Hawaii Silver Tsunami
Challenges and Opportunities
Early Detection: Alzheimer’s Disease

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Disclosure – Kore Liow, MD

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- Hawaii State Task Force ADRD
  Research, Prevention, Diagnosis and Treatment Workgroup

- Castle Medical Center
  Chair, Dept. of Medicine and Director of Neuroscience

- University of Hawaii John Burns School of Medicine
  Clinical Professor of Neurology, Family Medicine and Community Health (Volunteer)
Objectives

Early Detection Alzheimer’s Disease (AD)

- Why AD is important (especially to Hawai’i)
- Science of AD
- Benefits and Barriers to Early Detection
- Models of AD Care in Hawaii
How Serious is the Problem?
Alzheimer’s Disease is a Public Health Crisis

Estimated 5.2 million Americans living with AD

AD is 6th leading cause of death across all ages;

1 in 3 seniors dies with some type of dementia

www.alz.org/facts
How Costly is AD?
Alzheimer’s Disease is Costly (2012 $)

Medicare payments are **3x higher** for beneficiaries with Alzheimer’s disease.

Medicaid payments are **9x higher** for beneficiaries with Alzheimer’s disease.

www.alz.org/facts
What’s in Store for the Future?
Projected numbers of people aged 65 and over in the U.S. population with Alzheimer’s disease (in millions)  U.S. Census Bureau estimates of population growth
Are We Making Progress?

- Unlike other major diseases, which caused fewer deaths in 2008 than in 2000, AD deaths rose by 66%
How does this affect Hawai’i?

Hawai’i AD Statistics

• > 31,000 cases of known Alzheimer’s Dementia
  – Not including the 30-80% undiagnosed cases and other types of dementia
• 62,607 caregivers (2011)
• 71,296,910 hours of unpaid care
• about $864,118,545

U.S. Census, National Alliance for Caregiving, AARP and U.S. Dept. of Labor stats
2012 Facts and Figures of the Alzheimer’s Association
Hawai`i- growing number and % Elderly

- 2005: 17%
- 2020: 25%

People 60+
Objectives

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What is Dementia?

- It is NOT part of normal aging!

- A general term for memory loss and other intellectual abilities serious enough to interfere with daily life
Not ALL Dementias are Alzheimer’s Disease (AD)

- 60-80% Alzheimer’s Disease
  - Early onset
  - Late onset
- Vascular (Multi-infarct) Dementia
- Lewy Body Dementia
- Fronto-Temporal Lobe Dementias
- Other Dementias
  - Metabolic
  - Drugs/toxic
  - White matter disease
  - Mass effects
  - Depression
  - Infections
  - Parkinson’s

Some forms are reversible (treatable): Normal Pressure Hydrocephalus, Thyroid disorders, drug interactions, dehydration
# Top 10 Alzheimer Warning Signs

**Alzheimer Association**

<table>
<thead>
<tr>
<th>Signs</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory decline</td>
<td>Can’t remember a trip taken in the past</td>
</tr>
<tr>
<td>Difficulty performing familiar tasks</td>
<td>Bill paying, shopping</td>
</tr>
<tr>
<td>Disorientation</td>
<td>Getting lost in familiar places</td>
</tr>
<tr>
<td>Impaired judgment</td>
<td>Inviting strangers into the home</td>
</tr>
<tr>
<td>Impaired abstract thinking, problem-solving</td>
<td>Driving skills</td>
</tr>
</tbody>
</table>
## Top 10 Alzheimer Warning Signs

Alzheimer Association

<table>
<thead>
<tr>
<th>Signs</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Misplacing things</td>
<td>Losing valuable items in the home</td>
</tr>
<tr>
<td>Mood or behavior change</td>
<td>New-onset irritability, unusual habits or activities</td>
</tr>
<tr>
<td>Personality change</td>
<td>Withdrawn, increased socialization</td>
</tr>
<tr>
<td>Loss of initiative</td>
<td>Lost interest in hobbies</td>
</tr>
</tbody>
</table>
Brain is the most Interesting Organ! Understanding AD’s Brain…

