLE 18–3. Differences in clinical course of common arthritides

GOUT	OSTEOARTHRITIS	RHEUMATOID ARTHRITIS
• Early phase of prolonged hyperuricemia is asymptomatic. • Gout is an intermittent arthritis, but if not properly managed within 5–10 years, it can progress to a chronic disease. • Patients can also develop chronic kidney disease and progressive renal failure.	• Disease progression is slow. • There is increased vulnerability of the joints in ageing. Less matrix is produced by articular cartilage. • Muscles and ligaments become weaker and sensory impulses become slower, which lessens support to the joints.	• Damage from uncontrolled control of synovial inflammation is cumulative.

III. DIAGNOSIS OF ARTHRITIS

There is a need for correct diagnosis via thorough history and physical examination.

If the problem is arthritis, the following questions will help determine the type:

1. *Acute or chronic?*
   - Acute – two weeks or less
   - Chronic – more than two weeks
2. *With or without inflammation?*
   - Inflammatory – with joint swelling, erythema, prolonged morning stiffness, and symmetric pain even at rest (e.g. rheumatoid arthritis)
   - Non-inflammatory – morning stiffness that lasts less than one hour and pain that worsens with activity and abates with rest (e.g., osteoarthritis)
3. *Number of joints affected?*
   - Monoarticular – 1 joint (e.g., gout or septic arthritis)
   - Polyarticular – more than 5 joints (e.g., rheumatoid arthritis)
4. *With or without systemic involvement?*
   - Systemic involvement – rashes, oral/genital ulcers, Raynaud's phenomenon, pleuritis/pericarditis, dry eyes/mouth, ischemic symptoms (stroke) (e.g., systemic lupus erythematosus, psoriatic arthritis)

- Gout and septic arthritis are examples of acute inflammatory arthritis affecting one or two joints only.
- Osteoarthritis is an example of a chronic non-inflammatory arthritis of the weight-bearing joints.
- Rheumatoid arthritis is a chronic inflammatory polyarthritis with systemic manifestations.
- When an inflammatory arthritis is recurrent, it leads to scarring and eventual damage to the joint, resulting in secondary OA.

IV. CLINICAL PROFILE OF PATIENTS WITH ARTHRITIS

TABLE 18–4. Clinical profile of Filipinos with osteoarthritis and rheumatoid arthritis (chart reviews)

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS	OA (RACAZA, 2012)[4]	RA (PENSERGA, 2014)[5]
No. of patients	859	266 (Mean age: 44 years)
Setting	PGH and a private clinic	PGH
Mean age at diagnosis	63 y/o	
Mean time to diagnosis		5 years
Mean age at onset	59 y/o	
M:F ratio	1:3	1:9
Mean BMI	27.1 kg/m² (women overweight; men obese)	
Comorbidities	Hypertension (53%) Dyslipidemia (16%) Diabetes mellitus (13%)	Hypertension, tuberculosis, diabetes mellitus
Chief complaint	Pain (92.8%)	
Involved joints	Knees (62.5%) Knees and hands (14.3%) Generalized (13.5%) Hip (3%)	Symmetrical polyarthritis
Diagnostics	Radiographs: Kellgren-Lawrence score =2 (56.6%)	Rheumatoid factor positive in 66%

PGH, Philippine General Hospital; OA, Osteoarthritis; RA, Rheumatoid arthritis; PGH, Philippine General Hospital; BMI, Body mass index

Racaza GZ, Salido EO, Penserga EG. Clinical profile of Filipino patients with osteoarthritis seen at two arthritis clinics. *Int J Rheum Dis*. 2012;15(4):399-406.[4]

Penserga EG, Natividad TAL, Salido ES. Clinical profile of 266 Filipino patients with rheumatoid arthritis included in the Rheumatoid Arthritis Database and Registry (RADAR) of the Philippine General Hospital. *Int J Rheum Dis*. 2014;18(4):433-436.[5]

Gout in Filipinos[6-8]

- 3 hospital-based reviews, n=704 (Cebu, 1999; UST, 2005; PGH, 2014)
  - 86 to 91% were males
  - Age of onset: Mid-40s to 50s
  - Co-morbid illness: Hypertension and diabetes
  - Monoarticular in 7%
  - Tophi in 7–37%
  - Urolithiasis in 13–21%
  - Renal insufficiency in 4.8–52%
  - Mean creatinine: 1.7 mg%
  - Mean serum uric acid (SUA): 8 to 9 mg/dL

V. MANAGEMENT OF ARTHRITIS

A. Treatment goals

1. Control of pain
2. Maximize physical function
3. Emotional stability
4. Cure, remission, and disease modification
5. Improved quality of life

What kind of treatment do our elderly patients need?

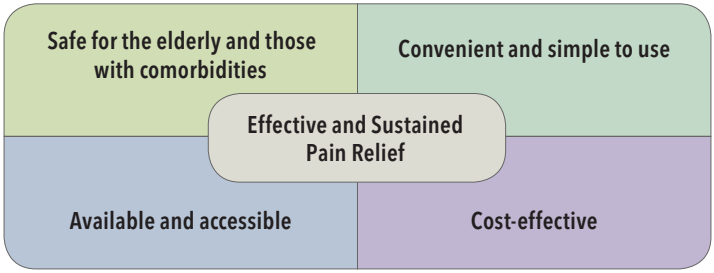

FIGURE 18–1. Ideal properties of arthritis treatment

B. Treatment Principles

1. *EARLY, AGGRESSIVE, AND CONTINUOUS management of arthritis*

TABLE 18–5. Principles of treatment for different types of arthritis

	OSTEOARTHRITIS	RHEUMATOID ARTHRITIS	GOUTY ARTHRITIS
Prognostication	ACR classification criteria 1. Joints involved 2. Imaging	2010 ACR-EULAR classification criteria 1. Joints involved 2. Chronicity 3. Serology 4. Acute phase reactants	2015 ACR-EULAR classification criteria 1. Joint involvement, tophi 2. Synovial fluid analysis, serum uric acid, Imaging
Goals	1. Control of pain 2. Modify risk factors 3. Delay progression	Remission	1. Control of inflammation during arthritis attacks 2. Maintain SUA<6mg/dl lifelong to prevent arthritis flares and disease complications

TABLE 18–5. Principles of treatment for different types of arthritis (cont.)

	OSTEOARTHRITIS	RHEUMATOID ARTHRITIS	GOUTY ARTHRITIS
Pharmacologic Treatment	1. Anti-inflammatory drugs a. NSAIDs b. Intraarticular glucocorticoids	1. Anti-inflammatory drugs a. NSAIDs b. Glucocorticoids 2. DMARDs a. Conventional–methotrexate b. Targeted–tofacitinib c. Biologics e.g., adalimumab d. Biosimilar	1. For acute arthritis – Anti-inflammatory drugs a. Colchicine b. NSAIDs c. Glucocorticoids 2. For uric acid reduction – Allopurinol or febuxostat
Duration of Treatment	Lifetime		

NSAIDs, Non-steroidal anti-inflammatory drugs; DMARDs, Disease-modifying anti-rheumatic drugs

2. *Adequate Pain CONTROL*
   - Chronic pain may have negative impact on:
     - Patient's ability to work
     - Enjoyment of social and family relationships
     - Overall mental health
   - Less than half (48%) of patients with chronic pain rate their overall quality of life as good.[9]
   - Modalities for controlling arthritis pain may be non-pharmacologic or pharmacologic (Table 18–6).

TABLE 18–6. Modalities for arthritis pain control

NON-PHARMACOLOGIC	PHARMACOLOGIC
Heat or cold modalities	Analgesics
Exercises	Muscle relaxants
Orthotics, braces, joint supports	Glucocorticoids
Occupational therapy	Intra-articular hyaluronic acid (for OA)
Physical therapy	Glucosamine sulfate (for OA)
Acupuncture	Definitive treatment: DMARDs, antibiotics, hypouricemic drugs
Psychological support	

OA, Osteoarthritis; DMARDs, Disease-modifying anti-rheumatic drugs

VI. PREVENTION OF ARTHRITIS

1. Recognize and correct modifiable risk factors

The major risk factors that lead to the increased susceptibility and predisposition to develop OA range from local to systemic, and modifiable to non-modifiable (Figure 18–2).

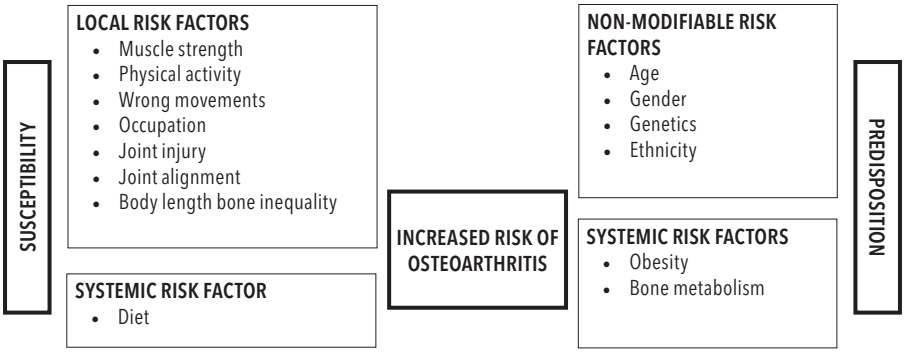

FIGURE 18–2. Risk factors for osteoarthritis

Reprinted with permission from "Osteoarthritis in the XXIst Century: Risk factors and behaviours that influence disease onset and progression" by G. Musumeci et al. *Int. J. Mol. Sci.* 2015, p 6096. © 2015 by the authors; licensee MDPI, Basel, Switzerland. Attribution 4.0 International (CC BY 4.0).[10]

- Obesity in Women and Knee Osteoarthritis[11]
  a. 5 kg more in weight → 36% extra risk for knee OA
  b. 5 kg reduced weight over 10 years → 50% less risk for symptomatic knee OA

2. Keep joints healthy

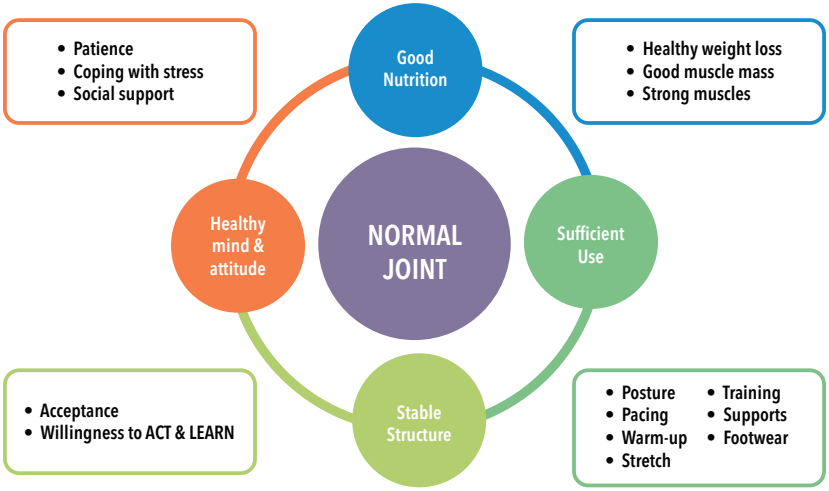

FIGURE 18–3. Points on keeping joints healthy in ageing

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OPEN FORUM HIGHLIGHTS

Moderator: DR. AILEEN ADELA J. MONTERO

Q: *Even as early as in our 20s, can we have arthritis?*

A: Yes. There are some forms of arthritis that we can see even among younger individuals, such as juvenile idiopathic arthritis, which is found in children. Gout can also occur among people younger than 30 years of age.

Q: *What is the best diagnostic procedure to diagnose RA?*

A: History and PE
ESR, CRP, anti-CCP, Rheumatoid Factor

Q: *Can you differentiate between osteoarthritis and rheumatoid arthritis if the rheumatoid factor is negative?*

A: Definitely. They can be differentiated through thorough history and PE.
When patients with rheumatoid arthritis wake up in the morning, they feel terrible for 1–2 hours.
Patients with osteoarthritis will also feel terrible; but once they start moving, they start to feel relief.
When the joints are swollen, especially the wrists, it is rheumatoid arthritis.

Q: *Is frozen shoulder due to osteoarthritis?*

A: Frozen shoulder is adhesive capsulitis, which is a soft tissue problem. In osteoarthritis, the joint space is narrowed.

Q: *Does beer aggravate gout?*

A: Alcohol is one of the more common triggers that can increase serum uric acid. We must advise patients with gout to limit alcohol intake.

Q: *How much meat or seafood should we take if we have gout?*

A: It is quite difficult to give a direct answer to this question. Meat and seafood increase uric acid, but research has shown that genetic factors have a larger effect on uric acid and risk of gout than diet.

Q: *Does the food supplement glucosamine help in management of arthritis?*

A: Clinical trials on glucosamine sulfate that are of pharmaceutical grade show that it can reduce pain among patients with osteoarthritis. There is some indication that it might prevent progression of cartilage damage and joint space narrowing.

Q: *Are there studies on the use of stem cells on the treatment of rheumatoid arthritis?*

A: There are currently registered trials on the use of stem cells in patients with rheumatoid arthritis and connective tissue diseases that present with arthritis.

Q: *What can RA patients do to prevent hand deformities?*

A: Even if you have the genes for RA, it does not always mean that you will develop the disease. You can do something to prevent it such as smoking cessation and oral hygiene. There is always a contribution from our environment.
Seek early management to prevent deformities.

Q: *How long should gout be managed? Do patients with a uric acid level of less than 6 mg/dL still need to take uric acid-lowering drugs?*

A: Urinary excretion of gout is the usual problem, which is, to a big extent, genetic. Hypouricemic drugs must be maintained for a life. If the target is reached, maintain the lowest dose. These drugs are intended for long-term use. Renal function must be assessed prior to giving allopurinol.

Q: *How about platelet-rich plasma injections for arthritis?*

A: They can be helpful for treatment of OA, but the data is not that strong. It is an option, and on a case-to-case basis.

Q: *Does menopause worsen arthritis? Will bisphosphonates treat the arthritis?*

A: Bisphosphonates will increase bone density but will not treat arthritis.

Q: *When do you use hyaluronic acid injections for the knee, and does it really work?*

A: Hyaluronic acid injection is a bit controversial due to studies with contradictory results. There are patients who respond, in terms of pain relief. This could be a possible treatment for patients who cannot take medications due to multi-drug allergy or intolerance to NSAIDs due to chronic kidney disease. It would be best if there is no active inflammation when hyaluronic acid injection is done.

REVIEW QUESTIONS

1. Which among the following is not among the most common arthritides in Filipinos?
   a. Osteoarthritis
   b. Septic arthritis
   c. Rheumatoid arthritis
   d. Gouty arthritis

2. Which among the following structures is affected in arthritis?
   a. Ligaments
   b. Muscles
   c. Cartilage
   d. Tendon

3. Which among the following has the most influence on the risk of gout?
   a. Age
   b. Diet
   c. Genetics
   d. Body mass index

4. How much weight must be lost in an obese patient to decrease risk of developing knee OA symptoms by 50%?
   a. 5 kg
   b. 8 kg
   c. 10 kg
   d. 15 kg

5. Which of the following is a conventional disease-modifying drug for rheumatoid arthritis?
   a. Abciximab
   b. Methotrexate
   c. Prednisone
   d. Ibuprofen

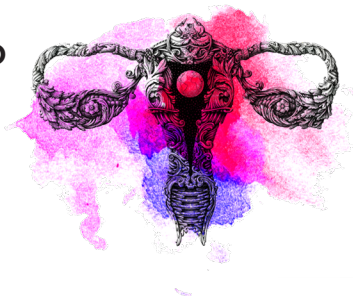
ANSWERS: 1. b; 2. c; 3. c; 4. a; 5. b

19 MENOPAUSE 101: WHAT YOU'VE ALWAYS WANTED TO KNOW

Marilyn D. David-Ruaro, MD, MHPED, FPOGS, FPSSTD, FPSUOG

Delivered as a webinar on April 12, 2019

https://bit.ly/ALMW_Ch19_Menopause



KEY POINTS

- Menopause can happen in several ways: natural, surgical, medical, and premature.
- We should be aware of its various presenting symptoms.
- We should always consult with our doctor to rule out illnesses or medical conditions that have symptoms similar to menopausal symptoms.
- We can do something about menopause, both nonpharmacological and pharmacological.

