INTRODUCTION

According to the definition provided by the World Health Organization (2017), dementia is “... an umbrella term for several diseases affecting memory, other cognitive abilities, and behavior that interfere significantly with a person’s ability to maintain their activities of daily living. Although age is the strongest known risk factor for dementia, it is not a normal part of aging.” It is a broad category of brain diseases that cause a long-term and often gradual decrease in the ability to think and remember that is great enough to affect a persons’ daily functioning. Other common symptoms include “emotional problems, language difficulties, and decreased motivation.” The definition provided by the U.S. National Institute of Neurological Disorders and Stroke (2018) is more detailed in that dementia is “... a group of symptoms caused by disorders that affect the brain. It is not a specific disease.” and “... memory loss is a common symptom of dementia. However, memory loss by itself does not mean having dementia. People with dementia have serious problems with two or more brain functions, such as memory and language. Although dementia is common in very elderly people, it is not part of normal aging.”

Many different diseases can cause dementia, including Alzheimer’s disease (AD), fronto-temporal dementia (FTD); Lewy body dementia, vascular dementia (VD), syphilitic dementia, mixed dementia (MD), senility dementia, or the combined effect of two or more types of dementia, and even stroke. About 10% of individuals present with MD, usually the combination of AD and another type of dementia such as FTD or VD.

However, not being a specific disease, the above potential contributors do not reach to the primary cause of the disease.
There lies our greatest shortcoming: unable to pinpoint the root cause of the disease, we are powerless in treating it. Sure, drugs are available to treat some of the symptoms of these contributing diseases, but not the diseases themselves. Likewise, drugs available for dementia can also only alleviate its symptoms; they cannot cure it or repair brain damage. They may improve symptoms or at best slow down the disease. And, indeed, there is no known cure for dementia. This is a sad observation on the state of the situation. It stems from our incomplete understanding of the deep biology of the contributing diseases and associated epigenetic/ecogenetic influences.[1-12]

EPIDEMIOLOGY OF THE DISEASE

With elongating lifespan in the developed world, dementia has emerged as an increasing public health concern. It was uncommon in pre-industrial times and relatively rare before the 20th century. As more people are living longer, and as risk factors are decreasing or better managed, dementia is becoming more common in the population as a whole. Alzheimer’s disease (AD) and other dementias are fifth among the top 10 global causes of mortality [Figure 1].

Worldwide, dementia affected ~50 million people (2017), 46 million (2015), and 35.6 million (2010), with projections of 82 million (2030) and 152 million (2050), much of the increase located in low- and middle-income countries (nearly 60% of people affected). Table 1 shows the increasing percentage of dementia with age. In 2013, dementia resulted in about 1.7 million deaths up from 0.8 million in 1990.

Causes of dementia depend on the age when symptoms began. Thus, Table 2 illustrates the variations of dementia with age of occurrence.

SIGNS AND SYMPTOMS

Most dementia types are slow and progressive. In their early stages, the onset is gradual to the point of not being clearly noticeable. Symptoms vary across types and stages of the disease and vary with the individual. Signs and symptoms evolve along three phases (early, middle, and late) that have been loosely categorized in Table 3 as psychological, memory, cognition, behavioral, and motor. Behavioral and psychological symptoms almost always occur in all types of dementia.[13]

RISK FACTORS

While most dementias have several common risk factors, each dementia type has its own risk factors, but most forms have several risk factors. These are summarized in Table 4.

STAGING OF THE DISEASE

Dementia has four progressive and subsequent stages. Scores in the mini-mental state examination are provided in Table 5.

MENTAL DISORDER CLASSIFICATIONS

The classification of mental disorders (also known as psychiatric nosology or taxonomy) is a key aspect of psychiatry and other mental health professions and an important issue for people who may be diagnosed. The following classifications are presented in Table 6.

Figure 1: Top 10 global causes of deaths, 2016. Source: Global Health Estimates 2016. Cause groups: Red (communicable maternal disease, neonatal, and nutritional conditions); blue (non-communicable diseases); green (injuries)
APPROACHES TO DIAGNOSIS

A diagnosis requires a change from a person’s usual mental functioning and a greater decline than one would expect due to aging. Being very similar in all types of dementia, symptoms cannot by themselves help to reach the correct diagnosis of dementia type(s). Diagnosis usually proceeds along the following lines (Table 7). Screening the general population for dementia is not recommended.\(^{[14-31]}\)

Table 8 provides the sensitivity and specificity of common tests for dementia.