Memory Loss

• Losses
  – Immediate recall
  – Recent events
  – Relationships

• Preserved abilities
  – Long ago memories
  – Emotional memories

Understanding

• Losses
  – Can’t interpret information
  – Can’t make sense of words

• Preserved abilities
  – Can get facial expression
  – Hears tone of voice
Brain is the most Interesting Organ!
Understanding AD’s Brain…

**Language**
- Losses
  - Can’t find the right words
  - Word Salad
  - Vague language
  - Single phrases
  - Sounds & vocalizing
  - Can’t make needs known
- Preserved abilities
  - singing
  - Swearing/sex
    - words/forbidden words

**Emotions**
- Losses
  - becomes labile & extreme
  - think it - say it
  - want it - do it
  - see it - use it
- Preserved
  - desire to be respected
  - desire to be in control
  - regret after action
Brain Atrophy - Shrinking

Normal

Alzheimer
The Pathological Cascade of AD

Clinical symptoms

Neurofibrillary tangles

TAU hypophosphorylation

APP

β-amyloid

Apo-E

PS1,2

Pathogenetic mutations

Neurodegeneration

Inflammation

Genetic risk factors

Environmental risk factors
The Hallmarks of AD

Plaques and Tangles:

- **Beta-Amyloid plaques**
  Dense deposits of protein and cellular material that accumulate outside and around nerve cells

- **Neurofibrillary tangles**
  Twisted fibers that build up inside the nerve cell
Normal Brain Cells

Neurotransmitters (AChE) - being sent - message being communicated to the next cell
Brain Cells with Alzheimer’s

- **Two processes**
  - Cells are shrinking & dying
  - Cells are producing less chemical to send messages

---

**plagues**

**tangles**

**Less neurotransmitter**

**Further to go to get to the next cell**

**Enzymes (AChE inhibitors) – get to them BEFORE they deliver their message**
Current Approved Therapies

- Does NOT cure
- Does NOT STOP Progression
- Only SLOW Progression

- Improve global function and cognition
- Temporary stabilization of ADLs
- Reduction in behavioral disturbances
- Delay nursing home placement
## Failure of AD Candidate Therapeutics

### Phase III randomized, placebo controlled, double-blind clinical trials

<table>
<thead>
<tr>
<th>Agent</th>
<th>Target/Mechanism</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Non-Aβ</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin; Simvastatin</td>
<td>Cholesterol (HMG CoA reductase inhibitor)</td>
<td>Negative</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Inflammation</td>
<td>Negative</td>
</tr>
<tr>
<td>Rosiglitazone</td>
<td>Insulin (PPAR gamma agonist)</td>
<td>Negative</td>
</tr>
<tr>
<td>Latrepirdine</td>
<td>Mitochondrial function</td>
<td>Negative</td>
</tr>
<tr>
<td><strong>Aβ</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AN1792 (Phase II)</td>
<td>Amyloid immunoRx</td>
<td>Negative (AEs)</td>
</tr>
<tr>
<td>Tramiprosate</td>
<td>Amyloid aggregation</td>
<td>Negative</td>
</tr>
<tr>
<td>Tarenflurbil</td>
<td>Gamma secretase</td>
<td>Negative</td>
</tr>
<tr>
<td>Semagacestat; Avagacestat</td>
<td>Gamma secretase</td>
<td>Negative</td>
</tr>
<tr>
<td>Bapineuzumab</td>
<td>Amyloid immunoRx</td>
<td>Negative</td>
</tr>
<tr>
<td>Solanezumab</td>
<td>Amyloid immunoRx</td>
<td>Negative (+/-)</td>
</tr>
</tbody>
</table>
Result of Treatment

Cognitive Function vs. Time

Onset

Presymptomatic stages

Treatment

AD
1) The diagnosis of AD cannot be certified clinically and needs a post-mortem confirmation to be ascertained
2) The diagnosis of AD can only be ‘probable’
3) The diagnosis of AD can only be made when the disease is advanced and reaches the threshold of dementia
Possible Result of Earlier Treatment