LEARNING OBJECTIVES

- To describe the epidemiology of menopause and the burden of this condition
- To elaborate on the signs and symptoms of menopause
- To discuss the available modalities in the management of menopause

I. DEFINITION AND EPIDEMIOLOGY

A. Natural Menopause

- Declining follicular activity with gradual loss of estrogen
- Average age: 51 years (range, 44 to 55) (worldwide); 48 (Philippines)
- Defined as no menses for 12 consecutive months; signals end of fertility

B. When Menopause is NOT natural

1. ***Surgical Menopause***
   - Surgical menopause starts at any age with removal of both ovaries
   - Surgical removal of both ovaries (bilateral oophorectomy) at any age = immediate menopause
   - Special conditions:
     - Removal of the uterus (hysterectomy) if one or both ovaries are left in place = no menopause; menses will stop
     - Removal of only one ovary = no menopause; menses go on as before
2. ***Medical: Chemotherapy and Pelvic Radiation***
   - Used in management of serious illnesses
   - May predispose to earlier menopause

- Cessation of menses may be temporary

3. ***Premature Menopause***
   - Occurs before age 40
   - Known also as premature ovarian failure (POF) and premature ovarian insufficiency (POI)
   - Cause:
     - 40% unknown
     - 30% thyroiditis, rheumatoid arthritis
     - Rarely: Genetic/chromosomal

C. Burden of Disease

Why should we be concerned about menopause?

1. Inevitable phase of a woman's life
   - Hormonal decline: natural progression in a woman's life
   - No one escapes menopause.
2. Increasing life expectancy of women
   - 2015–2020: Philippine population is projected to live longer.[1,2]
   - Women are expected to live until age 80.[2]
   - Women will spend up to 1/3 of their lives in the menopausal state.[3]
3. Affects women's quality of life
   - "Menopausal Syndrome/Perimenopause"
     - Signs and symptoms of estrogen loss may disrupt daily living and quality of life.
     - Most disappear with time but may last from 5–20 years.
4. Contributes to decline in women's health

II. SIGNS AND SYMPTOMS OF PERIMENOPAUSE AND MENOPAUSE

A. Definition of Perimenopause

- 'Transition years'
- Symptoms of estrogen loss can occur before menses stops.
- Symptoms may appear 4–8 years before, and may last until one year after onset of menopause (35–60 y/o).
- It may be the most misunderstood period in a woman's life.
- It can be a danger zone for unwanted pregnancy.
  - Pregnancy is possible during perimenopause.
  - An effective family planning method must be used up to 12 consecutive months after menses stop.

B. Common Signs and Symptoms of Perimenopause/Menopause (Table 19–1)

TABLE 19–1. Common perimenopausal symptoms

1. Fatigue	21. Irregular periods
2. Weight gain	22. Dry vagina
3. Headaches	23. Itchy crawly skin
4. Dizziness	24. Hair loss/thinning
5. Vertigo	25. More facial hair
6. Tingling extremities	26. Changed body odor
7. Electric shock feelings	27. Weakened fingernails
8. Bleeding gums	28. Allergies worsen
9. Burning tongue/roof of mouth	29. Joint and muscle pains
10. Chronic bad breath	30. Tense muscles
11. Ringing ears (Tinnitus)	31. Osteoporosis
12. Heart palpitations	32. Irritability
13. Hot flashes	33. Mood swings
14. Cold flashes	34. Trouble sleeping
15. Night sweats	35. Anxiety
16. Clammy feeling	36. Depression
17. Bloating	37. Lack of focus
18. Digestive issues	38. Poor concentration
19. Incontinence	39. Faulty memory
20. Sore breasts	40. Low sex drive

C. Menstrual Changes in the Perimenopause

1. ***Acceptable Menstrual Changes in the Perimenopause***
   - Shorter duration
   - Less, lighter flow
   - 'Missed periods'
2. ***Suspicious Menstrual Changes in the Perimenopause***
   - Longer duration
   - Increased flow
   - More frequent periods
   - Associated symptoms (e.g., pain, cramps)

   *Visit your gynecologist!
3. ***Abnormal Bleeding in Perimenopause***
   - Thorough history and careful physical (including pelvic) examination to exclude other causes, such as myoma
     - Myoma growths diminish in size with menopause.
     - There is a medical treatment to control uterine bleeding from myoma if still far from menopause.

D. Clinical Presentation of Menopause

1. ***Will every woman suffer menopausal signs and symptoms?***
   - 76% will have complaints; 40% will have severe symptoms
   - Symptoms vary from woman to woman.
     - Some women may have worse symptoms than others.

- Symptoms of surgical menopause can be more severe and start more suddenly.
- They may last 5 or more years.

2. ***Is the onset of menopause predictable?***
   - Information on menopausal symptoms, medical, obstetric and gynecologic history and physical examination may help.
   - Blood tests to measure hormone levels are inaccurate, expensive, and not used alone.
   - Hormone levels are erratic, and timing of extraction is difficult.
   - **2011 STRAW+10**, a nomenclature and staging system for ovarian ageing, can be used to grade one's stage in the reproductive cycle, including menopause[4]
3. ***What are the visible changes of menopause?***
   - Hips broaden
   - Breasts droop
   - Tummy bulges
   - Hair thins
   - Back stoops
   - Skin dries and wrinkles
   - Menses stops

   *For those who claim no or little symptoms, visible changes will happen soon enough.

E. Effects of Estrogen Deficiency

While we can't predict when it will happen, the projected timeline of symptoms progresses from the menopausal syndrome, genitourinary symptoms of menopause, and chronic disease (Figure 19–1).

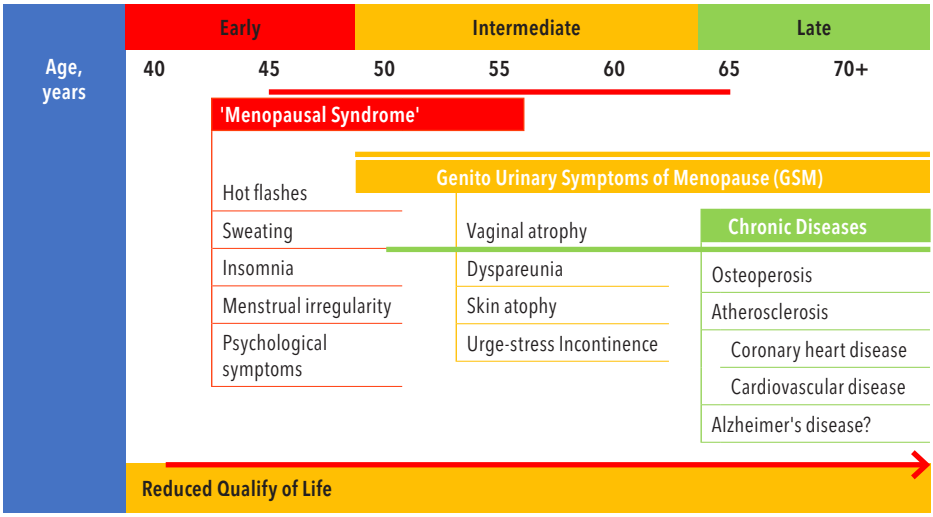


FIGURE 19–1. Stages of menopause

Source: Speroff L, Glass RH, Kase NG. *Clinical Gynecologic Endocrinology and Infertility*. 6th ed. Baltimore: William & Wilkins; 1999;[5] Van Der Mooren MJ, Kenemans P. Postmenopausal hormone therapy: Impact on menopause-related symptoms, chronic disease and quality of life. *Drugs*. 2004;64(8):821-836.[6]

- Estrogen deficiency plays a pivotal role in the incidence of climacteric symptoms and in the development of chronic diseases (Figure 19–2).

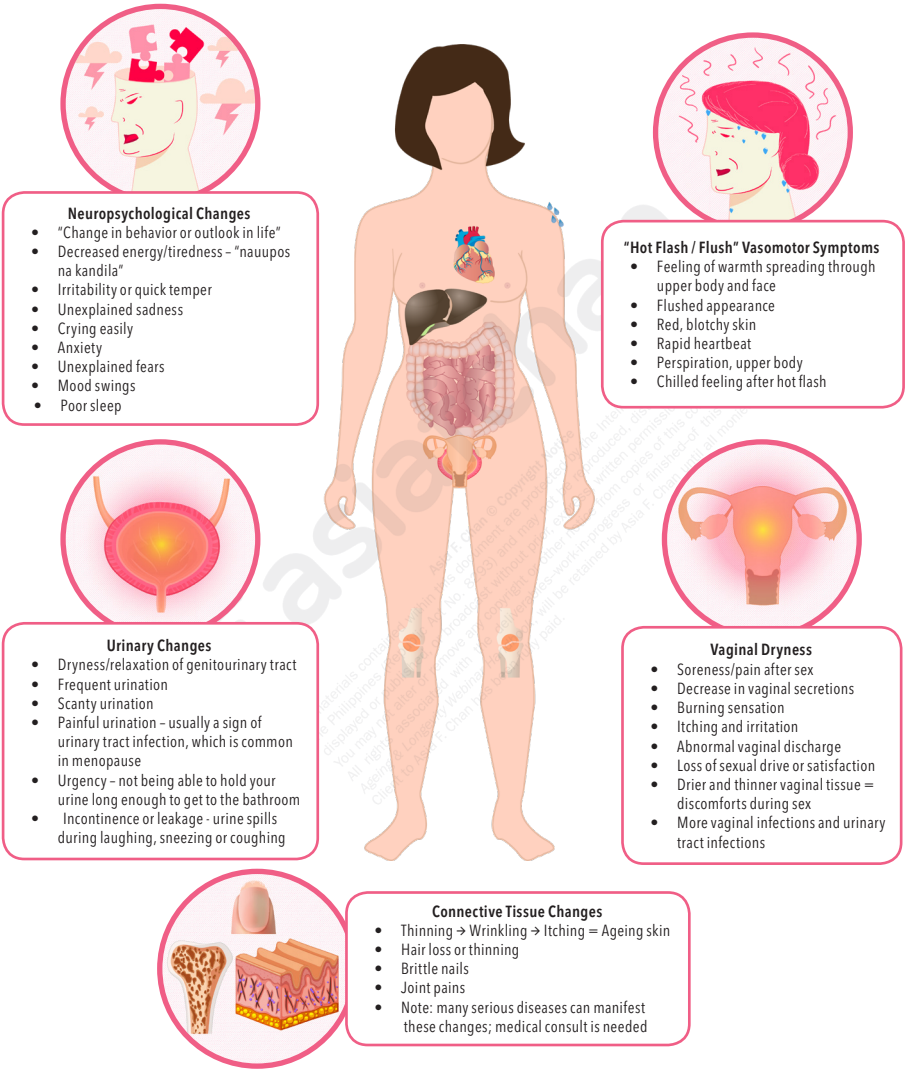


FIGURE 19–2. Changes in different organ systems during menopause

Women Nails Manicure Realistic Images Set designed by Macrovector - Freepik.com. https://www.freepik.com/free-vector/women-nails-manicure-realistic-imagesset_4301459.htm

Osteoporosis concept on white background designed by Brgfx - Freepik.com. https://www.freepik.com/free-vector/osteoporosis-concept-on-whitebackground_2758983.htm

Female younger skin and aging skin designed by Brgfx - Freepik.com. https://www.freepik.com/free-vector/female-younger-skin-and-aging-skin_2749585.htm

- The onset of genito-urinary symptoms of menopause (GSM) is around age 49, worsens with time, and if untreated, can be lifelong.

- Such symptoms and diseases contribute to impaired quality of life in climacteric and postmenopausal women.
- Long-term effects of menopause contribute to a decline in women's health, are often 'invisible' until complications occur, and may be irreversible.

III. MANAGEMENT OF MENOPAUSE

A. Treatment Principles

1. ***Discuss thoroughly.***
   a. Joint decision-making by the patient and her physician
      - A 'no treatment' decision is still a decision
   b. Recognition of signs and symptoms that affect work and lifestyle
   c. Agreement on treatment goals:
      - Reduce acute discomforts
      - Reduce potential complications
      - Introduce preventive health strategies
   d. Institution of appropriate treatment

2. ***Address important health issues.***
   During menopause, possible development of chronic disease must be recognized.
   a. Atherosclerosis
   b. Coronary heart disease
   c. Cardiovascular disease
   d. Osteoporosis
   e. Fractures
   f. Alzheimer's disease

B. Management Options for Menopause[12]

TABLE 19–2. Management options for menopause

1.	**Non-pharmacologic**	Lifestyle changes	Nutrition Exercise
		Counseling	
		Education	
2.	**Pharmacologic**	Hormone replacement therapy	Estrogens Estrogens + progestins Tibolone* – Selective tissue estrogenic activity regulator (STEAR) Low-dose oral contraceptives
		Non-hormonal	Selective estrogen-receptor modulators (SERMs) • Raloxifene • Ospemifene • Tamoxifene Bisphosphonates Calcitonin Calcium and vitamin D
3.	**Alternative therapy**	Phytoestrogens Traditional medicine	

*May be an alternative to MHT in reducing menopausal vasomotor symptoms but less effective; reported to have positive effects on sexual well-being and mood and improves dyspareunia and libido, but studies not consistent

Source: Tan, D. (2013). Amena RTD on menopause module 031013 [PowerPoint slides].[7]

1. ***Lifestyle Changes***
   - Stop smoking.
   - Eat healthy (low-salt, low-fat, baked, steamed).
   - Exercise regularly (30 minutes/day, 3–5x/week).
   - Supplements: Calcium 1200–1500mg, vitamin D 600–800mg
2. ***Intellectual Stimulation***
   - Read books.
   - Engage in brain-stimulating activities.
3. ***Menopausal Hormone Therapy (MHT)***[8-10]
   - Most effective treatment for menopausal related vasomotor symptoms
   - Relieves: Vasomotor symptoms, urogenital atrophy
   - Prevents and treats: Osteoporosis
   - May prevent: Cardiovascular disease, cognitive disorders and dementia, skin atrophy
   - Improves: Quality of life

   a. *How is MHT given?*
      - Tablets
      - Vaginal cream
      - Transdermal patch
      - Topical estrogen

   b. *Limitations of MHT*
      - MHT cannot be given to all women (Table 19–3).

TABLE 19–3. Contraindications to MHT

Undiagnosed vaginal bleeding
Active severe liver disease
Acute deep vein thrombosis
Acute thromboembolic disease
Recent breast cancer
Recent cancer of endometrium
Endometriosis
Congenital diseases of lipid metabolism

      - MHT is not used for primary prevention of CVD or osteoporosis.
      - 'Window of opportunity' of MHT is within 10 years of menopause (but not beyond).
      - Lifestyle modification is important.
      - Bone density is built before the age of 30 years with calcium and exercise.
      - Osteoporosis is irreversible.
      - Fracture/fall prevention is essential to bone health in menopause.