REVERSIBLE DISEASES

Hypothyroidism, Vitamin B12 deficiency, Lyme disease, and neurosyphilis are reversible diseases. All people with memory

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**Table 1: Percentage of dementia cases as a function of age**

<table>
<thead>
<tr>
<th>Age*</th>
<th>% for different populations</th>
</tr>
</thead>
<tbody>
<tr>
<td>65–74</td>
<td>75–84</td>
</tr>
<tr>
<td>Low-to-middle income (%)</td>
<td>3</td>
</tr>
<tr>
<td>Developed countries (%)</td>
<td>5</td>
</tr>
</tbody>
</table>

*Slightly higher in women than men at ages 65 and older

**Table 2: Dementia variations with age of occurrence**

<table>
<thead>
<tr>
<th>Age</th>
<th>Contributor (s)</th>
<th>Treatment effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40</td>
<td>Rare without other neurological disease</td>
<td>Treatment of underlying psychiatric illness, alcohol or drug abuse or metabolic disturbance</td>
</tr>
<tr>
<td></td>
<td>Genetic disorders can cause true NDD: AD, SCA 17 (dominant inheritance), X-linked ADL, GD type 3, MCLD, NPD, PKAN, WD</td>
<td>WD is particularly important since cognition can improve with treatment</td>
</tr>
<tr>
<td>&lt;65</td>
<td>AD is most frequent Inherited forms account for higher proportion FTLD and HD account for the rest VD in cases of repeated brain traumas CTE</td>
<td>Fully reversible with treatment</td>
</tr>
<tr>
<td>&gt; 65</td>
<td>Alzheimer’s dementia (AD), VD, or both and DLB occurring alongside either AD or VD or both Hypothyroidism NPH</td>
<td>Treatment may prevent progression and improve other symptoms</td>
</tr>
</tbody>
</table>


**Table 3: Signs and symptoms of dementia**

<table>
<thead>
<tr>
<th>Phase</th>
<th>Psychological</th>
<th>Memory</th>
<th>Cognition</th>
<th>Behavioral</th>
<th>Motor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early (gradual onset)</td>
<td>Lost in time and space</td>
<td>Forgetfulness</td>
<td>Speech and language difficulties</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle (progressing disease)</td>
<td>Communication difficulties Attention deficit Problem solving</td>
<td>Lost at home Forgetfulness Memory distortions Confusion</td>
<td>Increased speech and language difficulties (anomia)</td>
<td>Wandering Restlessness Repeated questioning Agitation Anxiety Apathy</td>
<td>Help personal care Balance problems Tremors Trouble eating and swallowing</td>
</tr>
<tr>
<td>Late (advanced disease)</td>
<td>Unaware of time and space Delusions Hallucinations Depression Disinhibition Impulsivity Psychosis</td>
<td>Serious memory disturbances Difficulty recognizing relatives and friends</td>
<td></td>
<td>Agitation Aggression Crying Anger</td>
<td>Total dependence and inactivity Difficulty walking</td>
</tr>
</tbody>
</table>
difficulty should be checked for hypothyroidism and B12 deficiency. For Lyme and neurosyphilis, testing should be done if there are risk factors for those diseases. As risk factors are often difficult to determine, testing for neurosyphilis and Lyme disease, as well as other unmentioned factors, may be undertaken as a matter of course in cases where dementia is suspected.

### CONTRIBUTING DISEASES

The main contributors to dementia are summarized in Table 9 with other (unlisted) minor contributors, including senilite dementia (SD) or senility, normal pressure hydrocephalus, and syphilis.

### TYPES OF COGNITIVE IMPAIRMENT

The following instances of cognitive impairment must be differentiated [Table 10].

### ON NEURODEGENERATIVE DEMENTIA

Dementia that begins gradually and worsens progressively over several years is usually caused by a neurodegenerative disease - that is, by conditions that affect only or primarily the neurons of the brain and cause gradual but irreversible loss of function of these cells. Less commonly, a non-degenerative condition may have secondary effects on brain cells, which may or may not be reversible if the condition is treated.
DISEASE MANAGEMENT

Except for the treatable types of dementia listed above and in the absence of a thorough understanding of its deep biology, there is currently no cure for the disease. Medical interventions remain, therefore, palliative with the aim to alleviate pain and suffering. They include:  
- Cognitive and behavioral interventions; 
- Education and support for the patient and the patient’s family and caregiver(s); and 
- Activity and exercise program.