Cognitive Function

Time

Onset

Presymptomatic stages

AD

Improvement
AD Biomarkers

Normal

Presymptomatic

Prodromal MCI

Dementia

Abnormal

CSF Aβ₄₂
Amyloid imaging
FDG-PET
MRI hippocampal volume
CSF Tau
Cognitive performance
Function (ADL)

modified from Aisen PS Alzheimers Dement. 2010
In 2011, the criteria were updated since the criteria was initially established in 1984
3 stages Alzheimer’s Disease “SPECTRUM”
1) AD dementia stage
2) Prodromal/MCI stage
3) Preclinical/Presymptomatic stage

Guidelines provide a framework for studying and characterizing the disease in earlier stages; critical for prevention and treatment
As biomarkers can be considered as surrogates for the histopathological changes,
Application of criteria and biomarkers in clinical practice is evolving rapidly.

- The entire course of AD from the asymptomatic onset to the severe/dementia form is captured.
- 3 stages Alzheimer’s Disease “SPECTRUM”
  - AD dementia stage
  - Prodromal/MCI stage
  - Preclinical/Presymptomatic stage
- Biomarkers are increasingly important in AD research – natural history and clinical trials and diagnosis in specific cases.
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Besides Potential for More Effective Treatments? Why Early Diagnosis in AD?

- **Early Detection**
  - Treat the treatable
  - Clinical trials with disease modifier treatments
  - Make lifestyle choices
  - Financial and legal plans while competent
  - Greater access to community support
  - Cost savings and delay institutionalization

- **Failure to do so:**
  - Mis-diagnosis, searching for other causes
  - Untreated problems
  - Unnecessary and costly testings
  - Patient and caregivers fear & stress
  - Safety issues

*from Cummings, 2011*
Early Detection of AD
Are We Doing a Good Job?

75% - estimated 36 million people living with dementia worldwide have not been diagnosed

20-50% - dementia cases in high-income countries are recognized

http://www.alz.co.uk/worldreport2011.

Cross-sectional study in 3 managed healthcare systems in US:
-18% with mild cognitive impairment had evidence within their medical charts of having been clinically evaluated for dementia.
-4% of the patients with moderate to severe impairment were offered treatments
-none of the patients with mild impairment, had been offered treatment.

Early Detection of AD
What are the Barriers?

- Attribution of cognitive impairment to normal aging
- Lack of a definitive tests
- Hesitant to assign a diagnosis of AD, esp. early disease
- Insufficient time
- Low rates of reimbursement for assessments and services
- Lack conviction that the benefits of diagnosing outweigh the burdens associated with diagnostic confirmation.
- Lack access and difficulty referring to specialized care

Is Early Detection in AD Altering Outcome?

American Academy of Neurologists (AAN) 2010 found that majority of neurologists endorsed providing diagnosis of MCI or early AD because it:

(1) Allows the patient to be involved in planning for the future,
(2) Motivate the patient to engage in risk reduction activities,
(3) Helps the patient and family with financial planning, and
(4) Helps clinicians when prescribing medications.

Majority of the neurologists offer these patients counseling regarding:
Physical (78%) and mental (75%) exercises, (63%) discuss dementia risk.

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What did other states do? California

• Since 1985, state invested more than $90 million in 10 Alzheimer’s Disease Centers, which raised over $500 million in federal and private research funding

• Comprehensive, multidisciplinary diagnostic and treatment evaluations

• Services offered by the centers include: professional training, specialty referral clinics, education and community services, research funding, and specialized knowledge provided to public and task forces
Missouri Alzheimer’s State Plan Task Force

• Recommendations include:
  – Early diagnosis, intervention, and support; use AD-8 as dementia screening tool
  – Implement innovative programs for dementia care, including community long term care services for young-onset AD patients
  – Ensure a dementia-conscious healthcare workforce
  – Fund to maintain Missouri’s status as a leader in AD research
    • Advocate for restoration of state funding to researchers for the AD and Related Disorders Research Program → SB268 and HB682 would increase individual grants from $30,000 to $50,000
Hawai‘i Pathway to Excellence in Dementia Care and Research
Hawaii Alzheimer’s Disease Center

- Clinical Core Comprehensive Care
- Tissue Core Research
- Education Core Life Enrichment