TABLE 19–4. Alternative therapies

Non-hormonal	**Centrally acting compounds:** belladonna/ergotamine/phenobarbital, clonidine, methyldopa, veralipride **Anti-depressants:** SSRIs/SNRIs (venlafaxine, desvenlafaxine, paroxetine, fluoxetine, citalopram), gabapentin, pregabalin	One Symptom: One Treatment Medical/Ob-Gyn Consult
Complementary and alternative therapies	Phytoestrogens, black cohosh, vitamin E, DHEA, other herbal remedies (evening primrose, dong quai, ginseng, wild yam), bioidentical hormone therapy.	Not enough conclusive evidence of effective relief nor safety
Mind-body, behavior therapies	Behavioral modifications, exercise, yoga, relaxation training, hypnosis, acupuncture	May reduce the frequency/intensity of hot flashes, sleeps, moods, stress, muscle and joint pains

Source: Pachman, D. R., Jones, J. M., & Loprinzi, C. L.. Management of menopause-associated vasomotor symptoms: Current treatment options, challenges and future directions. *Int J Women's Health*. 2010:2;123-135.[11]

4. ***Alternative modalities in the treatment of urogenital concerns during menopause – particularly for discomforts in sexual performance/ relationships:***
    - Self-help strategies
    - Use vaginal lubricants; moisturizers
    - Examine and address the "turn-ons" & "turn-offs"
    - Try new positions, stimulation and foreplay
    - Music, X-rated films
    - Sex toys: real or not
    - MHT
    - Ospemifene
    - Prasterone (dehydroepiandrosterone, DHEA)
    - Laser therapy
5. ***New modalities***
    - Aesthetic medical professional
    - Botox
    - Fillers
    - Mesotherapy
    - Sclerotherapy – veins
    - Non-surgical facelifts

SUMMARY

- There is no magic formula to good health in the menopausal period.
- Sometimes we have to fight for it.
- Accept ageing gracefully:
    - "God grant me the serenity to accept the things I cannot change; the courage to change the things I can; and the wisdom to know the difference." – Serenity Prayer, Reinhold Niebuhr, 1951

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OPEN FORUM HIGHLIGHTS

Moderator: MARY RANI M. CADIZ, MD, FPOGS

Q: *When would you recommend we start HRT? When or at what age?*

A: It depends on your level of discomfort. I think that age doesn't determine it. It's how much the symptoms are affecting your quality of life. Since the timing of perimenopause is retrospective, I would rely on symptoms. If you feel you are uncomfortable and you never felt that way before, it's time to seek help from your gynecologist who can help you decide whether you need the hormone or not.

Q: *When will be the best time to "freeze egg cells"?*

A: Whenever you want; usually when you're undergoing therapy for something, such as chemotherapy. We know that chemotherapy can have an effect on the ovaries so you might want to (especially if you are young or no matter how old you are) preserve your fertility by freezing your eggs. It will all depend on you and your understanding of the process of "freezing egg cells."

Q: *Is the transdermal MHT patch available in the Philippines?*

A: Yes, it is and we have the latest one, which is something that you apply on your skin. And you measure the dose by pumps. It is in gel form. A transdermal patch is actually one of the best preparations because it bypasses the liver. It is directly absorbed into your blood stream, without passing through the liver. Liver disorders present a problem with the absorption of the MHT. The transdermal patch is applied only twice a week.

Q: *What is the usual dose of estrogen for menopausal patients?*

A: It depends on the preparation that you have. There are equine estrogens and there are plant estrogens. I prefer plant estrogen. The dose of synthetic estrogens such as estradiol is 1-2 mg orally per day, or 0.025-0.10 mg transdermally per day. It depends on what you and your doctor will decide for you.

Q: *Is MHT safe for women with breast nodules BI-RADS 2 or 3 with myoma?*

A: You have two possible contraindications there. I think that if you have breast nodules you must have them examined first and find out whether they are malignant or not. If they are malignant, you cannot be given MHT because breast cancer is hormone- dependent. Myoma is also hormone-dependent. I have had cases where I had to make the patient choose between giving up her uterus or MHT. In my experience, my patients would rather lose the uterus than lose the benefits of hormones.

Q: *Is there any way we can delay menopausal stage?*

A: I wish, but no. This is a life situation. Women are born with a set number of follicles. Every time we menstruate or we ovulate, we lose thousands of follicles. Only one follicle usually releases an egg but the rest of the follicles will die. So therefore, there is a finite number. That's why we have menopause.

Q: *Does evening primrose oil (EPO) have a role in perimenopausal or menopausal management?*

A: EPO is part of complementary therapy and I think this must not be denied to anyone who believes that this improves her condition. Research shows that it will not perform as good as other preparations. But if the patient is happy with EPO or other herbal products she is using, then agree with her, but also tell her of other alternatives and advise her on regular check-ups.

Q: *What are the contraindications for transdermal patch preparations?*

A: The contraindications are 1) if the patch does not stick on your skin. 2) allergy to the adhesive. There is no problem with absorption into the skin.

Q: *What is the average age at which women with polycystic ovarian syndrome (PCOS) experience menopause?*

A: Honestly, I don't know. PCOS and menopause are totally unrelated because PCOS is a biochemical situation, while menopause is merely follicles dying, getting old and eventually not producing the necessary hormones.

Q: *What is atrophy? Is there a medicine to take or prevent it?*

A: Atrophy is actually ageing, not dryness. If this is regarding vaginal atrophy, we used to refer to dryness of the vagina as vulvovaginal atrophy or VVA, but now we call it GSM, encompassing both the external genitalia, vagina and the urinary tract.

Q: *What are the side effects of HRT and does the benefit outweigh the risk?*

A: I think this is something that you and your doctor must discuss. What I want to stress here is that women should have a say as to what is going to be done to them. That's part of education.

Q: *Can you determine the age of menopause based on the age of menarche?*

A: No, there is no association between age of menarche and age of menopause.

Q: *Until what age do we recommend pap smear?*

A: For as long as you're willing to go to your doctor. There is a guideline that says when there are 3 normal pap smears consecutively done, the patient no longer needs to go back to her doctor for a repeat pap smear. My personal principle is that – this is the only chance you get to examine your patient's blood pressure, her thyroid, her breasts – so I'd like them to come every year. You need to have a good evaluation of your patient every year for the rest of her life.

Q: *Is it true that your age of menopause is dependent on your mother's age of menopause?*

A: It has nothing to do with it.

Q: *Up to what age in women can the cervical cancer vaccine still be useful?*

A: You know that vaccines are given to people who are still unexposed. So we'd like our vaccines to be given to women who have not been exposed to the virus, which is sexually transmitted. But there was a clamor. Patients ask - what if I don't have the strain? So therefore, our principle is to just vaccinate them because they need protection. No matter what the age of the patient is, you may give the vaccine. If she so wants it, give her enough information and make her sign a waiver.

Q: *How can an individual with irregular period determine if she's already menopausal?*

A: You will know that you are into menopause if you have no menses for 12 consecutive months or you can check your hormonal levels through blood exams. However, if you are 55 years old and are still having irregular menses, it is a concern. A gynecologic evaluation is warranted in this case to check for extraovarian sources of estrogen.

REVIEW QUESTIONS

1. How is natural menopause defined?
    a. No menses for 6 consecutive months
    b. No menses for 12 consecutive months
    c. Increasing follicular activity
    d. Caused by ovarian failure or insufficiency

2. Which of the following is a suspicious menstrual change in the perimenopause?
    a. Shorter duration
    b. Less, lighter flow
    c. More frequent periods
    d. Missed periods

3. In which population is estrogen hormone therapy contraindicated?
    a. Women with acute deep vein thrombosis
    b. Congenital diseases of lipid metabolism
    c. Active liver disease
    d. All of the above

4. What is the most effective treatment for menopausal-related vasomotor symptoms?
    a. Hormone replacement therapy
    b. Selective Tissue Estrogenic Activity Regulator (STEAR)
    c. Behavioral modifications
    d. Evening primrose

5. Which is the most common perimenopausal symptom?
    a. Tinnitus
    b. Osteoporosis
    c. Hot flushes
    d. Incontinence

ANSWERS: 1. b; 2. c; 3. d; 4. a; 5. c

20 THE SCIENCE OF INTIMATE HEALTH CARE IN THE ELDERLY WOMAN

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Delivered as a webinar on June 14, 2019

https://bit.ly/ALMW_Ch20_ScienceofIntimateHealth

KEY POINTS

- Vaginal health is an important aspect of an ageing woman's femininity and overall health.
- Skin and mucosal laxity, dryness, and disruption of normal bacterial ecosystem in an ageing woman may lead to aesthetic and functional impairment.
- Intimate dysfunction may be caused by vulvovaginal atrophy and laxity, decreased vaginal lubrication, and lack of sensation. This may lead to urinary incontinence, frequent urinary tract infections, sexual dissatisfaction, and a poor quality of life.
- Non-surgical (e.g., radiofrequency treatment) and surgical procedures (e.g., labiaplasty and colpoperineorrhaphy) can restore vulvovaginal health and function.

LEARNING OBJECTIVES

- ➸ Review the basic facts of feminine intimate health
- ➸ Describe the anatomy and physiology of the vulvovaginal complex
- ➸ Increase awareness of the problem of intimate dysfunction in women
- ➸ Discuss methods for restoration, and renewal of the ageing vulvovaginal complex
- ➸ Understand the use of radiofrequency treatments to address the ageing vulvovaginal complex

I. BASIC FACTS OF FEMININE INTIMATE HEALTH

- Vaginal health is a topic that is least openly discussed among women and the medical community.
- From a medical perspective, the vagina is the most neglected intimate part of the female reproductive health system. Yet, it is an important part of a woman's overall health status and an expression of our femininity.
- Women take care of almost all body parts except the most intimate and vulnerable part, the vagina.
- In its youth, the vagina ensures our reproductive capacity, being an outflow tract in the childbearing years.
- Yet, like any female body part, it winds down together with our biological clock during the process of ageing.

II. ANATOMY AND PHYSIOLOGY OF VULVOVAGINAL COMPLEX

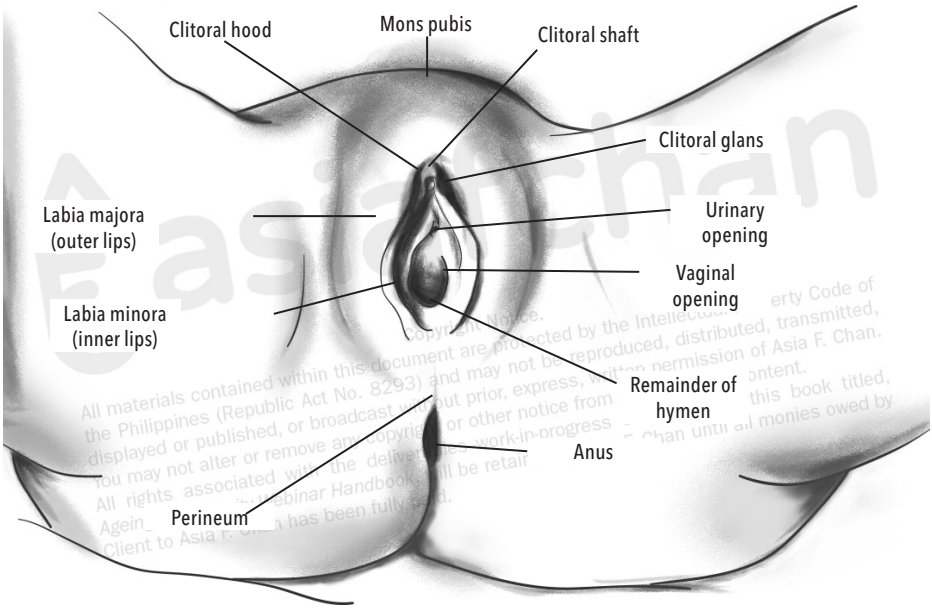


FIGURE 20–1. Gross anatomy of the vulvovaginal complex. Midline structures consist of clitoris, urethral opening, and vaginal introitus. Lateral structures are labia majora and minora, and perineum, which provide support.

A. Anatomy

- Normal Ageing
  - The vulvar skin is affected by the natural process of ageing.
  - Collagen and elastin are important protein structures in skincare as they provide strength, firmness, and shape of the skin.
  - Over time, the natural process of ageing depletes these fibers in the dermis resulting in the weakening and sagging of the skin due to loss of tensile strength and elasticity.
- During Vaginal Delivery
  - Stretching damages the connective tissue, which heals to a varying state of laxity that increases with each successive childbirth.
  - Loss of vaginal tissue, due to changes in cellular renewal and decreased collagen and elastin, can reduce the elasticity of the vagina and its opening.

B. Vaginal ecosystem

- Estrogen keeps the vagina moistened and at its optimal physiologic state (Table 20–1).
- Lactobacilli, the naturally occurring good bacteria, feed on the cells lined by estrogen and produces lactic acid. The more the lactobacilli feed on these cells, the more lactic acid is produced, which maintains the acidic pH.

- It is this acidic pH (3.5–4.5) that protects and prevents growth of bacteria from the anus.
- Any disruption in this ecosystem may cause inflammation, vaginal infections, and vaginal dryness.

TABLE 20–1. Estrogen and pH levels throughout a woman's lifespan

AGE GROUP	pH LEVEL	ESTROGEN LEVEL
Pre-reproductive period (Infancy to childhood)	5.0–7.0	Low estrogen
Reproductive period (Onset of menarche to childbearing years)	3.5–5.0	Sufficient levels of estrogen and estrogen stimulation
Post-reproductive period (Menopause, post-menopause and geriatric years)	>5.0	Declining levels or absence of estrogen

III. INTIMATE DYSFUNCTION

- Intimate dysfunction in a woman, more commonly termed female sexual dysfunction, occurs when a woman experiences persistent issues related to sex and intimacy, such as:
  - Physical changes
  - Dyspareunia
  - Lack of sexual drive
  - Inability to become aroused or excited during sex
  - Inability to achieve orgasm during sex
- Treatment of intimate dysfunction should address the anatomic and functional aspects of the vulvovaginal complex.
- Aesthetic gynecology is defined as the science of vulvovaginal restoration, and offers surgical and non-surgical procedures that address intimate dysfunction (Table 20–2).
- Apart from aesthetic goals (good form, function and pleasing appearance), it is equally important to address functional impairments such as excessive vaginal discharge, poor control of pelvic musculature, and psychological embarrassment to face their husbands, especially in postmenopausal women.