Other management approaches are as follows  
**Psychological and reminiscence therapies**

While benefits are small, these therapies can improve the quality of life, communication, and possibly mood in some circumstances. Areas covered include:  
- Quality of life, cognition, communication, mood, and cognitive reframing for caretakers; 
- Validation therapy; and 
- Mental exercises: Such as cognitive stimulation programs (for people with mild-to-moderate cognitive impairment).
### Table 9: Contributors to dementia

<table>
<thead>
<tr>
<th>Disease</th>
<th>Contribution (%)</th>
<th>Characteristics and symptoms</th>
</tr>
</thead>
</table>
| AD      | 50–70           | Cause: Death of nerve cells (neurons) in important parts of the brain  
Symptoms: Repetition, getting lost, difficulties keeping track of bills, forgetting to  
take medication, short-term memory loss, word-finding difficulties, trouble with  
visual-spatial areas, reasoning, judgment, insight  
Signs: Hippocampus, shrinkage of frontotemporal parts |
| VD      | 25              | Cause: Stroke (s); blood vessels diseases, hypertension, CVDs (particularly  
previous heart attack, angina), diabetes  
Symptoms: Minor strokes  
Signs: Lost or damaged ischemic brain areas |
| LBD     | 15              | Cause: Abnormal protein structures within brain cells. Treatable with  
medication  
Symptoms: PD (trembling, stiffness, and slowness), visual hallucinations,  
difficulty with visual-spatial function, problems with attention, organization,  
executive functions, “Parkinsonism” (tremor, rigid muscles, stiffness, slowness,  
and emotionless face).  
Signs: Vivid, long-lasting hallucinations; “act out of dreams,”  
occipital hypoperfusion hypometabolism |
| PDD     |                 | Cause: During the course of PD  
Symptoms: Very similar to DLB |
| FTD     |                 | Symptoms: Personality changes, abnormal social behavior, language  
difficulties (memory problems are not a main feature)  
Signs: Nerve cell loss in frontal and temporal lobes. Arises at earlier age than  
AD. 3 types: Behavioral, temporal (or semantic), and progressive non-fluent  
aphasia |
| MD      |                 | Cause: More than one (often AD and vascular)  
Signs: Over 80 years of age |
| PSP     |                 | Symptoms: Eye movement problems, falling backward, balance problems, slow  
movements, rigid muscles, irritability, apathy, social withdrawal, depression,  
progressive difficulty eating and swallowling, eventually talking. Misdiagnosed as PD  
Signs: Atrophied midbrain |
| CBD     |                 | Symptoms: Many different types of neurological problems, get worse over time  
Signs: Affected frontotemporal lobes; difficulty using only one limb (“alien limb”),  
asymmetric symptoms (myoclonus or jerky movements of one or more limbs),  
strange repetitive movements (dystonia), speech difficulty (inability to move  
mouth muscles in coordinated way), numbness and tingling of limbs, neglect one  
side of vision or senses |
| CJD     |                 | Cause: Prions  
Symptoms: Slow (at times rapid) progression |
| Encephalopathy |         | Causes: Brain infection (viral or sclerosing encephalitis) and WD  
Brain inflammation: LE; HE; CV; tumors (lymphoma, glioma); drug toxicity (e.g.,  
anticonvulsants) Metabolic causes: Liver or kidney failure, CSH |
| Immunologically mediated | | Causes: Chronic inflammatory conditions, BD, MS, sarcoidosis; SS, SLE, CD,  
and non-celiac gluten sensitivity  
Signs: Can rapidly progress. Good response to early  
treatment (immunomodulators and steroids) |
| Inherited conditions | | Causes: AD, CX, DPA, epilepsy, FFI, FXTAS, type 1 GA, KD, MSUD, type C  
NPD, NCL, neuroacanthocytosis, organic acidemias, PMD, type B SFS, type 2  
SCA, urea cycle disorders |

(Contd...)
Care in adult centers and special units in nursing homes and in the home
These institutions provide specialized care (supervision, recreation, meals, limited health care, music therapy,..., as well as providing respite for caregivers). Home care can provide one-on-one support and allow for the more individualized attention that is needed as the disorder progresses.\textsuperscript{[24,10,62]}

Psychiatric nursing
Can make a distinctive contribution to patients’ mental health.