- TREATMENT TRIALS, EARLY DIAGNOSIS, COGNITIVE RESEARCH, IMAGING.
- NEUROPATHOLOGY, GENETICS, CELL & MOLECULAR BIOLOGY, ANIMAL MODELS.
- LIFE ENRICHMENT PROGRAMS, EDUCATION OF PCPs, COMMUNITY LECTURES, INTRAMURAL SEMINARS.
Clinical Core
Comprehensive Clinical and “Preventive” Options

- Early and accurate diagnosis
- Treatable reversible causes
- Multidisciplinary Team
  Neurology, Geriatrics, Psychiatry, Neuropsychology, Psychology, Social work
- Multi Faceted Treatments
- Clinical Trials
  - Therapeutic Drug Trial
  - Prevention Trial
<table>
<thead>
<tr>
<th>Standard workup</th>
<th>Include when appropriate based on findings of standard workup</th>
<th>Optional/Research</th>
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<tbody>
<tr>
<td>Expanded History</td>
<td></td>
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<tr>
<td>Patient Caregiver</td>
<td></td>
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<tr>
<td>Cognitive Screening Instruments</td>
<td></td>
<td></td>
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<tr>
<td>MoCA, MMSE, AD8</td>
<td></td>
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<tr>
<td>CDT</td>
<td></td>
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<tr>
<td>Functional Instruments:</td>
<td></td>
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<tr>
<td>ADCS-ADL, FAQ, PSMS, Katz Index, Lawton IADL</td>
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<tr>
<td>Comprehensive Physical</td>
<td></td>
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<tr>
<td>Cardiovascular work up eg EKG, Holter Monitor, Echocardiogram</td>
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<td>Laboratory studies:</td>
<td></td>
<td></td>
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<tr>
<td>CBC, SMA, TSH, Vitamin B₁₂, folic acid, RPR, urinalysis/culture, Homocysteine</td>
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<tr>
<td>Specific laboratory studies:</td>
<td></td>
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<tr>
<td>Lyme, HIV, toxicology, heavy metal, methylmalonic acid, RPR, serum protein electrophoresis CSF analysis for infection</td>
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<tr>
<td>Imaging:</td>
<td></td>
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<tr>
<td>Brain MRI, Head CT</td>
<td></td>
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<tr>
<td>Chest x-ray</td>
<td></td>
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<tr>
<td>Neuropsychiatric exam or screening instrument to assess for behavior problems or depression; Beck Depression Inventory or Geriatric Depression Scale</td>
<td>Office exams</td>
<td></td>
</tr>
</tbody>
</table>

ADCS-ADL = Alzheimer's Disease Cooperative Study Activities of Daily Living; ApoE = apolipoprotein E; CBC = complete blood cell (count); CDT = clock drawing test; CSF = cerebrospinal fluid; CT = computed tomography; FAQ = Functional Activities Questionnaire; FDG = fluorodeoxyglucose; IADL = Instrumental Activities of Daily Living; MMSE = Mini-Mental State Examination; MRI = magnetic resonance imaging; PET = positron emission tomography; PSMS = Physical Self-Maintenance Scale; RPR = rapid plasma regain; SMA = smooth muscle antibody; TSH = thyroid-stimulating hormone
HADC Focus on “Prevention” Risk Factors for AD

Non-modifiable

- Age
- Genetic susceptibility (ApoE)
- Traumatic brain injury
- Family history of AD
- Down syndrome

Modifiable

- Cardiovascular risk factors
- Metabolic syndrome
- Diminished estrogen levels
- Hypertension
- Being overweight/obese
- Diabetes
- Chronic Inflammation
HADDEPT: (Hawaii Dementia Prevention Trial)
Can Targeted “Brain Foods” Prevent Dementia?