TABLE 20–2. General types of intimate dysfunction, symptoms and restorative procedures

TYPE	SYMPTOMS	PROCEDURES

1. Natural process of ageing	• Vulvovaginal dryness
	• Loss of vulvovaginal tone
	• Reduced vaginal secretion
	• Vulvar itchiness
		• Non-surgical:
		  ○ Radiofrequency
		  ○ Estrogen cream

2. Functional impairment	• Vaginal laxity and looseness • Reduced sensation during sexual intimacy • Urinary incontinence (with coughing, laughing, sneezing and straining) • Change in bowel function	• Non-surgical: Radiofrequency • Surgical: Colpoperineorrhaphy

3. Aesthetic imperfections	• Hypertrophy of the labia minora – with pain and discomfort from stretching and pulling of excess tissue
	• Sagging vulvar labial skin
	• Discoloration
		• Non-surgical: Radiofrequency
		• Surgical:
		  ○ Labial reduction
		  ○ Excess prepuce removal

TABLE 20–3. **Specific anatomic and functional changes and clinical course in intimate dysfunctions**

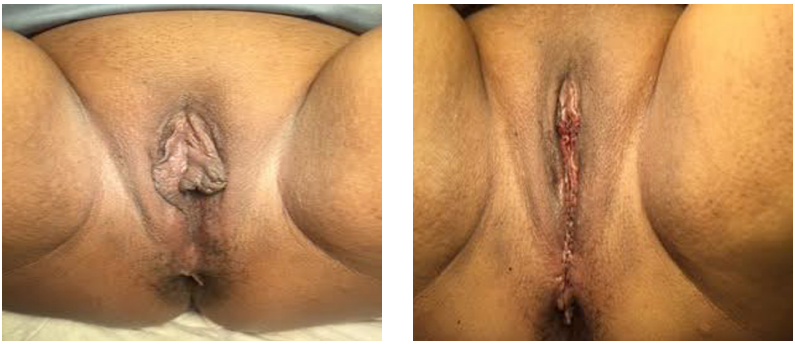
TYPE	CHANGES	CLINICAL COURSE
Vulvovaginal atrophy	• Absence or lack of estrogen • Insufficient lactobacilli • Changes in vaginal pH • Poor quality of connective tissue	• Chronic and progressive medical condition • Estimated to affect 10% to 40% of postmenopausal women ○ This rate is expected to increase with the rise in life expectancy. ○ Despite this significant prevalence of symptoms, it is believed that only 20% to 25% of symptomatic women seek medical attention.
Decreased vaginal lubrication	• Decreased elasticity due to loss of collagen and elastin • Shortening and narrowing of the vagina • Thinned and fragile vaginal mucosa	• Results in dyspareunia, itching, burning and discharge
Laxity and looseness[1]	• Laxity of the labia majora, resulting in vulvar itchiness • Laxity of fascial support – from childbirth or menopause • Natural results of delivery and trauma in advancing age	• Stress urinary incontinence – common issue after childbirth or menopause • Not limited to women who have given birth vaginally; up to 76% of women may experience decreased vaginal sensation due to laxity
Vaginal relaxation	• Due to loss of the optimum structural architecture of the vagina from ageing, pregnancy, and childbirth • Muscles are loose and weak, with poor tone and control • Internal and external widths increase • Muscles of the perineum have decreased strength and support	• Stress urinary incontinence • Change in bowel function • Feeling of looseness • Less sensation on intimacy
Insensitive skin	• Orgasmic dysfunction	• Reduced or absent coitus • Negative effect on sexual satisfaction and quality of life
Labial hypertrophy and/or discoloration	• Congenital in nature or due to pulling and stretching of excess skin	• Aesthetic imperfection

A. Surgical Procedures[2,3]

- Surgical procedures in aesthetic gynecology follow the principles of plastic surgery, which provide symmetrical, midline, clean and precise incisions.
- The desired result is to restore form, function, and appearance of the impaired body part.
- These are more permanent options to address functional impairment and aesthetic imperfections.

1. Labial reduction or labiaplasty
   - Indicated for labial hypertrophy
   - Involves removal of a portion of a hypertrophied labia minora
   - Aims to address aesthetic imperfections
2. Colpoperineorrhaphy (Anterior and posterior colporrhaphy with perineorrhaphy)
   - Indicated for vaginal relaxation (from sagging and laxity of labial and vulvar skin)

- Repair of vagina and perineum where muscles are reapproximated to improve aesthetic imperfections and reverse functional impairment
- The above surgical procedures may be combined to address these intimate dysfunctions.



(a) (b)

FIGURE 20–2. Labiaplasty and colpoperineorrhaphy (a) Before (b) After

B. Nonsurgical Procedures

- ***Temperature-controlled Radiofrequency (RF) (e.g., Thermiva)***
  - Non-invasive, non-surgical, energy-based device[4]
  - Unlike laser devices, which emit concentrated light with pure wavelengths to create microscopic columns of thermal damage in the skin, radiofrequency gently heats and massages the entire treated area.
  - Radiofrequency devices produce focused electromagnetic waves to generate heat in the underlying connective tissue. Heat (42–45°C) is delivered deeply into tissues using a delicately designed handpiece. The heat massages the area and stimulates blood flow. This improves lubrication and lessens friction in the vaginal canal, and stimulates collagen and elastin production that tightens and thickens the skin and mucosa.
  - Collagen immediately contracts after the 1st session; followed by collagen and elastin remodeling after the 2nd session, and long-term stimulation with new collagen and elastin formation after the 3rd session.
  - It is U.S. FDA-approved for dermatological conditions and general surgical procedures for electrocoagulation and hemostasis.[5]
  - It is also used for age-related gynecologic conditions, such as loose and sagging vulva and vagina (vulvovaginal laxity), vulvar and vaginal dryness (atrophic vulvovaginitis), and insensitive skin leading to sexual or orgasmic dysfunction.[4] Clinical evidence to support its use is still evolving but it seems to be an attractive, safe and effective option.[6]
  - It may also address mild to moderate stress urinary incontinence, overactive bladder or genitourinary symptoms, menopause symptoms, prolapse, or orgasmic dysfunction, but is not FDA-approved for these conditions.
  - Radiofrequency treatment of the vulvovaginal area takes 20 to 30 minutes: 10 to 15 minutes on the vulvar area, and 15 to 20 minutes in the vaginal area.
  - There is no downtime, pain, nor any side effects (such as burning) after the procedure.

- Anesthesia is not needed, and normal activities, including sexual intercourse, can be resumed right after.
- The recommended regimen for vaginal restoration is three monthly sessions with subsequent yearly maintenance.

IV. CASE SERIES

- Preliminary clinical experience by this author (Feb 2017–Feb 2019) using temperature-controlled RF device, once a month for 3 sessions
- Inclusion criteria:
  - Age: 25 to 80 y/o
  - Any of the following:
    - Vaginal looseness
    - Vaginal dryness
    - Vulvar laxity
    - Leaky urine
    - Desirous of pregnancy
- Exclusion criteria:
  - Abnormal pap smear
  - Pregnancy
  - Vulvar lesion/disease
- Results:
  - Demographic characteristics:
    - 82 patients (average age, 46 years)
      - 20–40 y/o: n=22
      - 40–60 y/o: n=40
      - >60 y/o: n=20
    - Most had a chief complaint of vaginal dryness. (Figure 20–3)

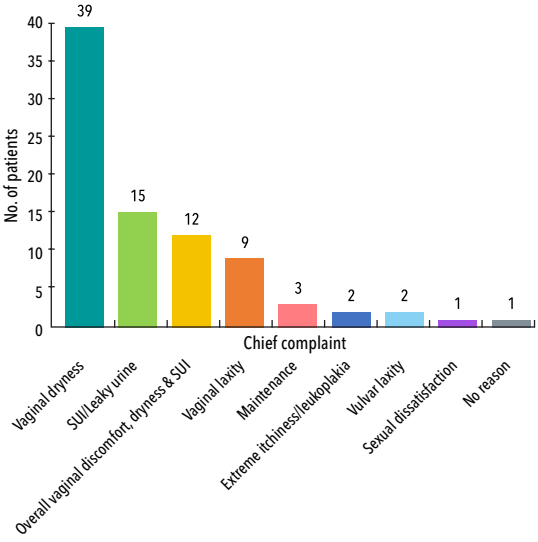


FIGURE 20–3. Distribution of patients' chief complaints prior to temperature-controlled radiofrequency sessions

SUI, Stress urinary incontinence

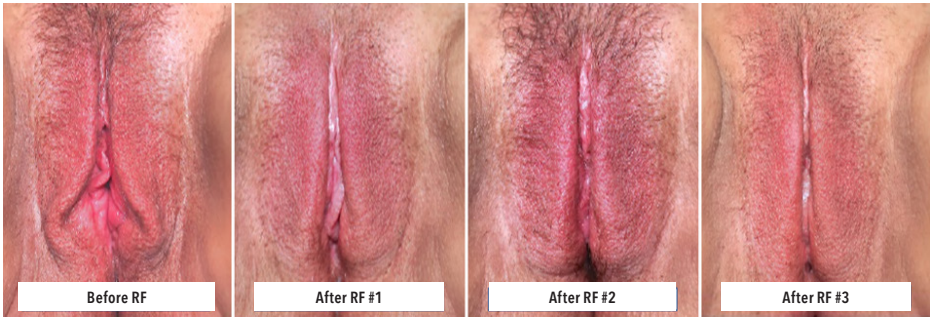
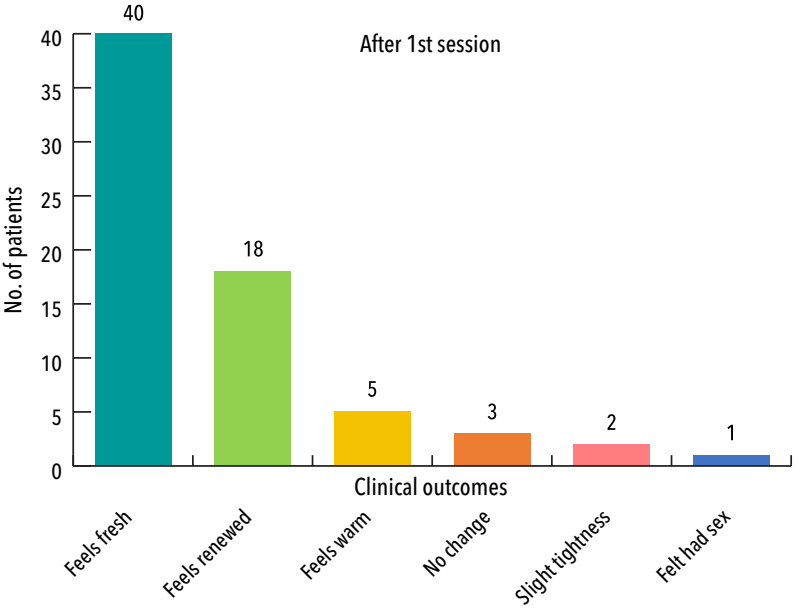


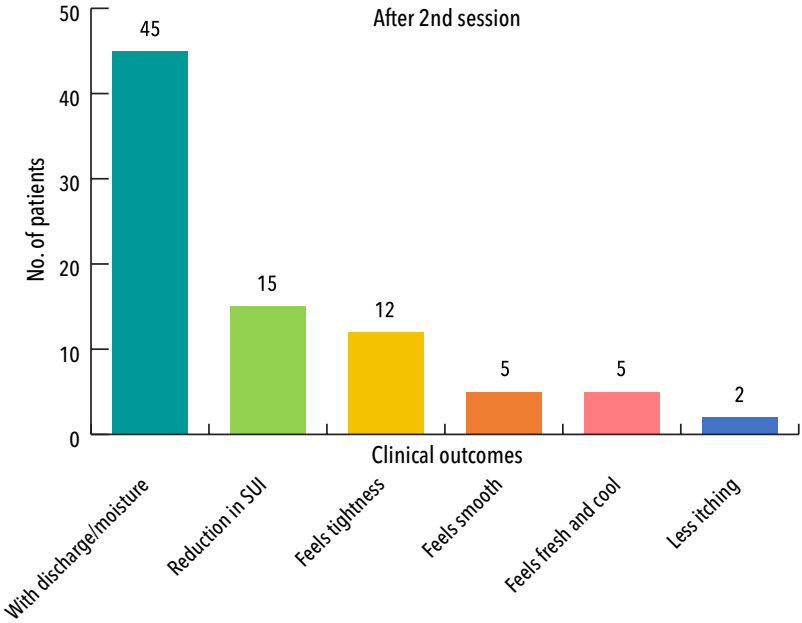
FIGURE 20–4. Vulvovaginal laxity treated with 3 sessions of temperature-controlled radiofrequency (RF)

TABLE 20–4. Patient-reported clinical outcomes post-radiofrequency treatment (Figure 20–5)

TIMING	CLINICAL OUTCOMES
After 1st session	• Generally, almost all felt refreshed, something that they never felt before. • Patients felt good, renewed, and satisfied. • Some felt they had sex while procedure was being performed. • Those who reported itching and dryness also felt warmth.
After 2nd session	• Generally, half of the patients reported increased vaginal discharge and moisture. • Five patients reported smoother and softer skin over the vulva. • Those who came for leaky urine reported a reduction in symptoms; less urinary frequency or urge to go to the bathroom, able to control urination, and had fewer toilet visits at night.
After 3rd session	• Over half experienced overall satisfaction. • About 1/3 experienced moderate wetness and increased tightness. • A number of patients experienced controlled urination and sexual satisfaction with long orgasms.
Summary of benefits	• Patients with complaints of vaginal dryness also reported vaginal tightening. • Patients with atrophic changes and dryness reported moist and comfortable feeling, and additionally, controlled urination. • Patients with mild to moderate stress urinary incontinence (SUI) had marked improvement with reduction in symptoms plus increased moisture and wetness. • Three patients reported longer orgasms.


After 1st session
No. of patients
Clinical outcomes
40
18
5
3
2
1
Feels fresh
Feels renewed
Feels warm
No change
Slight tightness
Felt had sex

(a)


After 2nd session
No. of patients
Clinical outcomes
45
15
12
5
5
2
With discharge/moisture
Reduction in SUI
Feels tightness
Feels smooth
Feels fresh and cool
Less itching

(b)

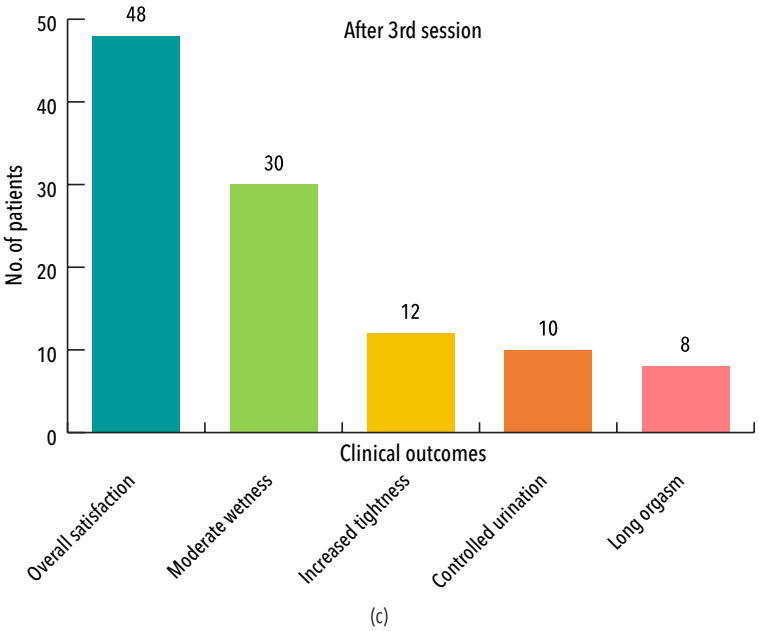


FIGURE 20–5. Distribution of patient-assessed outcomes after 3 monthly radiofrequency treatments (a) after 1st session (b) after 2nd session (c) after 3rd session

- ***Conclusion***
  - Many women who have valid indications are interested in these vaginal restoration procedures.
  - Each patient must be carefully assessed for risk and benefit and properly counseled. It is crucial to address the actual reason why the procedure is desired.
  - All were happy or very happy with results, would do it again, and would recommend the treatment to others.
- ***Recommendations***
  - There is a need for more studies.
  - Until further robust scientific data is available, the clinician must remain guided by the medical ethical principles of doing no harm, acting only in beneficence, and protecting patient autonomy.
  - Only a review of cases performed over time will ultimately answer questions on its efficacy and long-term safety.