Table 9: Continued

<table>
<thead>
<tr>
<th>Cognitive Impairment Type</th>
<th>Subtypes</th>
<th>Characteristics</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (MCI) MMSE=25–30</td>
<td>Amnestic</td>
<td>Memory loss develop Alzheimer’s disease</td>
<td>Difficult. Requires Petersen criteria: Memory or other cognitive Problem not severe enough Person must not have dementia</td>
</tr>
<tr>
<td>70% of people with MCI develop some form of dementia</td>
<td>Non-amnestic</td>
<td>Memory loss not primary Develop other dementias</td>
<td></td>
</tr>
<tr>
<td>Fixed (FCI) long-term effects</td>
<td>Various types of brain injury</td>
<td>Irreversible cognitive impairment</td>
<td>Diffuse axonal injury Localized damage due to neurosurgery Long-term effects on cognition</td>
</tr>
<tr>
<td>Temporary reduction in brain's blood or oxygen supply</td>
<td>Hypoxic/ischemic injury Strokes (ischemic stroke, intracerebral, subarachnoid, subdural or extradural hemorrhage) Infections (meningitis, encephalitis) Epileptic seizures Acute hydrocephalus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excessive alcohol use</td>
<td>AD WE KP</td>
<td>AD: Alcohol dementia, WE: Wernicke encephalopathy, KP: Korsakoff psychosis, FCI: Fixed cognitive impairment, MCI: Mild cognitive impairment, MMSE: Mini-mental state examination</td>
<td></td>
</tr>
</tbody>
</table>

PSYCHOPHARMACOTHERAPY FOR AD AND OTHER DEMENTIAS

Changes in medication management
The Medications Appropriateness Tool for CoMorbid Health - Dementia criteria can help to identify the ways that a diagnosis of dementia changes medication management for other health conditions.\textsuperscript{[63]}

Alternative therapies
- Aromatherapy and massage: Unclear benefits.
- Cannabinoids: Can relieve behavioral and psychological symptoms of dementia.
Table 10: Types of cognitive impairment

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Drugs</th>
<th>Precautions</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory problems Monitored 8-week course</td>
<td>Provide no cure: Cholinesterase inhibitors*: Donepezil (Aricept®), Rivastigmine (Exelon®), Galantamine (Razadyne®) Memantine (Namenda®): Used in combination with anti-cholinesterase NMDA receptor blockers Folate or Vitamin B12 Statins Blood pressure medications</td>
<td>Symptoms may worsen if the treatment is stopped or after treatment Periodic evaluation of the treatment required May cause increase in cardiovascular-related events</td>
<td>Nausea, vomiting, gastrointestinal upset, diarrhea, weight loss, fainting spells, difficulty sleeping with very vivid dreams (when taken at bedtime), muscle cramping, slow heart rate, and fainting in people with heart problem Dizziness, aggression, and hallucinations No improved outcomes No benefit No clear link with dementia</td>
</tr>
<tr>
<td>Behavioral symptoms</td>
<td>Environment change, physical exercise, avoiding triggers that cause sadness, socializing with others, engaging in pleasant activities Antipsychotics</td>
<td></td>
<td>Agitation, anxiety, irritability Not usually recommended due to little benefits, side effects, increased risk of death</td>
</tr>
<tr>
<td>Depression</td>
<td>Behavioral therapy and/or medications SSRI: Fluoxetine (Prozac®), Sertraline** (Zoloft®), Paroxetine (Paxil®), Citalopram** (Celexa®), Escitalopram (Lexapro®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety and aggression</td>
<td>Medications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep problems</td>
<td>Medications or/and behavior changes benzodiazepines (diazepam) and non-benzodiazepine hypnotics: To be avoided Melatonin, Ramelteon, Trazodone</td>
<td></td>
<td>Worsened confusion, increased risk of falls, increased cognitive impairment Little evidence to improve sleep in dementia patients</td>
</tr>
<tr>
<td>Pain</td>
<td>Medications</td>
<td></td>
<td>Decreased ambulation, depressed mood, sleep disturbances, impaired appetite, falls, and exacerbation of cognitive impairment, profound functional, psychosocial, and quality of life implications</td>
</tr>
</tbody>
</table>

(Contd...)
**PREVENTION**

No medications or supplements have shown good preventative evidence, including blood pressure medications. Efforts to prevent dementia include:

- Early education;
- Decrease in risk factors: High blood pressure, smoking, diabetes and obesity, hearing loss, depression, and social isolation;
- Lifestyle changes: Physical exercise and social activities;
- Computerized cognitive training: May improve memory.[64]

**CONCLUSIONS**

While much is known about dementia and the underlying and contributing factors and much has been published on the subject, we still do not understand the deep biology of the disease. Lacking this understanding, we have so far failed to find a cure and continue to be limited to symptomatic treatments that have limited or no effect. In the case of Alzheimer’s dementia, the main contributor, there is a ray of hope in the recent suggestion[21-40] that the root cause of Alzheimer may be an autoimmune disease gone rogue and that deposits (or plaques) of beta-amyloid (a protein) and the NFTs (disorganized masses of protein fibers within the brain cells) may only be the signs of a brain homeostasis that had broken down under an avalanche of brain insults. Similar innovative ideas and suggestions should be pursued for the other contributors to dementia.

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**Table 10: Continued**

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Drugs</th>
<th>Precautions</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eating difficulties</td>
<td>Assisted feeding,</td>
<td>Worsening pressure ulcers, fluid overload, diarrhea, abdominal pain, local</td>
<td>fluid overload, diarrhea, abdominal pain, local complications, risk of aspiration</td>
</tr>
<tr>
<td></td>
<td>gastrostomy, feeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>tube</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Precautions: Donepezil should be used with caution in people with: (a) Cardiac problems: heart disease, cardiac conduction disturbances, chronic obstructive pulmonary disease (COPD), severe cardiac arrhythmias; (b) asthma; (c) sick sinus syndrome (SSD); (d) peptic ulcer disease (PUD) or taking non-steroidal anti-inflammatory drugs (NSAID); and (e) in case of predisposition to seizures. **Sertraline and Citalopram do not reduce symptoms of agitation compared to placebo and do not affect outcomes, NMDA: N-Methyl D-Aspartate receptor blockers, SSRI: Selective serotonin reuptake inhibitors

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*Note on spirochetes*

These are neurotrophic in nature, meaning that they act to destroy nerve tissue and create inflammation. Inflammatory pathogens are an indicator of AD. Bacteria related to gum disease have been found in the brains of AD individuals. They invade nerve tissue in the brain, increasing the permeability of the blood–brain barrier and promoting the onset of AD among the elderly population.[41]

*Note on herpes simplex virus (HSV)*

It was found in over 70% of the 50 and older population, and it persists in the peripheral nervous system and can be triggered by stress, illness, or fatigue. High proportions of viral-associated proteins in amyloid-containing plaques or neurofibrillary tangles (NFTs) highly confirm the involvement of HSV-1 in AD pathology. HSV-1 produces the main components of NFTs, the primary marker of AD.