Steve Blake, Sc.D, George King, Ph.D., Nicole Kerr, R.D., M.P.H., Thomas Harding, Psy.D., Alana Taniguchi, BSc, David Kaminskas, M.D., Cheynie Nakano, MD, Michiko Inaba, MD, PhD, Kamal Masaki, MD, Kore Liow, MD, FACP,

MCI patients at HADC

- Reduce AGE (Advanced Glycation End products)
- Increase Antioxidants
- Ginkgo biloba
- Gotu kola
H3 (Hawaii Harvard Hupezine) Collaborative Trial

Hawaii-Based National Consortium

Study Extracts of Native and Cultivated Hawaiian Plants and Extract-Derived Compounds

Investigators from Harvard Medical School, University of Utah, Brigham and Women’s Hospital and Collaborators in Hawaii including:

HADC, JABSOM Department of Complementary and Alternative Medicine, University of Hawaii at Hilo College of Pharmacy Marine Biology Faculty at UH

“Collaborations is Key”
Tissues Core
Scientific Research

- Identifying, characterizing and genotyping patients in early stages or at risk for AD (unique to Hawaii and the Pacific island)
  - Cognitive Testings
  - Molecular genetics
  - Advanced Imaging Modalities with MRI and Ligand PET
Genetic Testings important to detect early onset AD and access risks

Risk genes
- Late Onset AD
  Apolipoprotein E-e4 (APOE-e4)
Increase the likelihood of developing a disease, but do not guarantee it will happen
  1 allele: 2-3 X
  2 sets: 8-12 X

Deterministic genes:
- Early Onset AD
  Amyloid precursor protein (APP)
  Presenilin-1 (PS-1)
  Presenilin-2 (PS-2)
  Trisomy 21
CSF AD Biomarker to access risk

AD = CSF has Low Aβ and High Tau

MRI Studies looking at Medial Temporal Lobe Atrophy

Atrophy in Alzheimer’s disease
- Prodromal AD 15%
- Mild dementia 25%
- Moderate dementia 40%

Choroid fissure
Temporal horn
Height of the hippocampus

Qualitative MTL Rating Scale
Scheltens, JNNP 1992
MRI Studies important to diagnose treatable causes:

Normal Pressure Hydrocephalus
MRI Studies important in Accurate diagnosis:
Frontotemporal Dementia (FTD)
AD Spectrum: Biomarkers

- CSF Aβ₄₂
- Amyloid imaging
- FDG-PET
- MRI hippocampal volume
- CSF Tau
- Cognitive performance
- Function (ADL)

Modified from Aisen PS Alzheimers Dement. 2010
New Imaging Technology for AD
Amyvid (florbetapir)
18F tracer;
FDA approved (2012)

PET scan

Amyloid detection

67 yo NL
79 yo AD

Nordberg
Lancet Neurology
2004
Subtle decrements in episodic memory can precede the onset of AD by several years and may serve as a marker for the imminent onset of dementia.

A reduced word repetition effect on the LPC may be an effective electrophysiological index of early AD.

Asymmetry in cognitive abilities may precede the onset of AD in a subset of elderly, and may serve as a marker for the imminent onset of dementia.
# Staging Categories for Preclinical AD (Research)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>$A\beta$ (PET or CSF)</th>
<th>Markers of Neuronal Injury (tau, FDG, sMRI)</th>
<th>Evidence of Subtle Cognitive Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>Asymptomatic cerebral amyloidosis</td>
<td>Positive</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Stage 2</td>
<td>Asymptomatic amyloidosis + “downstream” neurodegeneration</td>
<td>Positive</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Stage 3</td>
<td>Amyloidosis + neuronal injury + subtle cognitive/behavioral decline</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
</tbody>
</table>

R.A. Sperling et al. Alzheimer’s & Dementia;(2011) 1-13
Education Core
Life Enrichment Programs

- Education of physicians and other health professionals
- Referral center for all islands and working collaboratively with Primary Care Providers
- Life Enrichment Programs
- Social Needs
- Public awareness
HADC – Educational Hub
Developing “dementia-conscious” workforce

- University of Hawaii John Burns School of Medicine
- Tripler Army Medical Center
- Argosy University
- Residents Physicians, Fellows
- Medical Students
- Graduate Practicum Students
- Mainland Medical Student and Research Students
Creutzfeldt-Jakob Disease: A Case Report and Differential Diagnoses

Gotaro Kojima MD; Brent K. Tatsuno MD; Michiko Inaba MD; Stephania Velligas BS; Kamal Masaki MD; and Kore K. Liow MD

Abstract
Sporadic Creutzfeldt-Jakob disease is a rare neurodegenerative disorder of unknown etiology that causes rapidly progressive dementia. This disease is uniformly fatal and most patients die within 12 months. Clinical findings include myoclonus, ataxia, pyramidal signs, and cognitive dysfunction. The disease course follows rapid progression of cognitive and functional impairment toward atrophic encephalomalacia in the late stage, and eventually death, most often within 12 months of the disease onset.

Case Report
The patient was a 66-year-old woman who was referred to a memory clinic for further evaluation of a 5-month history of rapidly progressive dementia. The initial symptoms included memory loss, feeling odd, anxiety, and uncontrolled weight loss. At her first visit to the memory clinic, her son and husband reported that her cognitive problems had recently worsened over the previous two weeks. She had now problems with short-term memory and functional abilities, including getting dressed, using the toilet, and getting lost in her house. Her husband stated that she had emotional liability and at times, did not trust her own family. Her visuospatial was becoming blurry and she had become more disoriented. Her family denied that she had any myoclonic jerks, tremor, gait unsteadiness, or visual, auditory, or sensory hallucinations.

Her past medical history was non-contributory. She had not had any previous surgeries. Her family history was significant for a myocardial infarction in her father and fatal leukoencephalopathy in her mother, but there was no family history of dementia or prion disease. She had no known allergies and her medications consisted of nonsteroidal anti-inflammatory medications that she started for the onset of her symptoms. She had traveled to Holland and Belgium 5 years previously, but was a strict vegetarian at that time. She had also traveled to the Caribbean, Mexico, and Belize, but did not have any exposure to raw livestock or brain matter. She had previously been a journalist in Washington, DC, and did public relations for a real estate company in Hawaii. Her physical exam was significant for perseveration, anomia, aphasia, alexia, agnosia, and apraxia. Her muscle tone was normal in all four extremities and her cranial nerves were grossly normal. She had normal sensation and normal coordination. Her reflexes were symmetric and there were no Babinski reflexes. Her gait was slow but non-ataxic. She was able to complete the Mini-Mental State Examination (MMSE) and perform other collaborative tasks due to perseveration. For example, when asked about the month, day, and year, she answered “December” for each, when in fact, it was already March. When she answered “December” for the state, the MMSE was stopped. Blood work was normal and included a basic metabolic profile, CBC, thyroid studies, liver studies, vitamin B1, vitamin B12 and folate levels, lactate, and erythrocyte sedimentation rate (ESR), rapid plasma reagin (RPR), human immunodeficiency virus (HIV), angiotensin-converting enzyme (ACE) levels, and quantitative urinary and serum antibody tests were negative. Aspergillosis and infections were initially considered.

Discussion
Although definite diagnosis of CJD can only be made by examining post-mortem brain tissues in the brain, the diagnosis can be supported by protein assays were completed on E20 interspersed 14-3-3 protein in the CSF and abnormal rapid changes in cerebral and retinal protein on diffusion-weighted fluid-attenuated inversion recovery (FLAIR) MRI.

Keywords
sporadic Creutzfeld-Jakob disease, prion disease, rapidly progressing dementia

Introduction
Creutzfeldt-Jakob disease (CJD) is a progressive neurodegenerative disorder and one of the human prion diseases. It is uniformly fatal and the annual incidence rate is 1-2 per million worldwide. In addition to abnormal prion protein accumulation in the brain, CJD is characterized by spongiform change, neuronal loss, and gliosis. It is often difficult and challenging to diagnose CJD pre-mortem because of a low index of suspicion on the part of clinicians.

The most common form of CJD is sporadic Creutzfeldt-Jakob disease (sCJD) (85%-90%), while the rest are familial, inherited, and variant forms. The mean onset age of sCJD is 65 years, and most of the cases are distributed within the 30s and 80 years. In CJD patients aged less than 30 or over 80 years are rare. The etiology is still unknown and both genders are almost equally affected.

The clinical features mainly include a rapidly progressive dementia and multifocal neurological findings such as myoclonus, pyramidal, cranial, and pyramidal/extrapyramidal signs. The disease course follows rapid progression of cognitive and functional impairment toward atrophic encephalomalacia in the late stage, and eventually death, most often within 12 months of the disease onset.
Best Practices Medicare Annual Wellness

PCP Dementia Evaluations

A. Review HRA, clinician observation, self-reported concerns, responses to queries

- Yes: Signs/symptoms present
- No: Informant available to confirm

B. *Conduct brief structured assessment*
   - Patient Assessment: Mini-Cog or GPCOG or MIS
   - Informant assessment of patient: Short IQCODE, AD8, or GPCOG

Brief assessment(s) triggers concerns:
   - Patient: Mini-Cog ≤ 3 or GPCOG < 8 or MIS ≤ 4 or
   - Informant: Short IQCODE ≥ 3.38 or AD8 ≥ 2 or
   - GPCOG informant score ≤ 3 with patient score < 8

C. Refer OR conduct full dementia evaluation

AWV = Annual Wellness Visit; GPCOG = General Practitioner Assessment of Cognition; HRA = Health Risk Assessment; MIS = Memory Impairment Screen; MMSE = Mini Mental Status Exam; MoCA = Montreal Cognitive Assessment; SLUMS = St. Louis University Mental Status Exam; Short IQCODE = short Informant Questionnaire on Cognitive Decline in the Elderly

*No one tool is recognized as the best brief assessment to determine if a full dementia evaluation is needed. Some providers repeat patient assessment with an alternate tool (eg. SLUMS, or MoCA) to confirm initial findings before referral or initiation of full dementia evaluation.

<table>
<thead>
<tr>
<th>Screening or Assessment Tool</th>
<th>Time to Administer (~minutes)</th>
<th>Benefits</th>
<th>Limitations</th>
<th>Education bias</th>
<th>Available at:</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD8(^{27})</td>
<td>3</td>
<td>Simple to score</td>
<td>Considered informant-based</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDT(^{18})</td>
<td>≤1</td>
<td></td>
<td>Lacks standards for administering and scoring</td>
<td>Minimal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GPCOG(^{75}) Patient Informant</td>
<td>2-5</td>
<td>Developed/ validated for primary care setting</td>
<td>Best if used together</td>
<td>Little or no</td>
<td><a href="http://www.gpcog.com.au">www.gpcog.com.au</a></td>
<td>Available in multiple languages Informant component</td>
</tr>
<tr>
<td>GPCOG(^{75}) Patient Informant</td>
<td>1-3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mini-Cog(^{76})</td>
<td>2-4</td>
<td>Validated for primary care setting</td>
<td>Little or no</td>
<td></td>
<td>Available in multiple languages</td>
<td></td>
</tr>
<tr>
<td>MIS(^{2})</td>
<td>4</td>
<td>Verbal memory test; suitable for primary care</td>
<td>No executive function or visuospatial component</td>
<td>Little or no</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMSE(^{2})</td>
<td>7-10</td>
<td>Widely used</td>
<td>Best for at least moderate impairment; copyrighted</td>
<td>Yes</td>
<td>Proprietary – <a href="http://www.parinc.com">www.parinc.com</a></td>
<td></td>
</tr>
<tr>
<td>MoCA(^{14,20})</td>
<td>10-15</td>
<td>Designed to test for MCI</td>
<td>Lacks data in general practice settings</td>
<td>Yes</td>
<td><a href="http://www.mocatest.org">www.mocatest.org</a></td>
<td>Available in multiple languages</td>
</tr>
<tr>
<td>SBT (BOMC and 6-CIT)</td>
<td>4-6</td>
<td>Verbal test</td>
<td>No executive function Difficult to score</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIS(^{77})</td>
<td>2</td>
<td>Tests short term memory and orientation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLUMS(^{21})</td>
<td>7</td>
<td>Tests many domains</td>
<td>Limited information</td>
<td>No</td>
<td><a href="http://aging.slu.edu/pdfsurveys/mentalstatus.pdf">http://aging.slu.edu/pdfsurveys/mentalstatus.pdf</a></td>
<td></td>
</tr>
</tbody>
</table>

BAS = Brief Alzheimer Screen; CDT = clock drawing test; GPCOG = General Practitioner Assessment of Cognition; MIS = Memory Impairment Screen; MMSE = Mini-Mental Status Examination; MoCA = Montreal Cognitive Assessment; SBT = Short Blessed Test; SIS = Six item screener; SLUMS = Saint Louis University Mental Status test; SPMSQ = Pfeiffer Short Portable Mental Status Questionnaire; STMS = Short Test of Mental Status
Screening Tool: AD8- 8-item Informant Interview to Differentiate Aging and Dementia*

(PPV = 87% for CDR 0 vs CDR ≥ 0.5)

Score 1 for Changed, 0 Not Changed, > 2 = Impairment

1. Is there repetition of questions, stories, or statements?
2. Are appointments forgotten?
3. Is there poor judgment (eg, buys inappropriate items, poor driving decisions)?
4. Is there difficulty with financial affairs (eg, paying bills, balancing checkbook)?
5. Is there difficulty in learning or operating appliances (eg, television remote control, microwave oven)?
6. Is the correct month or year forgotten?
7. Is there decreased interest in hobbies and usual activities?
8. Is there overall a problem with thinking and/or memory?

*Adapted from Galvin et al, “The AD8: A Brief Informant-Interview to Detect Dementia”, Neurology. 2005;65:559-564.
Hawaii Brain Health Educational Initiatives

Increase awareness of the importance of ACCURATE and EARLY diagnosis of the different dementia types especially the Non Alzheimer’s Type and those with treatable and reversible dementias types and those with initial behavioral presentations.

Promote research and understanding of the neuroscience and pathophysiology of the various dementia types.

Increase awareness of the latest treatment options including behavioral modifications, clinical trials and life enrichment programs for patients and caretaker.

Promote collaborations and working together among the different disciplines involved in the care of dementia patients especially interactions and collaborations between different disciplines including basic science, clinical and social disciplines.

Kore Liow, MD, Kamal Masaki, MD, Wes Lum, PhD
Life Enrichment and Care Coordination @ HADC

• Early on care consultations and end-of-life decisions
• Discussion guardianship, driving, and legal issues
• Weighing risks vs benefits of aggressive treatment
• Patient centered home or SNF care – midlevel providers
• Early behavioral and psychosocial interventions
  – Non pharmacological interventions and structured socialization to facilitate cognitive and behavioral stimulation
  – Psychiatrist, psychologist, dementia and behavioral neurologist
• Education to the patient and appropriate caregivers
  – Supervision, concerns of safety, risk of falls, becoming lost, accidental drug overdoses; financial exploitation or mismanagement.
• Caretaker Burn outs and day care Options
  – Options for respite care, such as Adult Medical Day Care
    • Alzheimer’s Association, UH Social Work Department, Anna Loengard, MD
When to refer to Specialists

- Early onset (<60)
- Atypical Presentation
- Parkinsonism, focal findings
- Abnormal imaging findings
- Behaviors seemingly “untreatable”
- To document and monitor diagnosis, severity or progression
- Legal, financial, psychosocial, family caregivers Issues
Conclusions

• AD is the 6th leading cause of death and increasingly a public health and economic crisis

• 2011 New Diagnostic Criteria and the use of biomarkers and imaging rapidly changing our understanding of AD

• Accurate diagnosis EARLY ON offers best chance for appropriate interventions including treatment for reversible causes, care coordination, planning and lifestyle modifications

• Best Practices is established through education, community partnerships and access to specialized care
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- Steven Schachter, MD
- Many Other Collaborators

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- Argosy U, Neuropsy
- Alzheimer’s Association – Hawaii Chapter
- Medical Community
- Hawaii Community
- Harvard Medical School
- Many Other Institutions
With Gratitude to our Patients, Families and Clinical and Research Faculty, Staff and Students
Hawaii Alzheimer’s Disease Center
Hawaii Pacific Neuroscience www.HawaiiNeuroscience.com
To view Charlotte’s story, please see link below.