SUMMARY

Once considered taboo or an unspoken topic, intimate dysfunction has become more openly discussed. Changes in a woman's intimate health–due to pregnancy, childbirth, and the ageing process–are personal experiences that can affect her overall sense of feminine well-being. It is time to help women who suffer quietly to come out courageously and seek help when possible. The science of vulvovaginal restoration (surgical and non-surgical procedures) can provide safe, painless and, effective treatment options to women's most intimate dysfunctions.

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OPEN FORUM HIGHLIGHTS

Moderator: MA. STEPHANIE FAY S. SAMADAN-CAGAYAN, MD

Q: *Why is it that I do not hear about vaginal restoration, and just hear about vaginal rejuvenation? Is it a group of procedures that we offer to our patients – surgical and non-surgical?*

A: At the outset, it must be emphasized that vaginal rejuvenation is not a procedure. It is a term first defined and marketed as 'laser vaginal rejuvenation' and encompasses recognized surgical procedures for conditions such as labial hypertrophy, cystocele, and rectocele introduced and trademarked by Dr. David Matlock. Surgical procedures are more permanent.

Some women may not need surgical intervention but may benefit from a non-invasive, nonsurgical vaginal restorative procedure such as temperature-controlled radiofrequency (RF), which helps revive and restore loose sagging labial skin and loose vaginal wall, dry vulva and dry vagina, loose and insensitive vaginal mucosa, and loss of fascial support. This treatment is a healthy alternative for women who suffer not only from functional and aesthetic impairments but from the natural process of ageing.

Q: *How long is a surgical procedure?*

A: The surgical procedure takes around 90 minutes. The technique uses a pencil or a small probe that cuts, dissects, and tightens muscles of the upper bottom and external structures of the vulva for vaginal relaxation. It cleanly cuts the excessive labial tissue in hypertrophied labia; the procedure is bloodless.

Q: *How many of patients undergoing radiofrequency treatments belong to the younger age group?*

A: In our local setting, my 2-year clinical experience showed that half belongs to the 40- to 60- year-old age group, and 25% belong to the younger age group (20–40 y/o). The older age group (60 y/o and older) make up the remaining 25%.

My youngest patient was 26 years old and delivered her first baby at the age of 18 years. Since she was still young and sexually active, she desired some form of vaginal tightening, preferably a nonsurgical intervention. On the other hand, my oldest patient was 84 years old, who refused surgery and sought an

alternative solution–radiofrequency (RF) tightening for the reduction of her frequent urination of 4–5x night.

In a survey of 150 women comparing age groups 20 y/o and 60 y/o and above, contrary to expectations, stress incontinence (i.e., passage of urine upon coughing, laughing or, sneezing) was experienced by young and single respondents. The most probable reason for this result is the unusual active sexual practices of the young resulting in vaginal laxity and stretching of the vaginal wall (usually seen in childbirth and vaginal delivery).

Q: *Are there any side effects after having vaginal restoration? Are there any precautions for elderly patients with comorbidities?*

A: Surgical procedures for vaginal restoration have permanent results to address the specific need like vaginal relaxation or hypertrophied labia minora. Side effects are nil but downtime is longer.

On the other hand, there are no side effects and no downtime for patients who have undergone radiofrequency (RF) procedure whose science is basically heating with no burning nor scarring formation. A radiofrequency device is NOT a laser energy device. Radiofrequency treatment addresses both vulvar (labial, vaginal introital opening) and vaginal issues and concerns using only one probe for the whole procedure. This is very effective for patients who complain of vulvar and vaginal itchiness secondary to laxity of the labial wall, and lack of collagen and elastin fibers of the skin. I have used this procedure on my patients who experience chronic itching especially those with diabetes.

Q: *Is this covered by the PhilHealth packages or private health insurance?*

A: Unfortunately, this is not covered by PhilHealth. But some insurance companies may cover this surgical procedure, especially if there are anatomic reasons like pelvic organ prolapse (cystocele or rectocele). Nonsurgical radiofrequency procedure is an alternative solution to young breast cancer survivors who complain of vaginal dryness but are unable to use estrogen creams, and at times, may be covered by the insurance companies.

Q: *Are patients with underlying pathology, good candidates?*

A: It depends on the pathology. It is crucial to get a comprehensive history, provide appropriate counseling and ascertain the exact reason behind the request for the procedure.

Q: *Do we have medications in the market for stress urinary incontinence?*

A: There is really no permanent treatment for leaky urine. Temperature-controlled radiofrequency machines do not claim that it is a panacea or cure-all for this condition.

Q: *So you have stopped using laser procedures?*

A: Yes, I have stopped and have shied away from laser energy devices because of the side effects of perineal fibrosis, scarring, and cicatrization. Temperature-controlled radiofrequency (RF) procedure is safe since its science is purely heat therapy and massage over the affected and impaired area. There is no burning nor blister formation from the procedure.

REVIEW QUESTIONS

1. What leads to vulvovaginal atrophy?
    a. Absence or lack of estrogen
    b. Insufficient lactobacilli
    c. Changes in vaginal pH
    d. All of the above

2. What is the most common vulvovaginal complaint of female elderly patients?
    a. Vulvovaginal dryness
    b. Incontinence
    c. Itchiness
    d. Sexual dissatisfaction

3. Which of the following is true about radiofrequency energy treatment?
    a. Radiofrequency increases blood flow to impaired tissues
    b. Radiofrequency stimulates new and tighter collagen remodeling
    c. Radiofrequency tightens and thickens vaginal mucosa resulting in improved moisture, lubrication and friction during intercourse
    d. All of the above

4. What is the earliest symptom of vulvovaginal atrophy?
    a. Shortening and narrowing of the vagina
    b. Decreased vulvovaginal lubrication
    c. Decreased elasticity associated with the loss of collagen and elastin
    d. Urinary incontinence

5. Which of the following statements is incorrect regarding temperature-controlled radiofrequency?
    a. It is suitable for those with moderate to severe symptoms.
    b. It is a non-surgical option to address laxity of the labia majora and vaginal fascial support
    c. It reverses some of the changes due to ageing or childbirth.
    d. It can be used in women with breast cancer or gynaecologic cancer

ANSWERS: 1. d; 2. a; 3. d; 4. b; 5. a

21 AGEING AND LONGEVITY AMONG HEALTHCARE PROFESSIONALS

Carmencita M. David-Padilla, MD, MAHPS

Delivered as a webinar on March 8, 2019

https://bit.ly/ALMW_Ch21_AgeingandLongevity

Hibiscus rosa-sinensis 'Carmencita David-Padilla'

KEY POINTS

- Ageing is the process of growing older; longevity is the duration of life; and life expectancy (at birth) is the number of years that a newborn is expected to live.
- The population of the Philippines and the rest of the world is ageing, and there is a need to align health and social systems.
- Ways in which university health centers can commit to the global strategy and action plan on ageing are to develop age-friendly environments and provide measurement, monitoring and research on healthy ageing.

LEARNING OBJECTIVES

- ➟ Define ageing, longevity, and life expectancy
- ➟ Present the burden of ageing in the Philippine and global setting
- ➟ Discuss ways to align the programs for healthy ageing for health workers in institutions such as our university health sciences center setting to the Global Strategy on Ageing

1. *What are the differences between ageing, longevity, and life expectancy?*

- Ageing is the "lifelong process of growing older at the cellular, organ, or whole-body level throughout the life span."[1]
- Longevity is the duration of life.[2]
- Life expectancy (at birth) is the "average number of years that a newborn could expect to live, if he or she were to pass through life subject to the age-specific death rates of a given period."[3]

2. *Why do we need to know about ageing and health in the global and Philippine setting?*[4]

- By 2050, the proportion of the world's population aged 60 years and older will almost double from 12% (in 2015) to 22%.
- By 2020, there will be more people aged 60 years and older than children younger than 5 years.
- By 2050, majority (80%) of older people will be living in low- and middle-income countries.
- Our world population is ageing much faster than in the past.
- The world is facing major challenges to align their health and social systems to this demographic shift.

3. *What is the burden of ageing and life expectancy in the Philippines?*

- In 2020, an estimated 5M (4.86%) of the population are aged 65 or older (Figure 21–1).[5]
- Globally, older persons aged 60 and above account for only 13% in 2017. However, this age group is growing faster than the others, hence it is likely to double by 2050.[6]

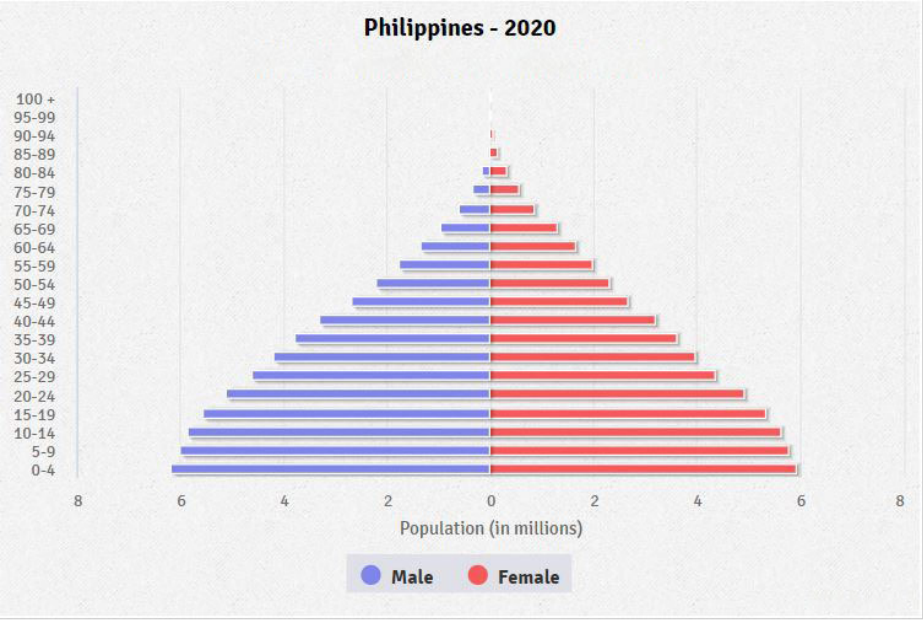

FIGURE 21–1. Population pyramid for the Philippines, 2020

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- Life expectancy for a Filipino born in
  - 1990 is 65–67 years
  - 2015 is 65(M)/ 72(F)
  - 2020 is 66.5 (M)/73.8(F)[5]

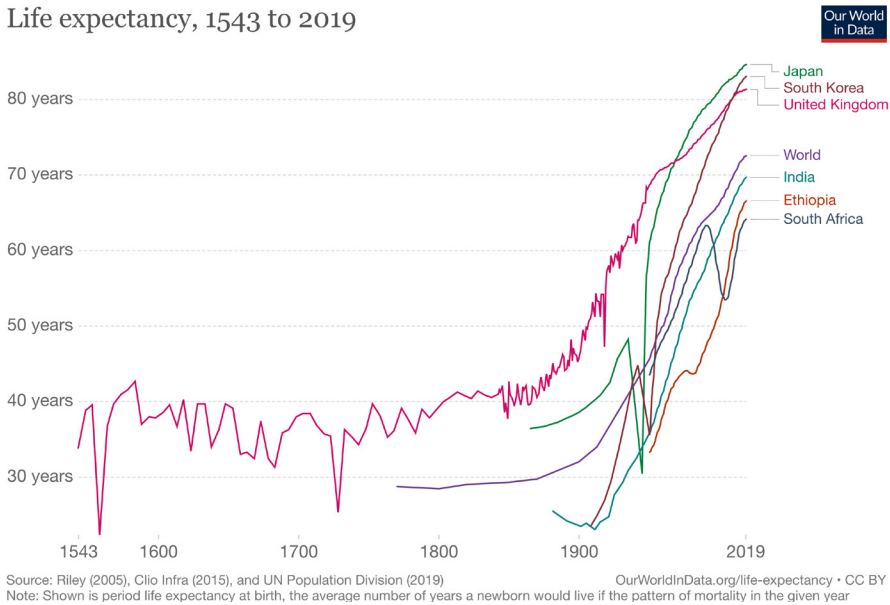

FIGURE 21–2. Life expectancy of Philippines and other countries

Reprinted from "Our World in Data" by University of Oxford. https://ourworldindata.org/grapher/life-expectancy?time=1844..2019&country=JPN+GBR+IND+ETH+OWID_WRL+KOR+ZAF+PHL
Copyright © 2019 University of Oxford (CC BY 4.0).[7]

4. *Why talk about Ageing now?*[8]

- Healthy ageing is the "process of developing and maintaining the functional ability that enables well-being in older age."
- "Functional ability is determined by the intrinsic capacity of the individual (the combination of all the individual's physical, mental, and psychosocial capacities) , the environment he or she inhabits, and the interaction between these."
- It is not enough to understand our body. It is also important to understand the environment to achieve healthy ageing.

5. *What contributes to increased life expectancy?*

- In low- to middle- income countries, increased life expectancy is the result of reduction in maternal and child mortality. In high income countries, it is mainly due to declining mortality in older age groups.[9]
- Throughout most countries, life expectancy steadily increases due to better health facilities, health care, and technology.[6]
- There is a **shift in the leading causes of disease and death:** from infectious and parasitic diseases (infants and children) to non-communicable diseases (adults and older people).[10]
- In the more developed countries, the infectious diseases resolve much earlier than in lower-income countries.

6. *What is Healthy Life Expectancy?*

- Biology and genetics
  - These contribute 30% to how we age and affect our disposition to disease.
- Environment and lifestyle
  - Compared to biology and genetics, these have a greater contribution to healthy life expectancy:
    - Improve nutrition and environmental sanitation.
    - Ensure screening, early diagnosis, improved disease management through medications (e.g., antibiotics, vaccines, anti-hypertensive and anti-diabetic drugs) and surgical techniques.
    - Implement safety measures in roads and workplaces.
    - Teach lifestyle modifications and better health-seeking behavior.

7. *What is the situation of ageing and longevity among healthcare professionals in UP Manila?*

- UP Manila is composed of 5,000 students, 1,000 faculty members, and 5,000 employees in a congested area in Manila.
- UP Manila has faculty and employees who belong to the ageing population and have been working for decades.

8. *What are the guiding principles of the Global Strategy and Action Plan on Ageing and Health (2016–2020)?*

TABLE 21–1. Guiding Principles (Global Strategy and Action Plan on Ageing and Health (2016–2020)

ITEM NO.	GUIDING PRINCIPLES
22	Ageing is a valuable, if often challenging, process. It is good to get old and that society is better off having older populations. It acknowledges that many older people will experience very significant losses, whether of physical or cognitive capacity or of family, friends and the roles they had earlier in life. Societal responses to ageing should not deny these challenges but seek to foster recovery, adaptation, and dignity.
23	This will require transformative approaches that recognize the rights of older people and enable them to thrive in the complex, changing, and unpredictable environment they are likely to live in now and in the future.
24	These approaches must foster the ability of older people to make multiple contributions in an environment that respects their dignity and human rights, free from gender- and age-based discrimination.

Source: World Health Organization. *Global Strategy and Action Plan on Ageing and Health*. 2017.[8]

- It is not easy to age in a healthy way, and we have to address the challenges along the way.
- It is OK to get old. We would like to reverse the notion that older people are a burden.

9. What are the strategic objectives of the Global Strategy?

TABLE 21–2. Vision, strategic objectives and action plan (Global Strategy and Action Plan on Ageing and Health, 2016-2020)

Vision	A world in which everyone can live a long and healthy life.
Strategic Objectives	1. Commitment to action on Healthy Ageing in every country. 2. Developing age-friendly environments. 3. Aligning health systems to the needs of older populations. 4. Developing sustainable and equitable systems for providing long-term care home, communities and institutions. 5. Improving measurement, monitoring, and research on Healthy Ageing.
Action Plan 2016-2020	1. Five years of evidence-based action to maximize functional ability that reaches every person. 2. By 2020, establish evidence and partnerships necessary to support a Decade of Healthy Ageing from 2020 to 2030.

Reprinted from "Global Strategy and Action Plan on Ageing and Health." by World Health Organization. 2017. p 6. Copyright @WHO (License: CC BY-NC-SA 3.0 IGO).[8]

- How does UP Manila align with these strategic objectives [SO]?
  - UP Manila will commit to action on Healthy Ageing. [SO1]
  - UP Manila will develop age-friendly environments [SO2].
  - UP Manila will provide measurement, monitoring, and research on Healthy Ageing [SO5].

10. How will Healthy Ageing happen in UP Manila?

- UP Manila administration will provide the leadership and coordination on providing services for the ageing community.
- With the focus on the ageing community, UP Manila will develop modules that will provide information on healthy lifestyle among health providers and employees.
- UP Manila is currently developing *13 Wellness Modules In The Workplace* (with a mobile app), which will include a module on Healthy Ageing.
- UP Manila will provide favorable work environment and promote healthy lifestyle among health providers and employees.
  - Evaluation of work assignments of ageing personnel and re-assignment if necessary
  - Provision of healthy choices for meals and assess the need to change policy on items for sale
  - Provision of comfortable and safe walking paths that are accident-free
  - Provision of board and lodging for employees with travel time of 4 hours a day
  - Provision of appropriate exercises for the aged (e.g., Zumba classes, Vinsaya Yoga) and
  - Monitoring of availment of free consultations and annual health check-ups for UP Manila employees at the UP Health Service
- UP Manila, through the National Institutes of Health (NIH) Institute on Ageing (IA), will provide the evidence that will be the basis for policies focused on the ageing community.
  - NIH-IA, led by Director Shelley de la Vega, will conduct a survey on health status of UP Manila employees.
  - IA will be responsible for monitoring the adequacy of UP Manila policies directed towards the ageing community.
  - IA will recommend policies, projects, and other activities that cater to the ageing community.

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OPEN FORUM HIGHLIGHTS

Moderator: JOHANNA PATRICIA A. CAÑAL, MD, MHA, MSc, FPCR

Q: *Will the modules (13 Workplace Wellness Modules) be free for everyone?*

A: So far, that is the plan. The Institute of Human Genetics National Institutes of Health (NIH), through a grant from the March of Dimes USA, developed wellness modules on various topics, i.e. hypertension, obesity, vaccination, and healthy pregnancy (via face-to-face meetings) with factory workers, and later NIH employees. There was good feedback and we are now in partnership with the UP Manila Open University to develop the online version that can be accessed either through the computer or a mobile app. After completing the wellness modules through 20-minute bite-sized lessons, participants will get a Certificate of Wellness. This set of modules will eventually be open to the general public. We will develop a module on healthy ageing in cooperation with the Institute of ageing. The modules are currently being tested by content experts before they are launched.

Q: *People are living longer. It used to be that people died of disease, and nowadays, people live with disease, mainly due to non-communicable disease.*

A: This is also partly due to better technology. In the past, if you have a heart disease, you will die. Now, we know that you can live, if diagnosis is picked up early, given correct medication and appropriate surgery if needed. It is important to age gracefully in a healthy manner.

Q: *Any opinions on how the Universal Healthcare (UHC) Law will impact the healthcare of the elderly population?*

A: If the UHC Law is implemented the way it should, then the elderly population will have a secure future. If the greater population of the audience will be in the health professions, we have to do our share now as the implementing rules and regulations are being developed.
It's still being written up, but this is the time to speak up. We have to work by groups and for each group of diseases, we have to be the voice.

Q: *What are the plans for food in UP Manila?*

A: Love water instead of soda. There will be access to clean water. There should be an alternative before we ban bottled water (and other bottled juices). All new buildings will have free and clean water in every floor. There is a plan for several cafeterias within UP Manila in around 2–3 years. Healthy food and not fast food will be provided.

Q: *Do we have any existing programs in our campus that address the health needs of the elderly employees?*

A: An annual physical examination is available but not everyone takes advantage of this. I will request the Geriatric Medicine Unit and Institute of Ageing to develop a different health checklist form appropriate for the elderly.

Q: *If we implement all of these, and we are foreseeing a healthier workforce, does that mean that the retirement age will be moved back?*

A: We are very functional beyond the age 65. I would like to believe that people one day will need to retire because there's really life after retirement. But I'd like them to retire in a very healthy condition so they can enjoy life outside of work.

REVIEW QUESTIONS

1. What is the definition of life expectancy?
    a. The duration of life
    b. The average number of years that a newborn would be expected to live if he or she is subject to the age-specific mortality rate during a given period
    c. The expected length of staying alive in an elderly given the environmental conditions
    d. The lifelong process of growing older at cellular, organ or whole-body level throughout the life span

2. Which of the following contributes to the improvement of life expectancy in low- to middle-income countries?
    a. Declining fertility rate
    b. Declining mortality in the elderly
    c. Reduction in maternal and child mortality
    d. Declining poverty rate

3. What is the life expectancy of a Filipino woman born in 2015?
    a. 70
    b. 71
    c. 72
    d. 73

4. What is the mobile app currently being developed by UP Manila with the Open University?
    a. 13 Wellness Modules in the Workplace
    b. 15 Healthy Ageing Modules in UP Manila
    c. 13 Healthy Ageing Modules in the Workplace
    d. 15 Wellness Modules in UP Manila

5. Which of the following is not a part of the strategic objectives of the Global Strategy and Action Plan on Ageing and Health (2016–2020)?
    a. Commitment to action on Healthy Ageing in every country
    b. Develop age-friendly environments
    c. Aligning health systems to the needs of older populations
    d. Developing programs to provide special attention to the ailments of the elderly

ANSWERS: 1. b; 2. c; 3. c; 4. a; 5. d

22 VACCINATION IN THE ELDERLY

Regina B. Pascua-Berba, MD, MSc, FPCP, FPSMID

Delivered as a webinar on July 12, 2019
https://bit.ly/ALMW_Ch22_Vaccination

KEY POINTS

- Immunization is public health's best buy, and remains one of the most cost-effective health interventions.
- Vaccines stimulate the body's immune system to respond swiftly against the pathogen.
- Herd immunity works through indirect protection of unvaccinated vulnerable members of the population.
- It is important for adults to get vaccinated to protect against potentially fatal but preventable diseases and to maintain overall health of self, family and community.
- The recommended vaccines in the elderly are:
  - Annual influenza vaccine (quadrivalent type)
  - Pneumococcal vaccine, the polysaccharide type (PPSV-23) and the conjugate type (PCV-13) once in a lifetime
  - Tetanus, diphtheria and acellular pertussis (TdaP) once-in-a-lifetime booster; Tetanus-diphtheria (Td) booster every 10 years
  - Herpes zoster vaccine - one or two doses in a lifetime
- Myths and fake news on vaccines should be dispelled with facts and scientific evidence.

LEARNING OBJECTIVES

- ➸ Describe the impact of immunization on public health
- ➸ Explain how vaccines work
- ➸ Discuss the recommended vaccines in the elderly
- ➸ Differentiate facts from fake news about vaccination

I. IMMUNITY: AN OUNCE OF PREVENTION IS WORTH A POUND OF CURE

- There is strong evidence that vaccines really work and can extend lives.
- Millions of cases of infectious diseases are prevented and billions of lives are saved because of vaccines.
- Immunization is an important public health strategy.
  - Smallpox was eradicated by vaccines in May 1980.
  - The last known case of naturally acquired smallpox in 1978 was Rahima Banu, a 3-year-old male from Bangladesh.
- In 1990, vaccination was declared one of the greatest public health achievements in the US (CDC, 1999).[1]

- Immunization saved more lives in the world in the last 50 years than any other health intervention; hence, it is the single most cost-effective health investment and a cornerstone in efforts to promote health.

II. HOW DO VACCINES WORK?[2,3]

- By mimicking disease agents, vaccines stimulate the body's immune system to build defenses against disease pathogens.
    - A vaccine is like a pathogen-impostor; it is recognized by the immune system as a bacteria or virus but does not make the person sick.
- Pathogens are covered with molecules, called antigens, that can trigger a specific immune response.
- Vaccination exposes the body to antigens that are similar to the antigens found on a pathogen.
    - By posing as a specific pathogen, the vaccine primes the immune system to respond with speed and strength if the body encounters the pathogen in the future.
- Primary response to a pathogen: Vaccines 'program' the immune system to remember a particular disease agent by allowing it to 'practice' on a weakened or killed version of the pathogen.
- Secondary response to a pathogen: If the pathogen invades the body again in full strength, the immune system is ready to respond with a swift and specific defense.
    - Secondary responses happen faster and at a greater magnitude than primary responses, which results to creation of more antibodies to fight the pathogen and more memory cells to fight it in the future.
- Herd immunity is recommended.
    - It is defined as the indirect protection of unvaccinated persons, whereby an increase in the prevalence of immunity interrupts transmission of infectious agents in vulnerable populations (e.g., very young, very old and immunocompromised) who are least likely to respond to vaccination.[4]

III. ADULT IMMUNIZATION RECOMMENDATIONS

- Local recommendations (2017-18)[5,6] are aligned with international recommendations.[7]
    - Annual influenza vaccine (quadrivalent type)
    - Pneumococcal vaccine – the polysaccharide type (PPSV-23) and the once-in-a-lifetime conjugate type (PCV-13)
    - Tetanus, diphtheria and acellular pertussis (TdaP) once-in-a-lifetime booster; Tetanus-diphtheria (Td) booster every 10 years
    - Herpes zoster vaccine - one to two doses in a lifetime

A. Influenza

- Overview of influenza
    - It is highly infectious and contagious and can potentially become a serious disease, especially in the elderly.
    - It is the 6th among the top ten causes of morbidity in the Philippines.[8]
        - One out of 100 Filipinos gets sick of influenza every year.
    - There are more influenza B strains seen in our country as well as in other Asian countries, Europe and America.
    - In the United States, the flu season is more distinct and starts around the winter season in

December and lasts around early March.
    - In the Philippines, it starts around the beginning of the rainy season, usually by June. Thus, vaccination of elderly should start around May until the end of October.[9] A study showed two peaks of influenza outbreaks (January to March, and July to September).[10]
    - Influenza causes a significant economic burden, directly (hospitalizations, consultations) or indirectly (absenteeism, lost productivity).[11,12]
  - Types of Influenza vaccine
    - All currently available vaccines are grown in embryonic hen's eggs, and then chemically inactivated and purified.
      - Split virion, inactivated or disrupted virus vaccines: Whole virus is inactivated by exposing it to organic solvents or detergents
      - Surface antigen inactivated vaccines: Contain H and N antigens prepared from disrupted viruses
    - There is a recent shift from trivalent (contains only 1 influenza B virus) to quadrivalent type (contains both influenza B viruses) of flu vaccine.
    - In the Philippines, the distributed influenza vaccine is the Southern hemisphere strain.
  - Recommendations:
    - Annual vaccination for all persons greater than 6 years of age
    - Persons aged 6 months or older including pregnant women and persons with no allergy to eggs can receive the inactivated vaccine.
    - Recommended for high-risk individuals in other countries:
      1. All those aged 65 years and over
      2. Residents of nursing homes and long-term care facilities
      3. Caregivers of people whose welfare may be at risk if the caregiver falls ill
      4. Pregnant women
      5. Immunosuppressed individuals
      6. Those with chronic illnesses (respiratory, cardiovascular, hepatic, neurologic, and renal)

B. Pneumococcal vaccine

  - Overview
    - Also called 'anti-pneumonia shots' or 'kontra-pulmonya', but may also protect against other infections caused by *Streptococcus pneumoniae*, such as otitis media, sinusitis, meningitis, bacteremia, endocarditis, peritonitis, and arthritis
    - Significantly reduced the incidence and risk of pneumonia
  - Indicated for:
    - Adults 65 years of age and older
    - High risk conditions: chronic heart and lung disease
    - Cigarette smokers
    - Diabetes mellitus
    - People without a spleen
    - Cancer patients undergoing chemotherapy
    - Persons living with HIV

- Types of Pneumococcal vaccine
  - Pneumococcal Polysaccharide Vaccines (PPSV23): serotype-specific capsular polysaccharides; 25 mcg each of polysaccharides from 23 serotypes
  - Pneumococcal Conjugate Vaccines (PCV13): serotype-specific polysaccharides "conjugated" to a protein carrier; contains 13 serotypes, one of which is not found in PPSV23
- Recommendations
  - PCV13 may be given first, followed by PPSV23 one year after. No revaccinations of either type needed.
  - Adult Filipinos more than 50 years of age who were previously given PPSV23 may be given PCV13 one year after.
  - Adult Filipinos who were previously vaccinated with PPSV23 at less than 50 years old, but who are now 50 years old, may receive PCV13 after at least one year, then another dose of PPSV23 one year after
  - Adult Filipinos more than 50 years old who were previously given PPSV23, without previous PCV13 vaccine may opt to be vaccinated with another dose of PPSV23 after 5 years. No revaccination thereafter.

C. Tetanus, Diphtheria and Pertussis

- Overview
  - Tetanus bacteria, upon entry through a break in the skin, attacks the neuromuscular system resulting in rigidity, spasm, and seizures. Diphtheria and pertussis are both acute respiratory infections with the former being characterized by a thick membrane in the mucosa.
- Types of vaccine
  - Td – Tetanus toxoid (20 IU) + adult diphtheria toxoid (at least 2 IU)
  - Tdap – Tetanus toxoid (20 IU) + adult diphtheria toxoid (at least 2 IU) + acellular pertussis (at least 8 μg)
- Recommendations
  - All adults 19 years old and older need a one-time Tdap booster.
  - Tdap should be administered regardless of interval since last tetanus or diphtheria-toxoid-containing vaccine.
  - Adults with no previous vaccination or incomplete vaccination of tetanus-diptheria combination (ie., 3-dose primary series) should receive the complete primary series that includes 1 dose of Tdap.
  - Follow-up boosters of Td are recommended every 10 years.

D. Vaccine for herpes zoster (shingles)

- Overview
  - Varicella is the primary infection caused by the varicella-zoster virus (VZV).
  - The VZV moves along the sensory nerve to the dorsal root ganglion where it establishes latency during primary infection, and is reactivated at a later time, resulting in herpes zoster.
  - Most adults worldwide are seropositive for VZV by age 40 years.
  - In the US, it is estimated that 32% of Americans will experience a zoster outbreak during their lifetime.
  - 1 out of 5 patients with zoster will get post-herpetic neuralgia.

- Age is the most important risk factor for zoster.
  - The risk is higher for persons aged 50 years and above.
  - 50% of people who live up to age 85 will get zoster.
  - 50% of post-herpetic neuralgia (PHN) cases occur in adults aged 85 and above.
- Types of zoster vaccine
  - Live attenuated zoster vaccine: 0.65 ml given once in a lifetime
  - Adjuvanted recombinant zoster vaccine: 50 μg given as 2 doses 2 to 6 months apart
- Recommendations
  - The live attenuated vaccine may be given to immunocompetent adults aged 60 or older.
  - The adjuvanted recombinant vaccine may be given to all adults aged 50 or older, regardless of whether they report a prior episode of herpes zoster.
  - Contraindication: Pregnancy or severe immunodeficiency

IV. FACTS VS. FAKE NEWS

1. *Myth 1: Are vaccines safe? (I heard on the news that childhood vaccinations cause autism)*
   Yes, vaccines are safe. No scientific evidence that it causes autism.
2. *Myth 2: I was vaccinated before and got vaccinated again; will I overdose on the vaccine?*
   False. There is no such thing as overdose in vaccines.
   a. Can I get all the vaccines at the same time?
   Yes. All vaccines can be administered at the same visit as all other vaccines.
   b. What if I miss a dose?
      i. Increasing the interval between doses, does NOT diminish the effectiveness of the vaccine
      ii. Decreasing the interval between doses, may interfere with antibody response and protection
3. *Myth 3: Better hygiene and sanitation will make diseases disappear – vaccines are not necessary.*
   False. The diseases we can vaccinate against will return if we stop vaccination programs. While better hygiene, hand washing and clean water help protect people from infectious diseases, many infectious diseases can spread regardless of how clean we are. If people are not vaccinated, diseases that have become uncommon, such as polio and measles, will quickly reappear.
4. *Myth 4: Vaccines have several damaging and long-term side effects that are yet unknown. Vaccination can even be fatal.*
   False. Vaccines are very safe. Most vaccine reactions are usually minor and temporary, such as a sore arm or mild fever. Very serious health events are extremely rare and are carefully monitored and investigated.
5. *Myth 5: Giving an elderly more than one vaccine at a time can increase the risk of harmful side effects, which can overload an elderly's immune system.*
   False. Scientific evidence shows that giving several vaccines at the same time has no adverse effect in a person's immune system. Our elderly patients are exposed to several hundred foreign substances that trigger an immune response every day.

6. *Myth 6: Influenza is just a nuisance and the vaccine is not very effective.*

   False. Influenza is real. It is a serious disease that kills 300,000 – 500,000 people worldwide every year. Pregnant women, small children, elderly people with poor health, and anyone with a chronic condition are at higher risk for severe infection and death. Vaccinations offer immunity to the three most prevalent strains circulating in any given season. It is the best way to reduce your chances of severe flu and of spreading it to others.

7. *Myth 7: Vaccines contain mercury, which is dangerous.*

   False. Thiomersal is an organic, mercury-containing compound added to some vaccines as a preservative. It is the most widely-used preservative for vaccines that are provided in multi-dose vials. There is no evidence to suggest that the amount of thiomersal used in vaccines poses a health risk.

"When meditating over a disease, I never think of finding a remedy for it, but, instead, a means of prevention." – Louis Pasteur

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OPEN FORUM HIGHLIGHTS

Moderator: DONA S. PARALA, MD

Q: *Are those aged 84 years and older still amenable for any vaccination?*

A: Yes. They should still get their annual flu shot and get themselves updated with the pneumonia shots. It's good to keep record of the vaccines administered.

Q: *Do dosages differ between young adults and elderly people?*

A: The same dosage is used for young adults and elderly people.

Q: *Can the four recommended vaccines for adults be given on the same day?*

A: Theoretically, yes but you shouldn't do it because the Tdap vaccine tends to be a little painful. The recommendation of the Philippine Society of Microbiology and Infectious Diseases (PSMID) is to give doses simultaneously during the same visit then space them out after a month before giving the next one.

Q: *Can PCV13 be used by adults aged less than 50?*

A: It can be used by adults who are ill especially those with HIV, cancer, chronic kidney disease and those whose immune system is lower than usual.

Q: *What if the elderly patient forgot the brand of the pneumococcal vaccine received and has no available documents?*

A: The patient should be asked how much was paid for the vaccine. The PCV13 (lifetime dose) tends to be more expensive than the other one. In fact, if you are already a senior citizen, you can go and ask the city hall or the barangays because there is a partnership between DOH and LGU for the pneumococcal vaccine.

Q: *Can patients with cancer also receive vaccines?*

A: Yes. However, for patients with cancer and others with very low immune system, such as patients with HIV and very low CD4 counts, we usually try not to expose them to live attenuated vaccines such as measles, mumps, and rubella vaccines. For patients with HIV, we wait for their CD4 counts to go up. For patients with cancer, let us stick with the attenuated vaccines or the antigenic vaccines and not the live ones.

Q: *When can we give vaccines to cancer patients who will undergo chemotherapy? How many days, months or years prior to the start of chemotherapy?*

A: The best time is to give it before undergoing chemotherapy, when the cells are not yet very weak. I don't think there's an exact number of days or weeks before giving it but I think it's best to give it 6 weeks before the chemotherapy.

Q: *If a person had pulmonary tuberculosis, which vaccine is more appropriate to get, a pneumococcal vaccine or a flu vaccine?*

A: Both vaccines should be given. If less than 50 years old, then give flu vaccine only yearly.

Q: *If quadrivalent flu vaccines are not readily available, are trivalent flu vaccines okay for the elderly too?*

A: Yes. But if you have a choice, go for the quadrivalent vaccine.

Q: *What allergies do we need to assess before giving the pneumococcal and influenza vaccines for the elderly?*

A: If you had prior allergic response to influenza vaccine, that's a contraindication for future use of the vaccine. For the pneumococcal vaccine, we haven't actually seen cases but it's also possible to get allergic reactions from it.

Q: *What are the contraindications to giving pneumococcal and influenza vaccines?*

A: Normally, there are no contraindications but we usually avoid giving them to those who are very ill. It is preferred that one is healthy when giving vaccines.

Q: *Do you still recommend an elderly to have zoster vaccine even if there is no history of prior varicella?*

A: Yes. There are no guidelines saying that it can't be given to those who didn't have primary varicella infection. All adults aged 50 years and above should be given the zoster vaccine.

Q: *How safe are the zoster vaccines?*

A: In general, they are safe. No occurrence yet of zoster coming out after the vaccine.

Q: *After administration of zoster vaccine, will one experience a fever?*

A: Although it's always possible, the incidence is not high.

Q: *What is the difference between the Zostavax and the Shingrix? Do I need Shingrix if I got a dose of Zostavax already?*

A: Shingrix, the newer and preferred herpes zoster vaccine of the two, is a recombinant zoster vaccine that is more effective compared to Zostavax, which is a live zoster vaccine. Yes, the CDC recommends two doses of Shingrix at least 8 weeks after previously receiving Zostavax.

Q: *Kindly repeat the recommendation for Tdap.*

A: As a child, DPT should have been received at 2, 4, 6 months of age then a booster shot during schooling age, then every 10 years thereafter. As an adult, we should receive at least 1 Tdap. After that, one can just get Td (Tetanus toxoid) every 10 years.

Q: *Can HPV vaccine be given to elderly patients especially those who are at high risk? How effective would HPV vaccine be in this age group?*

A: HPV vaccine is indicated for 9 – 26 years old. The benefit is not guaranteed for elderly patients because it is likely that they have been already exposed to the virus.

Q: *What are the vaccination programs of the DOH for the elderly?*

A: Right now, DOH is offering PPSV23 vaccine every 5 years. The flu vaccine is usually offered in work places because they have to prevent absenteeism in their employees. It is not yet offered by the government.

Q: *What are the prices of the four vaccines?*

A: It depends where you get the vaccines. The most expensive among the four vaccines is the herpes zoster vaccine, which is around 7,000 pesos. The PCV13 costs around 4,000 to 5,000 pesos. The PPSV23 costs around 2,000 to 3,000 pesos. The influenza vaccine costs around 800 to 1,500 pesos.

REVIEW QUESTIONS

1. How often is PCV13 administered?
   a. Once a lifetime
   b. Every year
   c. Every 5 years
   d. Every 10 years

2. What is the most important risk factor for acquiring herpes zoster?
   a. Chronic disease
   b. Gender
   c. Age
   d. Cigarette smoking

3. Which of the following is listed as the top 6 cause of morbidity in the Philippines?
   a. Herpes zoster
   b. Varicella
   c. Influenza
   d. Pneumonia

4. Which of the following statements is TRUE?
   a. Decreasing the interval between doses will not interfere with antibody response and protection.
   b. Immunization still remains one of the most cost effective health interventions.
   c. Vaccines contain mercury, which is dangerous.
   d. DOH offers free influenza vaccines, pneumococcal vaccines and vaccines against herpes zoster for elderly.

5. What is the recommended follow up booster for Tdap?
   a. Once a lifetime
   b. Every year
   c. Every 5 years
   d. Every 10 years

ANSWERS: 1. a; 2. c; 3. c; 4. b; 5. a

23 SPIRITUALITY IN AGEING

Fr. Gregory Ramon D. Gaston, S.Th.D

Delivered as a webinar on Dec 13, 2019

https://bit.ly/ALMW_Ch23_Spirituality

KEY POINTS

- Ageing may weaken or strengthen spiritual life.
- There is overwhelming evidence of positive health outcomes linked to spirituality and religious participation.
- It is a good idea to incorporate spirituality into medical care and the medical curriculum while the future doctors are still students.
- Spiritual issues for elderly are mainly coping with ageing and accepting the reality of death.

LEARNING OBJECTIVES

- ➸ To discern the changes in spirituality as one ages
- ➸ To find the connection between spirituality and health care outcomes
- ➸ To discuss ways to integrate the spiritual practice of the healthcare professional and the patient into healthcare delivery

I. CHANGES IN SPIRITUALITY AS ONE AGES

A. Spirituality as a universal experience

- Practically all cultures throughout history have spiritual practices.
- Unexplained phenomena make us try to discover. *These phenomena open us up to the possibility of something spiritual.*
- The experience of human weakness makes us think that there is something or someone greater than us.
- The reality of death makes us think of a possible transcendence.

B. Ageing may weaken or strengthen spiritual life.

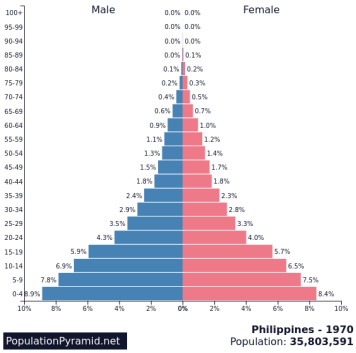
- It is a case-to-case basis.
- Each one has personal experience with spirituality.
- Our growth in the family, school and church taught us about spirituality.
- *Faith* and *Science* have the same goal → seek the truth (and both have the same source of truth: God)
  - If there seems to be conflict between *Faith* and *Science*, it means *we have to study more*.
  - Many great names in the sciences were clergymen (e.g., Mendel, Copernicus, Golgi).

C. Becoming closer to God and with each other

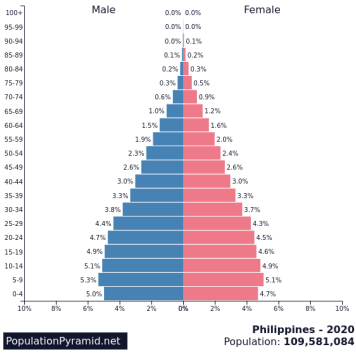
- Spirituality is very personal: me and my God.
- At the same time, it is also very communitarian. Our relationship with others will also bring us closer to God; vice versa.
- Persons intensely practicing the same faith get along well with each other.
- St. Paul: "For just as the body is one and has many members, and all the members of the body, though many, are one body, so it is with Christ." (1 Cor. 12:12 English Standard Version).

D. Relevance of spirituality as one ages

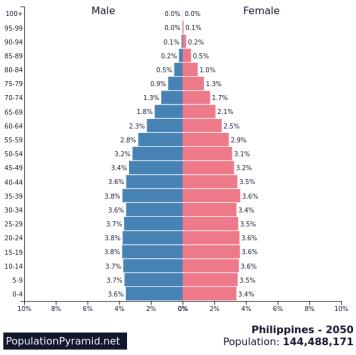
- Filipinos are deeply spiritual. When Filipinos are outside the country, they look for two things: fellow Filipinos and a church.
- Filipinos are ageing.
- There is a rapidly declining total fertility rate (TFR) in the Philippines; from 6 children per woman in the 1970s to 2.7 in 2017 (The World Bank, 2019).[1]
  - Experience in other countries show that a continuous decline below a fertility rate of 3 will lead to a below-replacement TFR of 2.1.
- The largest growing sector in Philippine population is not the children but the elderly.
  a. Comparing the population pyramids for 1970, 2020 and 2050, the number of children is decreasing in number relative to the elderly (Philippines Population Pyramids, 2019).[2]



(a) 1970



(b) 2020



(c) 2050

FIGURE 23–1. Philippine population pyramids

Reprinted with permission from 'Population Pyramids of the World from 1950 to 2100" from PopulationPyramid[2]
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II. CONNECTION BETWEEN SPIRITUALITY AND HEALTH CARE OUTCOMES

- There is increasing interest in academic research on the topic of spirituality and ageing.
- A systematic review in 2010 had a bibliography with 227 books and journals, which shows how interested people are in this topic.[3]
    - Researches find mixed connections. Some gave a positive correlation between spirituality and improved healthcare while others attributed improved health to other factors.
        - "Interest in spirituality and ageing has increased recently, owing to overwhelming evidence of positive health outcomes linked to spirituality and religious participation."[3]
    - Interest at the practical level
        - We are often faced with the question on whether or not to enter into spiritual topics.
        - "Improved understanding and respect for an individual's spiritual practice can help shape personalized medical care for older adults, and improve health outcomes."[3]
        - This does not mean that one should immediately discuss spiritual life. Rather, one can start by knowing the patient's spiritual preferences.
        - Even in government hospitals, we usually have a Catholic chaplaincy open to all religions.
    - Overcoming Difficulties in Integrating Spirituality

1. Uneasy feeling → remember that spirituality helps patients
2. Lack of time → consider it as an investment that will help patients
3. Inadequate training → one learns with experience

III. INTEGRATION OF SPIRITUALITY INTO HEALTHCARE DELIVERY

A. There is no harm in asking spiritual preferences.

Sample lead questions:

1. Would you like to talk with someone regarding spiritual matters?
2. Would you also like others to pray for you?
3. Would you like the chaplain to visit you?

B. Try prayer if it might help in medical care.

- This may be a case-to-case approach.
- Have an open dialogue if the patients are of different faiths. If of the same faith, one may share more freely.
- If they have a prayer card, crucifix, or some item of devotion, then we are sure they wish to pray.

C. Elderly Filipinos are usually religious.

- The patient would probably be interested in spiritual matters.
- Filipino patients are open to what doctors say, including spiritual matters.
- Most elderly patients would greatly appreciate prayers.
- In a special way, we also have the task of helping the elderly cope with ageing, and even accept the reality of death.

D. Integrate spirituality in the medical curriculum.

- Integrate spiritual topics, in general, with scientific literature.
- Allow students to live their spirituality outside classes.
- Medical practitioners are trained to save lives. They should also be trained to help patients and their families accept the end-of-life process.
- Assessing and integrating spirituality and considering patients' spiritual preferences should be standard operational procedure in health care.

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REACTORS

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1. ***REACTION FROM DR. A. GARCIA***

- Doctors need to remember that invoking the spiritual component among patients is very beneficial.
- In some healthcare studies, 75% of patients wish that their doctors would talk about spiritual issues. Patients who engage in religious/spiritual activities live 7 years longer. Preliminary studies in terms of spiritual participation with regards to healthcare show that those who have spirituality and receive religious care improve significantly.
- Filipino patients are deeply spiritual. In other cultures, it may be difficult to engage in this topic, but in the elderly Filipinos, it is not as challenging.
- "I shouldn't be afraid to label it as 'spirituality.' Prayer is what calms me down and decreases my inflammatory markers."
- Patients find relief when doctors understand that spirituality is important to them.
- It is a joy for patients to be prayed over if they are spiritual. When they are prayed over, they have more successful outcomes.
- A patient is not just a person with physical needs. A patient has all physical, spiritual, emotional domains. If we acknowledge their spiritual needs, it will be easier for them to follow and trust us.
- However, the challenging part for doctors is the limited time per consult.

2. ***REACTION FROM DR. D. GARCIA***

- We, doctors, are trained to measure what we can see, feel and hear.
- Spirituality is personal. Hence, doctors are hesitant to include it in medical treatment.
- It's hard to gauge if a person is spiritual or not. It's hard to ask them if they're spiritual. If they are spiritual, we then ask ourselves, "Am I equipped to talk about spirituality?" and "Do I have enough time?"
- Winning the trust of the caregiver of a child takes some time. It doesn't have to be a one-shot thing. It may take a number of consultations. It's an investment of time that will not only help the patient, but also the doctor. Compliance increases when trust is established.

OPEN FORUM HIGHLIGHTS

Moderator: CHRISTINE JOY S. ARQUIZA, MD

Q: *What do you think about euthanasia, especially if the elderly is already suffering so much?*

FR. GASTON:

- We have to distinguish between euthanasia (killing the patient) and allowing the dying patient to actually die.
- Doctors are trained to save lives, even when the patient is already dying. Death is an event, while dying is a process.
- 'Pulling the plug' or stopping certain procedures that do not really offer hope or extend the patient's life but simply extends the dying process – especially if these are burdensome to the patient and the patient's family, involving pain, harm and unnecessary costly expense – can be thought of as overly aggressive and may already be stopped. From a moral perspective, we are not required to apply procedures and medications that do not offer hope.
- We are accepting the reality of death. We should just take care of the ordinary health care needs, and not do any extraordinary measures. This is not killing the patient.
- Euthanasia is never acceptable, but withholding or even withdrawing certain medical procedures aforementioned is acceptable.

Q: *Can spirituality be used as an antidepressant for the depressed elderly?*

- **DR. A. GARCIA**: It can. There are studies that show that it can also decrease pain. There's a study on breast cancer patients whose pain decreased when they prayed. Consultation with a spiritual group or religious attendance can also help. There are also cases that show that medication is also important and can go hand in hand with spirituality.
- **DR. D GARCIA**: I had a recent patient with cerebral palsy and the treatment we were giving was not working. The delicate condition of the child prevented further procedures, and since the mother was a breast cancer survivor, it was difficult for the child to be brought to other specialists. The elderly aunt was frustrated and driven to helplessness and depression. At the end of their ropes and at the end of their wits, the only thing I could tell them was to pray with all their best effort, and things will turn out for the best. This brought a smile and tears to the aunt, and they went home feeling better with a much improved disposition.
- **DR. C. ARQUIZA**: Spirituality doesn't replace medication for pain but it can help. Miraculous supernatural healing can arise from answered prayers.

- **DR. A GARCIA**: Neurologic studies show that with prayer, parasympathetic system is heightened which is the relaxed state, while sympathetic system decreases. Spiritual healing has physical and physiologic basis.

Q: *How do we deal with elderly patients who are not Christians, that is, of other faith or atheists?*

- **FR. GASTON**: Listening would help a lot, but we should not impose our beliefs on the patients. Listening to the patient will teach us how to handle spiritual matters.
- **DR. D. GARCIA**: I agree with Fr. Gaston that we do not impose our own beliefs, but we remain to be spiritual and pray for the patient. Even if I cannot change the views of the patient, the way I regard and treat that patient improves, just because I prayed.

BLESSING BY FR. GASTON

I ask you for your prayers for us here in Rome, especially for Cardinal Tagle who has been assigned to the Vatican. Even if it may seem like a loss for Manila, it is a gain for the whole church.

I would like to ask for the intercession of the Blessed Virgin Mary to bless each one of us and our family this Advent season as we await the coming of Jesus.

We ask for the help of our brothers and sisters all over the world as we pray together and ask the Lord to strengthen all of us in this coming Christmas season.

All this we ask through Jesus Christ our Lord. Amen.

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APPENDIX

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ABBREVIATIONS

ACE	Angiotensin-converting enzyme
ACCORD	Action to Control Cardiovascular Risk in Diabetes
ACEI	Angiotensin-converting enzyme inhibitor
ACR	American College of Rheumatology
AD	Alzheimer's disease
ADDE	Aqueous-deficient dry eye
ADES	Asian Dry Eye Society
ADL	Activities of daily living
ADVANCE	Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evacuation Trial
AE	Adequate intake
AGS	The American Geriatric Society
AHA	Alpha-hydroxy acid
AI	Adequate intake
AIDS	Acquired immunodeficiency syndrome
AIN	Acute interstitial nephritis
AKI	Acute kidney injury
ALK	Anaphylactic lymphoma kinase
ALT	Alanine aminotransferase
AOM	Acute otitis media
ARB	Angiotensin II receptor blocker
ASH	American Society of Hypertension
AST	Aspartate aminotransferase
ATB	American Thoracic Society
α-TE	Alpha-tocopherol equivalent
BB	Beta-blocker
BEC	Blood eosinophil counts
BMD	Bone mineral density
BMI	Body mass index
BP	Blood pressure
BPPV	Benign paroxysmal positional vertigo
BSIT	Brief-smell identification test
Ca	Calcium
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CAP	Community-acquired pneumonia
CAT	COPD assessment test
CBC	Complete blood count
CBT	Cognitive behavioral therapy
CCB	Calcium channel blocker
CDC	Centers for Disease Control
CEA	Carotid endarterectomy
CFL	Compact fluorescent lights
CGA	Comprehensive geriatric assessment
CHD	Coronary heart disease
CHEP	Canadian Hypertension Education Program
CHF	Congestive heart failure
CKD	Chronic kidney disease
CO	Carbon monoxide
CO2	Carbon dioxide
COPD	Chronic obstructive pulmonary disease
COVID	Coronavirus disease
CPG	Clinical practice guidelines
CRP	C-reactive protein
CSF	Cerebrospinal fluid
CT	Computed tomography
CURB	Confusion, Urea, Respiratory rate, Blood pressure
CV	Cardiovascular
CVD	Cardiovascular disease
CXR	Chest x-ray
CYP	Cytochrome P

DALY	Disability-adjusted life years
dB	Decibel
DBP	Diastolic blood pressure
DED	Dry eye disease
DEQ	Dry Eye Questionnaire
DEWS	Dry Eye Workshop
DFE	Dietary folate equivalent
DHEA	Dehydroepiandrosterone
DKD	Diabetic kidney disease
DM	Diabetes mellitus
DMARD	Disease-modifying anti-rheumatic drug
DNA	Deoxyribonucleic acid
DOH	Department of Health
DOST-FNRI	Department of Science and Technology – Food and Nutrition Research
DPP-4	Dipeptidyl peptidase 4
DSM	Diagnostic and Statistical Manual of Mental Disorders
DXA	Dual-energy X-ray absorptiometry
ECG	Electrocardiogram
ECM	Extracellular matrix
ECOG	Eastern Cooperative Oncology Group
ECT	Electroconvulsive therapy
EDE	Evaporative dry eye
EF	Ejection fraction
EGF	Epidermal growth factor
eGFR	Estimated glomerular filtration rate
EML4-ALK	Echinoderm microtubule-associated protein-like 4
ECG	Electrocardiogram
ECM	Extracellular matrix
ECOG	Eastern Cooperative Oncology Group
ECT	Electroconvulsive therapy
EDE	Evaporative dry eye
EF	Ejection fraction
EGF	Epidermal growth factor
eGFR	Estimated glomerular filtration rate
EML4-ALK	Echinoderm microtubule-associated protein-like 4
EMR	Electromagnetic radiation
ENT	Ear, nose, and throat
EPO	Erythropoietin
EPV	Epstein-Barr virus
ERICA	Entorhinal cortex atrophy
ESA	Erythropoiesis-stimulating agents
ESC/ESH	European Society of Cardiology/ European Society of Hypertension
ESR	Erythrocyte sedimentation rate
ESRD	End-stage renal disease
EULAR	European League Against Rheumatism
FAQ	Functional Activities Questionnnaire
FBS	Fasting blood sugar
FBUT	Fluorescein breakup time
FCSRT	Free and Cued Selective Reminding Test
FDA	Food and Drug Administration
FDG-PET	Fluorodeoxyglucose-positron emission tomography
FeNO	Exhaled nitric oxide
FEV1	Forced expiratory volume
FIT	Fecal immunochemical test
FNAB	Fine needle aspiration biopsy
FOBT	Fecal occult blood test
FPG	Fasting plasma glucose
FVC	Forced vital capacity
GAD	Generalized anxiety disorder
GCA	Global cortical atrophy
GFR	Glomerular filtration rate
GINA	Global Initiative for Asthma

GLP-1	Glucagon-like peptide 1
GM	Genetically modified
GSM	Genito-urinary symptoms of menopause
HbA1c	Glycosylated hemoglobin
HDL	High-density lipoprotein
HF	Heart failure
HHC	Hearing Health Care
HIV	Human immunodeficiency virus
HPV	Human papillomavirus
HTN	Hypertension
HYVET	Hypertension in the Very Elderly Trial
IA	Institute of Aging
IADL	Instrumental activities of daily living
ICH	Intracerebral hemorrhage
ICS	Inhaled corticosteroids
ICU	Intensive care unit
IFG	Impaired fasting glucose
IgE	Immunoglobulin E
IGT	Impaired glucose tolerance
IHME	Institute for Health Metrics and Education
IMS	International Menopause Society
INR	International normalized ratio
IPL	Intense pulsed light
IPT	Interpersonal therapy
IR	Infrared
ISH	International Society of Hypertension
IU	International unit
JNC	Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure
K	Potassium
KGF	Keratinocyte growth factor
KUB	Kidney, ureter, and bladder
LABA	Long-acting beta-2-agonist
LAMA	Long-acting muscarinic antagonists
LED	Light-emitting diode
LTRA	Leukotriene receptor antagonist
LVEF	Left ventricular ejection fraction
MAPK	Mitogen-associated protein kinase
MCI	Mild cognitive impairment
MCV	Mean corpuscular volume
MDI	Metered-dose inhaler
MDS	Myelodysplastic syndrome
Mg	Magnesium
MGD	Meibomian gland dysfunction
MHT	Menopausal hormone therapy
MI	Myocardial infarction
MMP	Matrix metalloproteinases
MoCA-P	Montreal Cognitive Assessment – Philippines
MRC	Medical Research Council
MRI	Magnetic resonance imaging
MTA	Medial temporal atrophy
Nd	Neodymium-doped
NE	Niacin equivalent
NHSRC	Newborn Hearing Screening Reference Center
NIA-AA	National Institute on Aging-Alzheimer's Association
NIH	National Institutes of Health
NIHSS	National Institutes of Health Stroke Scale
NITBUT	Non-invasive tear breakup
NKTI	National Kidney Transplant Institute
nm	Nanometer

NNHeS	National Nutrition and Health Survey
NO2	Nitrogen dioxide
NPA	Neuropsychological assessment
NSAID	Non-steroidal anti-inflammatory drug
NSCLC	Non-small cell lung cancer
OA	Osteoarthritis
OGTT	Oral glucose tolerance test
OPD	Outpatient department
OSDI	Ocular Surface Disease Index
OSTA	Osteoporosis Self-Assessment Tool for Asians
PAB	Pure Asiatic brown
PABA	Para-aminobenzoic acid
PAF	Population attributable fraction
PAFP	Philippine Academy of Family Physicians
PAH	Polycyclic aromatic hydrocarbons
Pal-KTTKS	Palmitoyl pentapeptide
PANORS	Philippine Academy of Neurotology, Otology and Related Sciences
PAPA	Public Health and Air Population in Asia
PAW	Pure Asiatic white
PCCP	Philippine College of Chest Physicians
PCQ	Pure Caucasian white
PCR	Philippine College of Radiology
PCSK9	Proprotein convertase subtilisin/ kexin type 9
PCV	Pneumococcal vaccine
PDS	Philippine Dermatological Society
PET	Positron emission tomography
PG	Plasma glucose
PGH	Philippine General Hospital
PHN	Post-herpetic neuralgia
PHQ	Patient Health Questionnaire
PI3K	Phosphatidyl-inositol 3 kinase
PM	Particulate matter
PNRI	Philippine National Ear Institute
POF	Premature ovarian failure
POI	Premature ovarian insufficiency
PPSV	Pneumococcal polysaccharide vaccine
PRN	Pro re nata (as needed)
PSAUD	Philippine Society of Audiology
PSCO	Philippine Charity Sweepstakes Office
PSMID	Philippine Society for Microbiology and Infectious Diseases
PSO-HNS	Philippine Society of Otorhinolaryngology – Head and Neck Surgery
PSQI	Pittsburgh Sleep Quality Index
PT	Protime
PTH	Parathyroid hormone
PUFAs	Polyunsaturated fatty acids
RA	Rheumatoid arthritis
RAAS	Renin-angiotensin-aldosterone system
RAS	Renin-angiotensin system
RBC	Red blood cell
RBD	Refined, bleached, deodorized
RCT	Randomized controlled trial
RE	Retinol equivalent
RF	Radiofrequency
RNI	Recommended nutrient intake
ROS	Reactive oxygen species
RPG	Resting plasma glucose
rTMS	Repetitive transcranial magnetic stimulation
rtPa	Recombinant tissue plasminogen activator

SABA	Short-acting beta-2-agonist
SABR	Stereotactic ablative body radiation
SAH	Subarachnoid hemorrhage
SAMA	Short-acting muscarinic antagonists
SBP	Systolic blood pressure
SCCA	Squamous cell carcinoma
SCD	Subjective cognitive decline
SCINEXA	Score of Intrinsic and Extrinsic Skin Aging
SCLC	Small cell lung cancer
SD	Standard deviation
SERM	Selective estrogen receptor modulator
SHEP	Systolic Control of Hypertension in the Elderly Population
SIADH	Syndrome of inappropriate antidiuretic hormone secretion
SLE	Systemic lupus erythematosus
SLGT2	Sodium-glucose co-transporter-2
SNRI	Serotonin-norepinephrine reuptake inhibitors
SO2	Sulfur dioxide
SPF	Sun protection factor
SSRI	Selective serotonin reuptake inhibitors
STEAR	Selective tissue estrogenic activity regulator
STRAW	Stages of Reproductive Aging Workshop
SU	Sulfonylureas
SUA	Serum uric acid
SUI	Stress urinary incontinence
Td	Tetanus-diphtheria
TdaP	Tetanus, diphtheria, and acellular pertussis
TFOS	Tear Film and Ocular Surface Society
TFR	Total fertility rate
TG	Triglyceride
TGF-β	Transfer growth factor-beta
TH	T helper
TIA	Transient ischemic attack
TSH	Thyroid-stimulating hormone
TV	Television
U.S.	United States
UP	University of the Philippines
UTZ	Ultrasound
UV	Ultraviolet
VADT	Veterans Affairs Diabetes Trial
VATS	Video-assisted thoracoscopic surgery
VCO	Virgin coconut oil
VL	Visible light
VZV	Varicella-zoster virus
WBC	White blood cell
WHO	World Health Organization
YAG	Yttrium aluminum garnet

SYMBOLS

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AGEING AND LONGEVITY MEDICAL WEBINARS HANDBOOK is a quick reference companion to the year-long webinar series on common geriatric conditions streamed in 2019. Concise and jampacked with practical pearls on screening, diagnosis, and treatment, it can be used as a review for medical and allied medical students and healthcare professionals in primary care. The questions and answers from the interactive sessions are also provided, with review quiz items that can serve as a quick feedback on how well the reader comprehends the subject matter.

This ebook is a labor of love from the authors and editors, and is being shared for free to the medical community in celebration of 85 luminous years of the Mu Sigma Phi Medical Sorority.

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