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**Palliative care**

Recommended before the late stages of dementia. Given the progressive and terminal nature of the disease, palliative care can be helpful to patients and their caregivers by helping both people with the disorder and their caregivers understand what to expect, deal with loss of physical and mental abilities, plan out a patient’s wishes and goals including surrogate decision-making, and discuss wishes for or against cardiopulmonary resuscitation and life support.
Degeneration; CCMD: Chinese Classification of Mental Disorders; CD: Celiac Disease; CDT: Clock-Drawing Test; COPD: Chronic Obstructive Pulmonary Disease; CPR: Cardio Pulmonary Resuscitation; CRP: C-Reactive Protein; CSH: Chronic Subdural Hematoma; CT: Computed Tomography; CTE: Chronic Traumatic Encephalopathy; CV: Cerebral Vasculitis; CX: Cerebrotendinous Xanthomatosis; DPA: Dentatorubal Pallidolysian Atrophy; DSM: Diagnostic and Statistical Manual of Mental Disorders; DTBZ: (carbon-11) dihydrotetrabenazine (a radiotracer); ESD: Early Stage Dementia; FA: Folic Acid; FCI: Fixed Cognitive Impairment; FDA: (U.S.) Food and Drug Administration; FFI: Fatal Familial Insomnia; FTD: Fronto-Temporal Dementia; FTLD: Fronto Temporal Lobar Degeneration; TFTAS: Fragile X-Associated Tremor/Ataxia Syndrome; GD: Gaucher Disease; GDS: Geriatric Depression Scale; GPAC: General Practitioner Assessment of Cognition; HD: Huntington Disease; HE: Hashimoto encephalopathy; HXV: Herpes Simplex Virus; IQCODE: Informant Questionnaire on Cognitive Decline in the Elderly; KD: Krabbe Disease; KP: Korskoff psychosis; LBD: Lewy body dementia; LE: Limbic encephalitis; ICD: International Classification of Diseases; LDS: Late Stage Dementia; MATCH-D: Medications Appropriateness Tool for Co-morbid Health – Dementia; MCI: Mild Cognitive Impairment; MCLD: Meta Chromatic Leuko Dystrophy; MD: Mixed dementia; MS: Multiple Sclerosis; 3MS: Modified Mini-Mental State Examination; MMSE: Mini-Mental State Examination; MOCA: Montreal Cognitive Assessment Test; MRI: Magnetic Resonance Imaging; MSD: Middle Stage Dementia; MSUD: Maple Syrup Urine Disease; NCL: Neuronal Cereoid Lipofuscinosis; NICE: (U.K.) National Institute for Clinical Excellence; NIDDS: National Institute of Neurological Disorders and Stroke; NDD: Neuro Degenerative Disease; NFD: Neuro Fibrillary Tangles; NMEDA: N-Methyl D-Aspartate receptor blockers; NPD: Niemann-Pick Disease; NPI: Normal Pressure Hydrocephalus; NPI: Neuropsychiatric Inventory; Antipsychotics: NSAIAD: Non-Steroidal Anti-Inflammatory Drugs; PD: Precocious Dementia; PD: Parkinson Disease; PDD: Parkinson Disease Dementia; PDM: Psychodynamic Diagnostic Manual; PET: Positron Emission Tomography; PIB-PET: (carbon-11) Pittsburgh Compound B (a radiotracer); PFS: Progressive Non-Fluent Aphasia; PD: Peptic Ulcer Disease; PSE: Peripheral Nervous System; PSEE: Progressive Non-Fluent Aphasia; PNS: Peripheral Nervous System; PSNP: Progressive Supra Nuclear Palsy; PUD: Peptic Ulcer Disease; SASE: Sub-Acute Sclerosing Encephalitis; SAT: Self-Administered Test; SCA: Spino cerebellar Ataxia; SDF: San Filippo Syndrome; SFS: San Filippo Syndrome; SLE: Systemic Lupus Erythematosus; SPECT: Single Photon Emission Tomography; SS: Sjogren syndrome; SSD: Sick Sinus Syndrome; SSRI: Selective Serotonin Reuptake Inhibitors; TMT: Trail-Making Test; TSD: Tay-Sachs Disease; TSH: Thyroid Stimulating Hormone; VD: Vascular dementia; WE: Viral encephalitis (VE); WD: Whipple Disease; WD: Wilson Disease; WE: Wernicke Encephalopathy; World Health Organization (WHO).

**Diseases/Disorders Cited:** Acute Confusional State (or Delirium); Alzheimer Disease; Alexandre Disease: Alcohol Dementia; Adenoleukodystrophy; Behcet Disease; Cortico Basal Degeneration; Celiac Disease; Chronic Obstructive Pulmonary Disease; Chronic Subdural Hematoma; Chronic Traumatic Encephalopathy; Cerebral Vasculitis; Cerebrotendinous Xanthomatosis; Dentatorubal Pallidolysian Atrophy; Early Stage Dementia; Fixed Cognitive Impairment; Fatal Familial Insomnia; Fronto-Temporal Dementia; Fragile X-Associated Tremor/Ataxia Syndrome; Gaucher Disease; Geriatric Depression Scale; General Practitioner Assessment of Cognition; Huntingron Disease; Hashimoto Encephalopathy; Herpes Simplex; Krabbe Disease; Korskoff psychosis; Lewy body dementia; Limbic encephalitis; Late Stage Dementia; Mild Cognitive Impairment; Mixed dementia; Multiple Sclerosis; Neuronal Ceroid Lipofuscinosis; Neuro Degenerative Disease; Niemann-Pick Disease; Precocious Dementia; Parkinson Disease; Parkinson Disease Dementia; Pantothenate Kinase-Associated Neurodegeneration; Pelizaeus-Merzbache Disease; Progressive Supra Nuclear Palsy; Progressive Non-Fluent Aphasia; Progressive Supra Nuclear Palsy; Peptic Ulcer Disease; Sub-Acute Sclerosing Encephalitis; Spino cerebellar Ataxia; Syphilitic Dementia; San Filippo Syndrome; Systemic Lupus Erythematosus; Sjogren Syndrome; Sinus Syndrome; Tay-Sachs Disease; Vascular dementia; Viral encephalitis; Whipple Disease; Wilson Disease; Wernicke Encephalopathy.

**Drugs Listed:** Anticholinergics; Antipsychotics; Benzodiazepines (central nervous system depressants); Blood pressure medications; Cholinesterase inhibitors: Donepezil (Aricept®), Rivastigmine (Exelon®), Galantamine (Razadyne®); Folates; Hypnotics (benzodiazepines: diazepam; non-benzodiazepine: Memantine (Namenda®); N-Methyl D-Aspartate receptor blockers; Memantine; Nicotinamide; Selective Serotonin Reuptake Inhibitors: Fluoxetine (Prozac®), Sertraline (Zoloft®), Paroxetine (Paxil®), Citalopram (Celexa®), Escitalopram (Lexapro®); Sleep aids (melatonin; ramelteon); Statins; Vitamin B12.

**REFERENCES**

3. American Speech Language Hearing Association. Dementia Signs and Symptoms. Rockville, MD, USA: American Speech...
Fymat, et al. Dementia and cognitive disorders

APPENDIX 1

The top 10 causes of death
(World Health Organization, 24 May 2018)

Of the 56.9 million deaths worldwide in 2016, more than half (54%) were due to the top 10 causes. Ischemic heart disease and stroke are the world’s biggest killers, accounting for a combined 15.2 million deaths in 2016. These diseases have remained the leading causes of death globally in the past 15 years.

Chronic obstructive pulmonary disease claimed 3.0 million lives in 2016, while lung cancer (along with trachea and bronchus cancers) caused 1.7 million deaths. Diabetes killed 1.6 million people in 2016, up from <1 million in 2000. Deaths due to dementias more than doubled between 2000 and 2016 make it the fifth leading cause of global deaths in 2016 compared to fourteenth in 2000.

Lower respiratory infections remained the most deadly communicable disease, causing 3.0 million deaths worldwide in 2016. The death rate from diarrheal diseases decreased by almost 1 million between 2000 and 2016 but still caused 1.4 million deaths in 2016. Similarly, the number of deaths by tuberculosis decreased during the same period but is still among the top 10 causes with a death toll of 1.3 million. HIV/AIDS is no longer among the world’s top 10 causes of death, having killed 1.0 million people in 2016 compared with 1.5 million in 2000.

Road injuries killed 1.4 million people in 2016, about three-quarters (74%) of whom were men and boys.

APPENDIX 2

The World Health Organization Dementia Fact Sheet # 362
(April 2012)
Fymat, et al. Dementia and cognitive disorders

Infographic on dementia
(This infographic includes information about the symptoms of dementia, cause, number of people affected, and cost)

Facts

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Decreased ability to think and remember, emotional problems, problems with language, decreased motivation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usual onset</td>
<td>Gradual</td>
</tr>
<tr>
<td>Duration</td>
<td>Long term</td>
</tr>
<tr>
<td>Causes</td>
<td>Alzheimer's disease, vascular dementia, Lewy body dementia, frontotemporal dementia</td>
</tr>
<tr>
<td>Diagnostic method</td>
<td>Cognitive testing (mini-mental state examination)</td>
</tr>
<tr>
<td>Differential diagnosis</td>
<td>Delirium</td>
</tr>
<tr>
<td>Prevention</td>
<td>Early education, prevent high blood pressure, prevent obesity, no smoking, exercise, social engagement</td>
</tr>
<tr>
<td>Treatment</td>
<td>Supportive care</td>
</tr>
<tr>
<td>Medication</td>
<td>Cholinesterase inhibitors (small benefit)</td>
</tr>
<tr>
<td>Frequency</td>
<td>46 million (2015)</td>
</tr>
<tr>
<td>Deaths</td>
<td>1.9 million (2015)</td>
</tr>
</tbody>
</table>

Signs and symptoms
Dementia affects each person in a different way, depending on the impact of the disease and the person’s personality before becoming ill. The signs and symptoms linked to dementia can be understood in three stages.

Early stage: The early stage of dementia is often overlooked because the onset is gradual. Common symptoms include:
- Forgettingfulness
- Losing track of the time
- Becoming lost in familiar places.

Middle stage: As dementia progresses to the middle stage, the signs and symptoms become clearer and more restricting. These include:
- Becoming forgetful of recent events and people’s names
- Becoming lost at home
- Having increasing difficulty with communication
- Needing help with personal care
- Experiencing behavior changes, including wandering and repeated questioning.

