Annual Meeting Syllabus

Saturday November 7 – Sunday November 8
Dallas Renaissance Hotel

Includes presentations available at time of print
Increasing Market Pressure and Cost is Driving VBP

Federal

State

Commercial


<table>
<thead>
<tr>
<th>Volume to Value</th>
<th>2016</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Track 1: Value-based payments</td>
<td>65% of all Medicare payments</td>
<td>90% of all Medicare payments</td>
</tr>
<tr>
<td>Track 2: Alternative payment models</td>
<td>30% of all Medicare payments</td>
<td>50% of all Medicare payments</td>
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Focus Areas

**Incentives**
- Promote value-based payment systems
  - Test new alternative payment models
  - Increase linkage of Medicaid, Medicare FFS, and other payments to value
  - Bring proven payment models to scale

**Care Delivery**
- Encourage the integration and coordination of clinical care services
- Improve population health
- Promote patient engagement through shared decision making

**Information**
- Create transparency on cost and quality information
  - Promote HIT at the point of care with meaningful use
Major Commercial Payor Developments Nationally

Movement toward consumer driven health plans and payment models
Retail Health Care and New Technologies e.g. CVS, Wal-Mart clinics, telemedicine

Growth in Provider Sponsored Health Plans
Medicaid Managed Care/ACOs

Payers Building Delivery Systems
- Highmark ---- purchases seven hospitals/physician practices
- Cigna --------- Primary Care Network (PCNM) – Phoenix
- United ------ Healthcare Monarch physicians group (2,300 physicians)
- Aetna ------- purchases Active Health
- DaVita -------- acquires Healthcare Partners

Partnering with MSSP ACOs
- UniversalAmerican (34 MSSPs)
- Alignment (5 ACO’s), e.g. AdvoCare and SAE, e-1 Arizona Priority Care ACO

Components of New Payment Models
- Transformational funding e.g. funding ACO start-up cost
- Care management
- Shared Savings

Early Adopters include the Following
- Regional Blue Cross plans (WI, MA, IL, HA, etc.)
- Aetna, Cigna, Humana, etc.

Value Based Payment Models Provide a Path to Full Accountability

The Methodist Patient Centered ACO (MPCACO) is a physician-led program that benefits patients, physicians, the health system and the communities we serve. Created in 2012, the MPCACO was designed to:

- IMPROVE - Improve the quality and coordination of health care to the communities served by Methodist Health System
- ENHANCE - Enhance patient experience with a coordinated patient-centered model focused on quality, value, and service
- SHARE - Share savings with Methodist and the physicians who participate in programs operated by the MPCACO
- CONTRACT - Demonstrate success to payors and employers

Core Competencies
- Data Analysis/Spending Identification
- Physician Engagement
- Post-Acute Quality and the Provider Network
- Risk Stratification and benchmarking, Resource Matching
- Collection of GPRO Quality Metrics
Medicare Shared Savings Program
- 15,000 attributed Medicare beneficiaries
- >350 total participating physicians
- Top-quartile performance on 33 quality metrics including CAHPS patient experience
- Incentivized performance improvement across the continuum
- Generated $12.7 million year 1, $12.6 million in year 2
- 1 of 52 out of 220 nationally to qualify for shared savings
- 13th in overall quality ranking

Physician Led
- 10 physician Governing Board (with admin and beneficiary participation as well)
- Committees: Governance and Nominating, Finance, Clinical Oversight, Care Coordination

Professional Support Staff
- 1 Clinical Director, 1 LCSW, 2 Health Coaches, 2 Clinical Coordinators
- 4 Population Health Managers, 8 Beneficiary Care Navigators
- et. al.

Data/Expenditure Analysis

<table>
<thead>
<tr>
<th>Expense for MPCA</th>
<th>Assigned Beneficiaries</th>
<th>All MSSP ACOs</th>
<th>Impact of 5% Cost Reduction</th>
<th>Impact of Reaching MSSP Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>$11,494</td>
<td>$9,684</td>
<td>$7,308,138</td>
<td>$21,236,584</td>
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<tr>
<td>ESRD</td>
<td>$68,541</td>
<td>$56,829</td>
<td>$970,942</td>
<td>$4,040,411</td>
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<tr>
<td>Inpatient</td>
<td>$3,550</td>
<td>$3,280</td>
<td>$1,257,938</td>
<td>$6,455,161</td>
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<tr>
<td>Part B Physician</td>
<td>$3,318</td>
<td>$3,113</td>
<td>$2,159,638</td>
<td>$2,604,171</td>
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<tr>
<td>Skilled Nursing</td>
<td>$1,088</td>
<td>$891</td>
<td>$692,058</td>
<td>$2,509,422</td>
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<tr>
<td>Home Health</td>
<td>$1,664</td>
<td>$527</td>
<td>$1,058,028</td>
<td>$14,462,779</td>
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</tbody>
</table>

Home health alone could generate over 3x the savings as compared to inpatient expenses

HHC and SNF Quality Measures

Home Health Agencies
- Care initiated within 48 hours of at least 96% of the time
- Patients’ wounds improved/healed of at least 86% of the time
- Patients required hospital admission less than 17% of the time
- Patients required hospital admission less than 20% of the time

Skilled Nursing Facilities
- Average readmissions <13%

Referrals
- 90% sufficiency
- Discharge to Community Percentage
- Discharge to Acute Percentage
- Measures within 5% of national average

Data review of quality measures
- Quarterly meetings
- Measures evaluated annually
- Lists published 2x year
- Distribution to stakeholders
Physician Engagement

Monthly Newsletter — detailing MPCACO news and resources
Nurse Navigators — providing communication between providers and allied services
Population Health Management — gap closure activity and risk assessment

Distribution of shared savings keyed to published metrics:
- Minimum quality scores in prevention and diabetes
- Attendance at “Learning Collaboratives” on quality and performance
- Completion of POSA performance improvement projects utilizing measurable data
- Engagement in committees
- Use of a certified EHR

NCQA PCMH level 3 recognition and BTE recognition of most primary care practices, extended hours, open access, population health management

Quality review performed by EHR review and DMPN (physician credentialing group) and individual providers provided with reporting and guidance on performance.

Quality Provider Network

Risk Stratification and Resource Matching

- All patients do not need the same amount of help and support
- Systems and standardized approaches can be designed which are most appropriate for the patients’ needs
- High risk patients are the ones who are most likely to benefit from intense care management
- High risk patients tend to generate the highest costs for the system; therefore, provide the most opportunity for cost savings (80/20)
- Pro-active care management and tracking of high risk patients keeps them from “falling through the cracks” or getting lost in the system
Nurse Navigators

- Risk stratification of entire population
- Nurse navigation based upon medical complexity
- Personalized navigation
  - Work collaboratively and maintain active communication with physicians, nursing, and other members of care-team to execute a care plan
  - Attend physician visits, communicate with patients between visits
  - Provide follow-up during transitions of care
  - Medication reconciliation during transitions of care
  - Advanced directives
  - Social services e.g. meals on wheels, transportation vouchers, scales for CHF patients, engaged family and neighbors

Collection of GPRO Quality Metrics

- 357 ACOs reporting data across the country
- 22 measures in 15 modules
- Each ACO is required to report on the first 411 consecutively ranked and assigned beneficiaries for each of the 15 modules
- MPCACO reported on 8,077 denominator elements

MSSP Performance Year 2 Performance

Market Comparison

<table>
<thead>
<tr>
<th>ACO</th>
<th>Legal Business Name</th>
<th>Score</th>
<th>Total Assigned Beneficiaries</th>
<th>Denominator Services Methodologies</th>
<th>Aggregate Beneficiaries</th>
<th>Non-Beneficiary Utilization Impact</th>
<th>Financial Shared Savings</th>
<th>3M Change</th>
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<tbody>
<tr>
<td>1st</td>
<td>Methodist Patient Centered ACO</td>
<td>85.12%</td>
<td>12,612,997</td>
<td>$5,260,901</td>
<td>87.61%</td>
<td>14.94</td>
<td>27.43</td>
<td>87.47</td>
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<tr>
<td>2nd</td>
<td>Physicians ACO</td>
<td>74.84%</td>
<td>13,222,555</td>
<td>$4,849,165</td>
<td>79.51%</td>
<td>15.07</td>
<td>30.66</td>
<td>11.26</td>
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<tr>
<td>3rd</td>
<td>Genesis Accountable Physician Network, LLC</td>
<td>74.84%</td>
<td>10,920,532</td>
<td>$5,351,061</td>
<td>84.10%</td>
<td>15.47</td>
<td>48.76</td>
<td>16.67</td>
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<tr>
<td>4th</td>
<td>UT Southwestern Accountable Care Network</td>
<td>76.25%</td>
<td>6,010,275</td>
<td>$2,945,035</td>
<td>81.04%</td>
<td>14.81</td>
<td>70.76</td>
<td>25.25</td>
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</table>

Methodist Patient Centered ACO 2nd year to achieve shared savings
Renewal application successfully submitted August, 2015 for 3 years
New ACO Partnerships and Commercial Contracting Opportunities

Collaborative Accountable Care

- An experienced, successful clinically integrated network of physicians leading the way in improving healthcare
- Single agreement contracting ability
- Easing the burden of government regulations and requirements
- Physicians provide the intellectual capital and change agency necessary to efficiently deliver exemplary patient care in a new era
- Access to IT, personnel, and operational support

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Where physicians lead the way in improving health care
Creating a Clinically Integrated Accountable Care Organization For Independent Physicians

November, 2015

Keeping Independent Physicians Strong

• Payors are driving change from traditional FFS to value-based, shared savings, and risk contracting
  • Decreasing FFS rates on traditional IPA contracts
  • Increasing FFS rates and incentives on ACO contracts
• Independent physicians are building Clinically Integrated Networks
• Independent physicians are entering into Accountable Care Organization (ACO) contracts

Keeping Independent Physicians Strong

• In 2-3 years ACO contract participation will be required to stay financially viable (replace loss of traditional FFS rates)
• Clinically Integrated Networks (ACOs) are the only mechanism that allows a network of Independent Physicians to negotiate FFS rates
• What are your options as an independent physician?
  • Join a hospital-based ACO
  • Join a physician-led ACO
The Basics of Shared Savings Contracts

- **Patient Population:** Based on historic visits and claims the payer assigns/attributes covered patients to a group of participating PCP physicians.

- **Three Types of Physician Payments:**
  1. Physicians still receive traditional FFS reimbursement
  2. Shared Savings Payments - if the cost of care for the assigned population is less than projected costs (risk-adjusted + inflation)
     - Payer splits some portion of the savings (% differs by contract)
  3. ACO offers financial incentives for quality reporting, quality improvement, and other process changes

Example: Shared Savings or Capitated/Risk Contracting

<table>
<thead>
<tr>
<th>Payor</th>
<th>ACO Risk Common</th>
<th>ACO/Clinically Integrated Network</th>
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</thead>
<tbody>
<tr>
<td>PCP</td>
<td>$800</td>
<td>$2,100</td>
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<tr>
<td>SCP</td>
<td>$5,300</td>
<td>$1,000</td>
</tr>
<tr>
<td>Hosp</td>
<td>$10,000</td>
<td></td>
</tr>
<tr>
<td>Post</td>
<td>$100</td>
<td></td>
</tr>
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</table>

Total Costs:

- Greater than budget creates a loss, leading to reduced provider payments.
- Less than budget creates a savings, leading to provider bonuses.
An ACO’s Quality Score Comparison - 2014

MSSP Contract – GAPN 2014/2015
Cost & Utilization Trend*

MSSP Contract - GAPN 2014/2015
Inpatient Utilization Trend*

*Data Reported by CMS for GAPN’s 2014 Performance Trend for 16,000 Medicare patients
*Data Reported by CMS for GAPN’s 2015 Performance Trend for 12,000 Medicare patients
MSSP Contract - GAPN 2014/2015
Post-Acute Utilization Trend*

*Data Reported by CMS for GAPN's 2014 Performance Trend for 16,000 Medicare patients
*Data Reported by CMS for GAPN's 2015 Performance Trend for 12,000 Medicare patients

MSSP Contract – GAPN 2014/2015
High Cost Radiology Utilization Trend*

*Data Reported by CMS for GAPN's 2014 Performance Trend for 16,000 Medicare patients
*Data Reported by CMS for GAPN's 2015 Performance Trend for 12,000 Medicare patients

MSSP Contract Performance:
TX ACOs in 1st Year of Performance-2014

"54% of Texas 1st Yr. ACOs Reduce Costs!"
MSSP Contract Performance – N.Texas
ACOs in 1st & 2nd Year of Performance

An ACO’s Financial Distribution of Shared Savings: 2014

- 82 Physicians with Attributed Patients
  - 122 Physicians (Specialists) without Attributed Patients
- The Top Physician Bonus:
  - $88,186 with 762 Patients
  - 78.6% Quality Performance Score
  - 66% Participation Score
- The Lowest Physician Bonus:
  - $2,979 with 16 Patients
  - 52.9% Quality Performance Score
  - 33% Participation Score
- Median Physician Reward: $11,473

An Independent Physician’s ACO Pivot:
UT Southwestern Accountable Care Network
Affiliating to sustain clinical integration * momentum!

UTSW Faculty Physicians
1,600
Community PCPs (UTSCAP)
175
Genesis IPA (PCP & Specialist ACO Members)
400
MSSP + 5 Commercial ACO Contracts
5
Square miles in North Texas
400

*Contracting; IT Services; Practice Transformation; Care Team Support; Etc.
What is mindfulness?

Present moment awareness

“Paying attention to something, in a particular way, on purpose, in the present moment, non judgmentally”

Kabat-Zinn, 2003

What is mindfulness

Historically Buddhist, but in reality it constitutes a more universal human capacity that fosters clear thinking and openheartedness

In medicine one of the aims is to take greater responsibility for one’s life choices

Part of the professional development of physicians, it helps with effective decision making, reducing medical errors

JAMA 2008

JAMA, September 17, 2008
Benefits

Don’t be put off by the word “meditation.”

Think about it as becoming better at dismissing distracting thoughts.

Be fully present.

When we aren’t present it makes us feel dissatisfied

Leads to doubt and loneliness

Our mind checks out and goes to the past or the future

We endlessly replay errors of our past criticizing ourselves and blaming ourselves repeatedly

This ironically leads to more anxiety

When we allow the mind to rest in the Present we conserve energy. Our mind remains fresh and open and ready to respond

Benefits

Decreased perception of pain therefore decrease use of analgesics and consequently, decrease in toxic effects

Increased ability to tolerate pain or disability

Reduced stress anxiety or depression

Increase motivation to make lifestyle changes

Enriched interpersonal relationships

Alterations in biological pathways including the autonomic nervous system, neuroendocrine function and immune system

JAMA 2008
Why are we interested

- The goal of mindfulness is to maintain awareness moment to moment
- Disengaging from strong attachments to thoughts or emotions
- Developing a greater sense of emotional balance and well-being
- Promotes neuroplasticity

Brain structures relevant to Mindfulness

<table>
<thead>
<tr>
<th>Prefrontal cortex</th>
<th>Amygdala</th>
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<tbody>
<tr>
<td>Planning</td>
<td>Processing of emotions</td>
</tr>
<tr>
<td>Organizing</td>
<td>Autonomic responses</td>
</tr>
<tr>
<td>Regulates attention</td>
<td>Fear</td>
</tr>
<tr>
<td>Decision making</td>
<td>Hormonal secretion</td>
</tr>
<tr>
<td>Motivation</td>
<td></td>
</tr>
<tr>
<td>Moderates behavior</td>
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Mindfulness is associated with changes in the brain when confronted with stress we have an emotional reaction that perseverates. In the brain this is expressed as prolonged activation of the amygdala.
Changes in the Brain

Mindfulness is associated with prefrontal cortex activation (PFC)
reduced bilateral amygdala activity
the PFC activation inhibits the limbic system and may disrupt automatic affective responsiveness
Cresswell et al. Psychosomatic Medicine 69:560-567

The hippocampus plays a central role in mediating some of the benefits of meditation, due to its involvement in the modulation of cortical arousal and responsiveness.

The hippocampus also contributes to the regulation of emotion (Corcoran and Maren, 2001; Corcoran et al., 2005; Milad et al., 2007)
The structural changes in this area following mindfulness practice may reflect improved function in regulating emotional responding.

What 's going on in the brain?

Mindfulness practice leads to increases in regional brain gray matter density
Britta K. Hölzel*,a,b, James Carmodyc, Mark Vangel a, Christina Congleton a, Sita M. Yerramsetti a, Tim Gard a,b, and Sara W. Lazar a

a Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
b Bender Institute of Neuroimaging, Justus Liebig Universität Giessen, Germany
c University of Massachusetts Medical School, Worcester, MA, USA

Abstract
Therapeutic interventions that incorporate training in mindfulness meditation have become increasingly popular, but to date, little is known about neural mechanisms associated with these interventions. Mindfulness-Based Stress Reduction (MBSR), one of the most widely used mindfulness training programs, has been reported to produce positive effects on psychological well-being and to ameliorate symptoms of a number of disorders. Here, we report a controlled longitudinal study to investigate pre-post changes in brain gray matter concentration attributable to participation in an MBSR program. Anatomical MRI images from sixteen healthy, meditation-naive participants were obtained before and after they underwent the eight-week program. Changes in gray matter concentration were investigated using voxel-based morphometry, and compared to a wait-list control group of 17 individuals. Analyses in a priori regions of interest confirmed increases in gray matter concentration within the left hippocampus. Whole brain analyses identified increases in the posterior cingulate cortex, the temporo-parietal junction, and the cerebellum in the MBSR group compared to the controls. The results suggest that participation in MBSR is associated with changes in gray matter concentration in brain regions involved in...
A longitudinal study of gray matter changes associated with a mindfulness-based intervention.

To identify brain regions that changed in association with participation in an eight-week Mindfulness-Based Stress Reduction course (MBSR; Kabat-Zinn, 1990).

The MBSR program consists of eight weekly group meetings

Lasting two and a half hours each

One full day (6.5 hours) during the sixth week of the course.

All participants were scanned during the 2 weeks before (Pre) and after (Post) participation in the program.

Control participants were also scanned twice, approximately two months apart.
Changes in the Brain and immune function

Abstract:

Aim: To investigate changes in brain and immune function produced by mindfulness meditation.

Methods:

1. A randomized controlled trial was conducted among 60 healthy volunteers. Participants were randomly assigned to either a mindfulness-based stress reduction (MBSR) group or a control group. The MBSR group received an 8-week intensive program of mindfulness meditation, including group sessions, individual sessions, and daily practice.

2. The immune function was assessed by measuring the levels of cytokines and immune cells before and after the intervention.

Results:

The results showed a significant increase in the levels of cytokines and immune cells in the MBSR group compared to the control group. The changes in the brain function were also observed, with a significant increase in connectivity between the prefrontal cortex and the hippocampus.

Conclusion:

The findings suggest that mindfulness meditation may change brain and immune function in a positive manner, and contribute to the treatment of anxiety disorders.
The default network

**Effects on the brain**

Different kinds of “networks” in the brain for different kinds of experiences

The Narrative Focus (NF) = rumination and worry

The Experiential Focus (EF) = grounding without so much rumination

**Automatic thought and self-referential thinking**

According to cognitive neuroscience we have two types of mental processes
controlled and automatic

Automated thoughts are initiated unconsciously and are not easy to interrupt (Raz et al. National Rev of neuroscience 2006)

When attention drifts away the default mode network (DMN) is activated

Objective awareness of automatic thoughts is a mechanism by which mindfulness decreases symptoms of depression, anxiety and stress.
Meditation affects decision making.

Behavioral evidence suggests that meditation related interventions can increase sensitivity to thoughts, sensations and feelings.

It can lead to more sustained attention, cognitive flexibility and working memory.

Decreases rumination, negative automatic thinking and habitual responding.

Thus, with short or long-lived intentions, meditation can help decision makers to reach conclusions with more reflective consideration.

Enhanced efficiency of the anterior cingulate cortex (ACC).

Enhanced efficiency of the anterior cingulate cortex (ACC).

The basic process of mindfulness

Notice: the thought
Accept it without judgment
Dismiss it without engaging
Return your attention back to the target
Repeat

Basic process of mindfulness

1. Set your intention to pay attention
2. Select something to pay attention to: breath
3. Notice everything about your breathing
4. Notice now that you are being distracted by thoughts
5. Acknowledge this thought
6. Don’t judge it
7. Just let it go
8. Gently return your attention to your breathing
9. Repeat this exercise for about 1 to 2 minutes
   you can increase the time gradually
Common obstacles

- I didn’t have time
- I can’t stay focused
- I don’t know how to do it right
- This doesn’t work for me
- I fell asleep
- Mindfulness is too “religious” for me
- I felt silly doing it
- It’s boring
- I don’t see how this could possibly help me

Basic relaxation breathing

Breathing technique that is very helpful deactivating the stress response

Deep breathing or diaphragmatic breathing: relaxation breathing

Abdominal breathing

- Place one hand on your navel and one on your chest
- Relax your abdomen
- Breathe in through your nose and fill your lungs
- Allow your lungs to expand downward and move the bottom hand
- Avoid shallow chest breathing or raising your shoulders
- Exhale through the mouth
Core Practice

• Pause → listen → Breathe
• find yourself a comfortable position
• close your eyes
• pay attention to your breathing
• breathe slowly through your nose and out the mouth
• imagine the air slowly filling your lungs and body and slowly flowing out again
• when you notice your mind wandering, acknowledge it, and then bring your attention back to the breath
• notice your abdomen moving as you take slow abdominal breaths
• continue for one minute
• open your eyes and return to the room

Beginning a sitting meditation practice

• sit down on a chair, or on a cushion on the floor
• make sure you are comfortable and have enough room in your chest and abdomen to breathe
• focus your attention on your breath; find the places in your body where you are most aware of the breathing sensations
• don’t try to change your breath; just turn your attention to the breath
• rest your attention in the constantly changing sensations of the breath
• each time your mind wanders away from the awareness of breath, GENTLY bring it back

Mindfulness of emotions

• There are three basic components to an emotion to be mindful of
  • Thoughts
  • Physical sensations
  • Emotional mood or tone in the mind
Awareness of the emotion process
• notice the feeling and how it shows in your body
  • observe it: pleasant/unpleasant
  • accept it: don’t judge it
  • stay present with it: don’t fight it
  • don’t identify with it: you are not the emotion
  • identify the trigger for this emotion

mindfulness on the go ....
Use of the non dominant hand teaches us laughter, patience, compassion for anyone who is unskilled
When eating, just eat when eating or drinking don’t do anything else
Sit down and enjoy
Appreciate: color, textures, smells, flavors
Listen to sounds
Listen to obvious sounds and subtle ones
This is a potent way of quieting the mind
Disengaging from the endless ruminations
Waiting

Just before his enlightenment the Buddha described the qualities of the mind that he had developed over many years his mind had become
Concentrated
Purified
Unblemished
Malleable
Rid of imperfections
Imperturbable
“If we are to make peace in the world, we must first make peace in ourselves”

The Dalai Lama
HPI

CC: SOB

50 year old Caucasian male
- SOB x6 weeks, worsening
- Dry cough x2 months, recently worsened → coughing fits → vomiting
- Cough productive of milky yellow sputum x1 week
- Slept on right to improve SOB and pleuritic pain.
- Night sweats, 30-40 lb weight loss in 5 months, decreased appetite, subjective fevers

HPI

- 30 days prior to admission presented to OSH for coughing fits. CXR unremarkable. Sent home with 14 day course of Bactrim for UTI.

+ROS: chills, orthopnea, LE edema, sick contact (granddaughter)
- ROS: dysuria, hematuria, hemoptysis
History

PMH: none except recent UTI

PSH: none

Home medications:
- Completed a 14 day course of Bactrim a month ago for UTI
- Ibuprofen prn

Allergies: NKDA

History

Family:
- mother: brain tumor
- father: lung CA (heavy smoker)

Social:
- tobacco: denies
- alcohol: denies
- drugs: denies

Works as a truck driver; on the road for weeks at a time. Lives with wife. Has not gone to doctor in about 20 years.

Physical Exam

HR 94
BP 127/62
RR 28
Temp 97.9
O2 sat 98% on 2 L NC

Gen: ill-appearing Caucasian male lying on R side in NAD
HEENT: PERRL, EOMI, MMM, poor dentition
Neck: supple, no LAD, no JVD
CV: tachycardic, regular rhythm, no m/r/g
Chest: decreased breath sounds on R, CTA on left, tachypneic, no accessory muscle use
Abd: +BS, soft, NT, ND
Ext: 1+ pitting edema, no cyanosis, no clubbing
Neuro: AAOx3, CN II-XII grossly intact
Labs

<table>
<thead>
<tr>
<th>CMP</th>
<th>CMP</th>
<th>CBC</th>
<th>Differential</th>
<th>Miscellaneous</th>
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<tbody>
<tr>
<td>Na 135</td>
<td>Gluc 124</td>
<td>WBC 19.8</td>
<td>Segs 53%</td>
<td>Globulin 6.2</td>
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<td>K 4.8</td>
<td>Ca 8.7</td>
<td>HB 10.6</td>
<td>Bands 8%</td>
<td>HbA1c 5.8</td>
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<tr>
<td>Cl 105</td>
<td>Albumin 2.5</td>
<td>HCT 31.6</td>
<td>Lymphs 16%</td>
<td>Lactate 2.3</td>
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<tr>
<td>Bicarb 20</td>
<td>T bil 1.7</td>
<td>Platelets 394</td>
<td>Mono 7%</td>
<td>ESR 85</td>
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<tr>
<td>BUN 39</td>
<td>Alb. Pn 0.95</td>
<td></td>
<td>Ery 0%</td>
<td>CRP 15.9</td>
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<tr>
<td>Cr 2.6</td>
<td>AST/ALT 14/15</td>
<td></td>
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</tr>
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</table>

UA: specific gravity >1.030, pH 5.5, trace protein, negative blood/glucose/ketones, positive bil, urobilinogen 4.0, negative nitrite, trace leukocyte esterase
Microscopic urine: RBC 5-10, WBC 90-100, epith cells few, hyaline casts 10-15, bacteria light
UCx: negative

CXR

Large right pleural effusion with leftward tracheal deviation.

Hospital Admission

- Cultured and started on vanc, Zosyn, Levaquin
- Failed bedside thoracentesis
- CT chest/abdomen/pelvis
- Renal US for AKI
Renal US

Right kidney shows chronic severe hydronephrosis. Debris within the collecting system is nonspecific and could be infectious, hemorrhagic, or proteinaceous debris. Therefore, pyonephrosis is a consideration. Shadowing calculi and a possible staghorn calculus.

CT

1. Nephrolithiasis with multiple hypodense cystic structures within the right kidney. There is necrosis into the right psoas muscle, which likely represents a perinephric abscess.
2. Large right pleural effusion with complete atelectasis of the entire right lung.
3. Cholelithiasis and biliary sludge.
4. Note pattern of right kidney which is a “classic” finding.

Hospital Course

- **HD1:** IR for thoracentesis (2 L cloudy yellow fluid) and nephrostomy tube
  - Pleural fluid grew E. coli; consistent with exudative process
  - Urine from nephrostomy grew E. coli (10,000-50,000 CFU/ml)
  - Urology, pulmonary, CTS consulted
  - Urology recommends outpatient nephrectomy
- **HD4:** VATS, mini thoracotomy, decortication, and placement of chest tubes x2 (3.5 L purulent fluid removed).
  - Cr 1.9 in pleural fluid
  - Cultures negative
Hospital Course

- HD7: ID recommends narrowing antibiotics to Rocephin. PICC placed for prolonged course of abx.
- HD9: chest tubes removed
- HD9: Discharge planning for outpatient Rocephin and nephrectomy in two weeks.
- HD12: EGD

EGD

Dieulafoy’s lesion in duodenal bulb; injected with epi and clipped x5

Hospital Course

- High risk for rebleeding. H/H remained stable. GI cleared for discharge.
- Repeat CT for worsening CXRs
Abscess in the right retroperitoneum is not significantly changed. Superior aspect of the abscess tightly abuts the right hemidiaphragm with a suspected fistulous connection to the right pleural space.

Hospital Course

- Urology reconsiders
- HD21: radical nephrectomy, drainage of psoas abscess, open cholecystectomy (inflamed and edematous GB)

Hospital Course

- HD27: discharge with close follow-up
- Pathology from kidney confirmed diagnosis
Pathology

Lymphoplasmacytic infiltrate effacing the normal kidney parenchyma. Prominent thickening of the arterioles. Greater than 75% of the glomeruli demonstrate global sclerosis.

Pathology

Lipid laden macrophages

Xanthogranulomatous Pyelonephritis (XGP)

- Rare form of chronic pyelonephritis
- First described in 1916
- Typically unilateral in the setting of chronic obstruction from stones
- Common pathogens: E. coli, Proteus mirabilis, Klebsiella, Enterococcus, Pseudomonas
Presentation

- Symptoms:
  - Most common: flank pain, fever
  - Common: malaise, weight loss, anorexia, palpable mass
  - Less common: dysuria, increased urinary frequency
  - Rarely: hematuria, sepsis
- PE: may have palpable, tender, unilateral flank mass
- Labs: anemia, leukocytosis, elevated ESR
- Urine: pyuria, bacteriuria; cultures sterile in 25-35%

Who gets it?

- More common in women (2.5:1)
- Middle age (47-61)
- Predisposing factors
  - Recurrent UTIs
  - Obstruction
  - ? Diabetes/immunocompromised state

Differential Diagnosis

- Renal cell carcinoma
- Nephrolithiasis
- Pyonephrosis
- Perinephric abscess
- Renal TB
Diagnosis: Imaging
- CT scan is preferred method for diagnosis
  - Enlarged kidney, hydronephrosis, retained contrast
  - Renal stones (simple or staghorn)
  - Round, low density areas surrounded by enhanced rim of contrast (dilated calyces with debris/purulence) ("bear claw" sign)
  - Will show extent of involvement (fistula?)

Diagnosis: Pathology
- Gross pathology: enlarged necrotic kidney with stones
- Histopathology: lipid filled macrophages
  - Inflammatory necrosis of pericalyceal fat → cannot drain from obstructed kidney
  - Phagocytic disturbance → impaired bacterial degradation

Complications
- Psoas muscle abscess
- Fistula
  - Usually to colon or duodenum
  - Less commonly to lung, skin, spleen
Treatment

- Radical nephrectomy and antibiotics
- Good prognosis if infected kidney resected

References


Meyrier A. Xanthogranulomatous pyelonephritis. UpToDate.


Heart of Darkness

Putting Together the Puzzle
Typical and Atypical Presentations of Disease

Evaluation of Apparent Incongruent History

Treating the Underlying Disease Process

History of Present Illness

50 year old Caucasian Female
CC: “I hurt my back during yoga”
Inability to perform the stretches
Lower extremity numbness
Weakness in the left leg and moving to the right leg

Associated Symptoms:
- Visual aura
- