Recent advances in diagnosis and treatment of early Alzheimer's Disease

Abhilash Desai MD

Geriatric Psychiatrist

8-26-24

Dr.abhilashdesai@icloud.com

Financial disclosures

- I have no relevant financial relationships to disclose.
- I do not intend to discuss any off-label, investigative use of commercial products or devices.

Learning objectives

- Describe the role of biomarkers in early accurate diagnosis of Alzheimer's disease.
- Discuss role of new FDA approved medications for Alzheimer's disease in clinical care.

2024 Diagnosed Dementia Estimates

- Noninstitutionalized population age 65 and older.
- Self report or report by reliable informant that they have been diagnosed to have dementia
- Age group 65-74: 1.7%
- Age group 85 and older: 13.1%

• CDC. National Health Statistics Reports #203. June 13, 2024.

2024 Diagnosed Dementia Estimates

Clinical implication: Many individuals have undiagnosed dementia (possibly 50% or more, especially in over 85-year-old population)

New revised Alzheimer's Disease (AD) Criteria

- AD is defined biologically meaning that if you have positive biomarkers (and asymptomatic), you have AD.
- Biological staging of AD is proposed.

New revised Alzheimer's Disease (AD) Criteria

- Core 1 biomarkers for diagnosis (just one is needed for diagnosis)
- Core 2 biomarkers for prognosis (when abnormal, will increase confidence that AD is contributing to symptoms)

Core 1 biomarkers

- Amyloid PET
- Approved CSF biomarkers
- Accurate plasma biomarkers (especially phosphorylated tau 217)

Core 2 biomarkers

- CSF or plasma biomarkers (e.g., MTBR-Tau243, eMTBR-Tau243)
- Tau PET

- Jack Jr. et al. Revised criteria for diagnosis and staging of Alzheimer's disease: Alzheimer's Association Workgroup. Alzheimer's Dement. 2024; 1-27.
- A plasma test for tangles. Alzforum 8-22-24

Other biomarkers

- N: Neurodegeneration (e.g., NFL, anatomic MRI, FDG PET)
- I: Inflammation (e.g., GFAP)
- V: Vascular injury (e.g., Infarction in MRI, CT, WMH)
- S: Alpha Synuclein seed amplification assay

Clinical judgment is essential

- Biomarkers have limitations
- Head trauma or cardiorespiratory arrest may transiently increase ptau values
- Certain medications, CSF dynamic disorders and impaired renal function can alter values of plasma biomarkers

AD neuropathology in centenarians

- AD neuropathology present but no clinical symptoms Resilience
- AD neuropathology absent Resistant

• Pearls T. Cognitive Trajectories and Resilience in Centenarians - Findings From the 100-Plus Study. JAMA Network Open 2021.

P-tau217

- Improved diagnostic accuracy of PCP from 61% to 91%.
- Improved diagnostic accuracy of dementia experts from 73% to 91%.

• Palmqvist et al. Blood Biomarkers to Detect Alzheimer Disease in Primary Care and Secondary Care. JAMA July 28, 2024.

Monoclonal anti-amyloid antibodies - mABs

- Lecanemab (Leqembi) Eisai and Biogen
- Donanemab (Kisunla) Eli Lily

Biomarkers and mAbs – what does primary care need?

- Ms. J's test result is just posted in the EMR.
- Ms. J was recently diagnosed with Mild Cognitive Impairment and she wanted to get Lecanemab, so she got herself tested for plasma phospho tau 217.
- Trying to avert alarm, her specialist Dr. A calls her.
- 45 minutes of rapid-fire questions ensue.
 - Chen and Erickson. Alzheimer's disease, biomarkers and mAbs What does primary care need. NEJM. 2024.

Biomarkers and mAbs – what does primary care need?

- Dr. A explains that "elevated" phospho tau confirms the suspicion that Alzheimer's is a cause of Ms. J's symptoms and avoids the term "positive" for the phospho tau test.
- Dr. A explains that depression, anticholinergic medications and OSA may also be contributing to her symptoms.
- Dr. A explains that she may be eligible for mAb therapy, but a separate evaluation is needed.
 - Chen and Erickson. Alzheimer's disease, biomarkers and mAbs What does primary care need. NEJM. 2024.

Genetic testing

- Familial Alzheimer Disease (onset even in 30s and 40s)
 - Presenilin 1 (PSEN1)
 - Presenilin 2 (PSEN2)
 - Amyloid Precursor Protein (APP)
 - Down's syndrome has three copies of APP
- APOE 4

https://www.genetestornot.org

- Genetic counseling
 - Alzheimers Society Canada. <u>https://alzheimer.ca/sites/default/files/documents/research_understanding-genetics-and-alzheimers-disease.pdf</u>

APOE E genotype for white population

- APOE E4 two copies eight to 12-fold increased risk compared to E3
- APOE E4 one copy three times increased risk compared to E3
- APOE E2 has reduced risk compared to E3

Early Alzheimer's Disease

- Mild Cognitive Impairment (MCI) due to AD
- Mild dementia due to AD

Diagnostic test

There is no single test that can give a definite diagnosis of MCI or dementia.

Diagnosis

MCI and dementia are clinical diagnoses – meaning that diagnosis is given by clinicians after careful gathering medical history, doing a physical exam, interpreting office based cognitive tests, assessment of activities of daily living and work-up (e.g., laboratory tests, brain scans).

Diagnosis of early AD

MCI-AD and mild dementia due to AD require biomarker evidence

A/T/N Classification

- Amyloid (and corresponding biomarkers)
- Tau (and corresponding biomarkers)
- Neurodegeneration (and corresponding biomarkers)

• Jack et al. A/T/N: An unbiased descriptive classification scheme for Alzheimer's disease biomarkers. Neurology 2016.

A/T/N/I/V/S Classification

- Amyloid
- Tau (T1 [P-tau 217], T2 [MTBR-tau243])
- Neurodegeneration Inflammation
- Vascular injury
- Alpha Synuclein

Blood / Plasma Biomarkers – Not FDA approved

- Plasma Abeta42/40 (reduced in AD) and Phospho-tau levels (elevated in AD)
- Neurofilament light chain (NFL) (elevated if there is neurodegeneration)
- Glial Fibrillary Acidic Protein (GFAB) (elevated if there is neuroinflammation)

• Johannson C et al. Plasma biomarker profiles in Autosomal Dominant Alzheimer's Disease. Brain 2023; 146:1132-1140.

FDA approved CSF Biomarkers

- Abeta 42/40 ratio (reduced in AD)
- Phospho Tau / Abeta 42 ratio (better than Abeta 42/40 ratio) (increased in AD)

• Biomarkers for dementia detection and research. Fact Sheet. National Institute on Aging. 2020.

Brain imaging biomarkers

- Amyloid PET (FDA approved)
- Tau PET

• Biomarkers for dementia detection and research. Fact Sheet. National Institute on Aging. 2020.

Artificial Intelligence

FDA has approved *BrainSee*, an AI-driven software platform that uses MRI data, along with scores from routine cognitive tests, to predict the likelihood that a person with mild cognitive impairment will develop AD dementia within five years.

Treatment of early AD - update

- Disease modifying therapy (lecanemab, donanemab)
- Symptomatic therapy (brexpiprazole, suvorexant)
- CMS GUIDE model for Comprehensive Dementia Care

Disease modifying treatment of early AD

- Early AD = MCI-AD and mild dementia AD
- Diagnosis of "early AD" requires biomarker evidence (CSF or amyloid imaging)
- Lecanemab (Leqembi) and Donanemab (Kisunla) have full approval by the FDA for treatment of Early AD.
- Lecanemab DID NOT receive approval by the EMA (European Medicines Agency in July 2024).

Anti-amyloid antibody therapies – Lecanemab and Donanemab immunotherapies

- Human monoclonal antibody
- Given via intravenous infusion every two weeks (lecanemab) and every four weeks (donanemab)

FDA label

Requires MRI before and periodically after the infusion begins to monitor for ARIA

- Lecanemab: baseline, before fifth, seventh, and 14th infusions.
- Donanemab: baseline, before second, third, fourth, and seventh infusions. More frequent because Donanemab has higher risk of ARIA compared to Lecanemab with most serious reactions occurring early.

Annual Cost

\$26.5K for Lecanemab and \$32K for Donanemab plus cost of treatment – total around \$90K annually per person

Benefits

Reduced markers of amyloid and "moderately" (20-30% according to UCSF) less decline in measures of cognition and function at 18 months (6 months slowing according to UCSF).

• van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388:9-21.

ARIA – Amyloid Related Imaging Abnormalities

- Microhemorrhages
- Macrohemorrhages
- Superficial siderosis

- van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388:9-21.
- Sims et al. Donanemab in early symptomatic Alzheimer's disease. JAMA 2023.

Lecanemab and Donanemab : Adverse effects

- Brain bleed and brain swelling in 17% of patients lecanemab and 24% for donanemab.
- Black box warning for individuals on anticoagulants and two copies of APOE 4
- 4% of ARIA symptomatic for lecanemab and 6% for donanemab

- van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N* Engl J Med. 2023;388:9-21.
- Sims et al. Donanemab in early symptomatic Alzheimer's disease. JAMA 2023.

Lecanemab and Donanemab : Adverse effects

- Symptoms: headache, dizziness, confusion, balance problems, vision changes, diarrhea, falls, syncope (some the symptoms mimic stroke)
- Rare: seizures, strokes (less than 1%)

- van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388:9-21.
- Sims et al. Donanemab in early symptomatic Alzheimer's disease. JAMA 2023.

Lecanemab and Donanemab : Deaths & IRRs

- 3 deaths so far with lecanemab and 5 with donanemab
- Infusion related reactions (IRRs): flushing, chills, nausea, sweating
- 3 cases of anaphylaxis (donanemab)

- van Dyck CH, Swanson CJ, Aisen P, et al. Lecanemab in early Alzheimer's disease. *N Engl J Med*. 2023;388:9-21.
- Sims et al. Donanemab in early symptomatic Alzheimer's disease. JAMA 2023.

Lecanemab and deaths in primary care

- Two deaths have been reported so far from the clinical use of lecanemab.
- Both were APOE 4 homozygous who developed severe ARIA-E and seizures.

 Alzheimer's Association International Conference 2024. Reported in Alzheimer's Forum 8-16-24

FAERS - Lecanemab

- Food and Drug Administration Adverse Event Reporting System
- First death: December 2023 in an individual age 84.
- Second death: May 2024 in an individual age 80 (after the third infusion, sudden severe ARIA-E).
- Both developed severe ARIA-E, received steroids, developed uncontrollable seizures and died.

• Alzheimer's Forum (alzforum). 8-16-24.

High risk group for ARIA

- Cerebral amyloid angiopathy (detected by MRI)
- APOE e4 gene (two copies have highest risk of ARIA) APOE genotype recommended prior to starting DMT but not mandated.

- Cummings J, et al. Lecanemab: appropriate Use Recommendations. J Prev Alzheimer's Dis. 2023
- Haller S, et al. Cerebral Microbleeds: imaging and Clinical Significance. *Radiology*. 2018;287:11-28

High risk group for ARIA

- Anticoagulants (blood thinners such as warfarin, DOACs [direct acting oral anticoagulants, used to treat Atrial fibrillation, peripheral artery disease and venous thromboembolism])
- Pre-existing microbleeds

- Cummings J, et al. Lecanemab: appropriate Use Recommendations. J Prev Alzheimer's Dis. 2023
- Haller S, et al. Cerebral Microbleeds: imaging and Clinical Significance. *Radiology*. 2018;287:11-28

To reduce risk of death with DMTs

- Avoid giving it to individuals with CAA cerebral amyloid angiopathy
- Catch ARIA early
- Avoid thrombolytics if stroke is suspected in individuals receiving DMT

Lecanemab: when to stop

At least 18 months of treatments

Donanemab: when to stop

- May stop infusion therapy if tests show that most amyloid plaques have been removed from the brain (e.g., amyloid PET scan shows plaque load below 11 centiloids or twice consecutively below 25 centiloids).
- In the pivotal trial, two thirds on donanemab were amyloid negative at the end of one year.

Donanemab vs Lecanemab

MMSE cut off was lower (20) for donanemab compared to 22 for lecanemab.

Donanemab vs Lecanemab

- For APOE 4 positive individuals, lecanemab may be preferred due to lower risk of ARIA
- For individuals who live further way, donanemab may be preferred due to less frequency of infusions

Inclusion - Exclusion criteria for mABs

- VA criteria
- Alzheimer's Association criteria

Medicare coverage

- Both antibodies are covered by Medicare
- Out of pocket cost \$7000 per year suggested by some experts

New FDA approved medication for symptomatic therapy of cognitive symptoms of AD

- Benzgalantamine (Zunveyl) serves as a prodrug (precursor to the active compound galantamine)
- Supposed to have less gastrointestinal adverse effects relative to other cholinesterase inhibitors (e.g., galantamine, donepezil, rivastigmine)
- FDA approved it in July of 2024

Agitation associated with Alzheimer's Dementia (AAD)

Brexpiprazole is the only drug approved by the FDA for the treatment of Agitation related to Alzheimer Disease Dementia.

Insomnia due to AD

Suvorexant – FDA-approved medication

CMS GUIDE model of Dementia Care

- Guiding an Improved Dementia Experience (GUIDE)
- Care management and coordination
- Caregiver support and education
- Respite services (\$2,500 per year)

CMS: <u>https://www.cms.gov/priorities/innovation/innovation-models/guide</u>

CMS GUIDE model of Dementia Care

- Team based approach to dementia care
- Addresses needs of unpaid caregivers
- Adds patient care navigator to standard clinical team.
- Higher payments based on severity of dementia, presence or absence of a family caregiver and level of caregiver burden.

CMS: <u>https://www.cms.gov/priorities/innovation/innovation-models/guide</u>

Brain Health Tracking Tool

Brain Care Score. McCance Center for Brain Health. Massachusetts General Hospital. Freely available on the internet.

eBooks available upon email request

- *Dementia Prevention*. Abhilash Desai, MD and Faith Galliano Desai, PhD.
- Agitation Associated with Dementia Management without Antipsychotics. Abhilash Desai MD.
- Dementia Family Caregiver Wellness. Abhilash Desai, MD and Faith Galliano Desai, PhD.

Namaste

- Shukriyaa
- Dhanyawaad
- Muchas Gracias
- Merci
- Thank you

The new face of Alzheimer's

The story of Dr. Rebecca Chopp

- Diagnosed with early AD in 2019 at age 67.
- After the diagnosis, Dr. Chopp retired from her job as a chancellor of the University of Denver at the pinnacle of her career.
- She was also an ordained minister, prolific author and former president of Swarthmore College and Colgate University

- Neurologist told her she wouldn't be able to button her clothes or feed herself within two years.
- Today, she rises at dawn to take her dog for a walk, starts her daily routine of vigorous exercise and a strict diet, and is passionately involved in painting, is on the board of directors for Voices of Alzheimer's, (an advocacy group to promote the views of patients and try to gain access to treatments) she launched along with Mr. Gutis.
- She is currently working on a book entitled Art, Spirit, Body: Ways to Live While Dying from Alzheimer's.

- When she told her friends that she had been diagnosed to with earlystage Alzheimer's disease, her friends started talking more loudly. There was nothing wrong with her hearing.
- Dr. Chopp has stopped eating processed foods (e.g., potato chips) and sweets. She has adopted a vegetarian diet.
- Dr. Chopp "made" her husband (age 75) take ballet lessons with her.

- Her friend, Ann-Charlotte Grandholm-Bentley, the director of the university's Knoebel Institute for Healthy Aging provided her brain health and wellness guidance.
- She has stopped driving at night. Sometimes, she puts ice cream in the pantry and salad in the freezer.
- Dr. Chopp, while urging Medicare to cover Lecanemab, does not know whether she would use it. "I have had such good luck with lifestyle interventions" she said.

Joe's story

• Joe was almost 74. He was still working part-time. He noticed he was becoming more forgetful at work. He felt frustrated that it was so hard to find the right words to describe something. His boss told him that he missed a couple of meetings. He started to wonder if he had a serious problem.

• Joe's wife took him to get a complete health check-up. The doctor told Joe that he had mild cognitive impairment, also called MCI. Joe felt better knowing that there was no reversible cause that was being missed. He enthusiastically joined the group comprehensive brain wellness program at the local YMCA. Joe also started using memory tools such as daily to-do lists.

National Institute of Health. <u>https://www.nia.nih.gov/health/what-mild-cognitive-impairment</u> (with modification)

Valene and Patricia Campbell

- Valene Campbell's mom, Patricia (age 71) kept holding up the line at the airport and seemed strangely confused by the entire process of boarding (they were going to London).
- Baseline for Ms. Patricia "a very neat packer and a sense of style is everything to her"
- When Ms. Valene opened the suitcase, everything was in total disarray.
- A year later, Ms. Patricia diagnosed with Alzheimer's disease dementia.

• Lynya Floyd. Prevention. *Alzheimer's in Black and White.* September 2023.

Mitzi Miller and her mother

- When her mom (age 71) forgot to pick Ms. Mitzi (age 47, a TV executive in LA) up at the airport, she knew something was wrong.
- When Ms. Mitzi entered her mother's home, she found windows covered, aluminum foil over the electrical outlets, and a new laptop smashed.
- Her mother was paranoid and erratic.
- Her physician misdiagnosed her as having Schizophrenia and admitted for one month into a psychiatric inpatient unit. She had Alzheimer's Disease dementia. Her mother's mother had dementia.

• Lynya Floyd. Prevention. *Alzheimer's in Black and White*. September 2023.

Is AD a normal part of aging?

NO

• Pearls T. Cognitive trajectories and resilience in centenarians – findings from the 100-plus study. JAMA Network Open. 2021;4(1):e2032538.

Types of Alzheimer Disease Dementia

- Early onset (EOAD) (onset of dementia before age 65) vs Late onset (LOAD)
- Sporadic vs Familial (autosomal dominant; ADAD Autosomal Dominant Alzheimer's Disease)

• Alzheimer's Association. 2024 Alzheimer's Disease Facts and Figures.

ICD 11: Behavioral and Psychological Symptoms of Dementia

- 6D86.0 Psychotic symptoms in dementia
- 6D86.1 Mood symptoms in dementia
- 6D86.2 Anxiety symptoms in dementia
- 6D86.3 Apathy in dementia
- 6D86.4 Agitation or Aggression in dementia
- 6D86.5 Disinhibition in dementia
- 6D86.6 Wandering in dementia

Vascular cognitive impairment (VCI)

- Vascular contributions to cognitive impairment and dementia (VCID)
- Post-stroke dementia (within 6 months)
- Multi-infarct dementia
- Subcortical ischemic vascular dementia

• Iadecola et al. Vascular cognitive impairment and dementia. Journal of the American College of Cardiology 2019; 73:3326-3344.

Lewy body dementia (LBD)

- Chronic REM sleep behavior disorder
- Visual hallucinations
- Parkinsonism (within one year of dementia)
- Early visuospatial impairment

Lewy Body Dementia Association <u>https://www.lbda.org</u>

Skin biopsy for diagnosing synucleinopathies

- Syn-One[™] can help early diagnosis of synucleinopathies including PD and LBD.
- Medicare pays for this test.

- Han Y et al. Skin alpha-synuclein deposit patterns: A predictor of Parkinson's disease subtypes. eBioMedicine 2022. The Lancet discovery science.
- <u>https://cndlifesciences.com/introducing-syn-one-test/</u>

Blood test for Parkinson's disease (PD)

Plasma alpha synuclein assay may be able to detect PD up to 10 years before clinical diagnosis.

• Kiani L. Blood test for early Parkinson's disease. Nature Reviews. May 2024.

Frontotemporal dementia

- Behavioral variant (most common presentation is disinhibition and inappropriate behaviors)
- Language impairment variant (such as semantic dementia in which the meaning of the patient's speech is unclear; impaired fluency of speech)

• The Association for Frontotemporal Degeneration https://www.theaftd.org

What are the realistic expectations from Lecanemab and Donanemab ?

- "Slowing of cognitive and functional decline"
- Experts debate about whether the degree of slowing is worth the risks and costs (on the person, their family and society at large).
- No improvement of memory and other cognitive functions
- They are not a cure
- There is no cure
- In the Donanemab study, 29% of placebo group DID NOT decline over one year.

Risks and Harms of Lecanemab and Donanemab

- Physical harm in terms of brain bleeds and brain swelling, risk of seizures, strokes and death – especially in certain high-risk patients)
- Psychosocial harm: tremendous strain caregiver / family resources for the majority because of high burden of treatment (e.g., intravenous infusion every two-four weeks, periodic brain scans)
- Psychosocial harm: High anxiety with any development of headache or dizziness or confusion that may be thought to be due to the drug leading to rushing to ED

Decision making

- Patient and family will need lot of education and guidance regarding decision to take or not to take these drugs.
- It is a very emotional issue very difficult for patients and their family to be rational and wise.
- Takes 1-5 hours of physician time to do a good job of education and guidance.

DICE approach

- Describe
- Investigate
- Create
- Evaluate

 The DICE approach online training program for caregivers to better manage agitation in individuals with dementia. <u>https://diceapproach.com</u>

Caregiver training in De-Escalation

- University of Washington STAR-Caregivers: A standardized intervention
- <u>https://www.caregiver.org/resource/star-c-managing-difficult-behaviors/#</u>

Post Diagnostic Dementia Support - PDS

- The Next Steps: Dementia Post-Diagnostic Support Guidance (Ireland)
- The 5 Pillar Model of Post Diagnostic Support (Scotland)
- Life After Diagnosis (USA)
- No PDS for special populations (e.g., ASD, IDD)

Websites created and managed by individuals with ADRD

- Voices of Alzheimer's <u>https://www.voicesofad.com</u>
- National Council of Dementia Minds <u>https://dementiaminds.org</u>

Website – Caregiver education

The Aliviado Health program (from the Hartford Institute for Geriatric Nursing at New York University Rory Meyers College of Nursing) trains long-term care and hospice team members in dementia care principles. <u>https://aliviado.org</u>

Website – Virtual team care UCSF

- The Care Ecosystem. UCSF Memory and Aging Center. https://memory.ucsf.edu/research-trials/professional/care-ecosystem
- Trains care team navigators in dementia care
- Embeds navigators within a clinical team with dementia-specific care protocols

Website – IDD, ASD and Dementia

National Task Group on Intellectual Disabilities and Dementia Practices. <u>https://www.the-ntg.org/autism-and-dementia</u>

Website – IDD, ASD and Dementia

Examining Adults with Neuroatypical Conditions for MCI/Dementia During Cognitive Impairment Assessments – Report of the Neuroatypical Conditions Expert Consultative Panel. The National Task Group on Intellectual Disabilities and Dementia Practices and the LuMind IDSC Foundation. https://www.the- ntg.org/screeningassessment. [Revision V. June 27, 2022]. Janicki, M.P., Hendrix. J., & McCallion, P., and Neuroatypical Conditions Expert Consultative Panel. (2022). https://www.the-

ntg.org/ files/ugd/8c1d0a 40b5805be7a44ef39684898913e49466.pdf



GeriPal – A Geriatrics and Palliative Care Podcast by geriatricians Dr. Alex Smith and Dr. Eric Widera. UCSF. December 2, 2022. Transforming the culture of dementia care: Podcast with Anne Basting, Ab Desai, Susan McFadden and Judy Long. One hour.

Saint Alphonsus Wellcast (Podcasts)

- Unlocking the Mind: Exploring Modifiable Risk Factors for Dementia. 16 minutes. 6/15/23
- Ageism: Combating common myths surrounding aging. 17 minutes.
 7/27/23

Confronting Reality – Atul Gawande

We're caught in a transitional phase. However miserable the old system has been, we are all experts at it. We know the dance moves. With this new way, in which we together try to figure out how to face mortality and preserve the fiber of a meaningful life with its loyalties and individuality, we are plodding novices. We are going through a societal learning curve, one person at a time.

Book: Being Mortal – Medicine and What Matters in the end.

Success stories

- Scotland: Anyone in Scotland receiving a diagnosis of dementia is entitled to at least one year's post-diagnostic support from a named and trained person called a Dementia Link Worker (or similar job title).
- Cognitive screening is a mandatory requirement of the driver's license renewal process for older people in Japan, while walk-in clinics are available for screening and consultation in memory centers in Korea. The emergence of telecare-enabled specialist support has helped to empower PCP sites in the United States.
- Hep C curable. One pill a day for 12 weeks. \$25K. Egypt eradicated it. Made their own pill – copyright issues. Hep C causes liver failure, liver cancer, inflammation, CKD, diabetes. Two companies make the pill. NETFLIX strategy.