Late stage: The late stage of dementia is one of near total dependence and inactivity. Memory disturbances are serious and the physical signs and symptoms become more obvious. Symptoms include:
- Becoming unaware of the time and place
- Having difficulty recognizing relatives and friends
- Having an increasing need for assisted self-care
- Having difficulty walking
- Experiencing behavior changes that may escalate and include aggression.

Common forms of dementia
There are many different forms of dementia. Alzheimer’s disease is the most common form of dementia and may contribute to 60–70% of cases. Other major forms include vascular dementia, dementia with Lewy bodies (abnormal aggregates of protein that develop inside nerve cells), and a group of diseases that contribute to frontotemporal dementia (degeneration of the frontal lobe of the brain). The boundaries between different forms of dementia are indistinct and mixed forms often coexist.

Rates of dementia
Worldwide, around 50 million people have dementia, with nearly 60% living in low- and middle-income countries. Every year, there are nearly 10 million new cases.

The estimated proportion of the general population aged 60 and over with dementia at a given time is between 5 and 8 per 100 people.

The total number of people with dementia is projected to reach 82 million in 2030 and 152 in 2050. Much of this increase is attributable to the rising numbers of people with dementia living in low- and middle-income countries.

Treatment and care
There is no treatment currently available to cure dementia or to alter its progressive course. Numerous new treatments are being investigated in various stages of clinical trials.
However, much can be offered to support and improve the lives of people with dementia and their carers and families. The principal goals for dementia care are as follows:

• Early diagnosis to promote early and optimal management
• Optimizing physical health, cognition, activity, and well-being
• Identifying and treating accompanying physical illness
• Detecting and treating challenging behavioral and psychological symptoms
• Providing information and long-term support to carers.

Risk factors and prevention
Although age is the strongest known risk factor for dementia, it is not an inevitable consequence of aging. Further, dementia does not exclusively affect older people - young-onset dementia (defined as the onset of symptoms before the age of 65 years) accounts for up to 9% of cases. Some research has shown a relationship between the development of cognitive impairment and lifestyle-related risk factors that are shared with other non-communicable diseases. These risk factors include physical inactivity, obesity, unhealthy diets, tobacco use and harmful use of alcohol, diabetes, and midlife hypertension. Additional potentially modifiable risk factors include depression, low educational attainment, social isolation, and cognitive inactivity.

Social and economic impacts
Dementia has significant social and economic implications in terms of direct medical and social care costs and the costs of informal care. In 2015, the total global societal cost of dementia was estimated to be US$ 818 billion, equivalent to 1.1% of global gross domestic product (GDP). The total cost as a proportion of GDP varied from 0.2% in low- and middle-income countries to 1.4% in high-income countries.

Impact on families and carers
Dementia is overwhelming for the families of affected people and for their carers. Physical, emotional, and economic pressures can cause great stress to families and carers, and the support is required from the health, social, financial, and legal systems.

Human rights
People with dementia are frequently denied the basic rights and freedoms available to others. In many countries, physical and chemical restraints are used extensively in care homes for older people and, in acute-care settings, even when regulations are in place to uphold the rights of people to freedom and choice.

An appropriate and supportive legislative environment based on internationally accepted human rights standards is required to ensure the highest quality of service provision to people with dementia and their carers.

The World Health Organization (WHO) Response
The WHO recognizes dementia as a public health priority. In May 2017, the World Health Assembly endorsed the Global action plan on the public health response to dementia 2017-2025. The Plan provides a comprehensive blueprint for action - for policy-makers, international, regional, and national partners, and WHO - in areas such as increasing awareness of dementia and establishing dementia-friendly initiatives; reducing the risk of dementia; diagnosis, treatment and care; research and innovation; and support for dementia carers.

An international surveillance platform, the Global Dementia Observatory, has been established for policymakers and researchers to facilitate monitoring and sharing of information on dementia policies, service delivery, epidemiology, and research.

The WHO has developed iSupport and an e-health solution that provides information and skills training for carers of people living with dementia. The first study of the usability and effectiveness of iSupport is taking place in India.

Dementia is also one of the priority conditions in the WHO Mental Health Gap Action Program (mhGAP), which aims to scale-up care for mental, neurological, and substance use disorders, particularly in low- and middle-income countries.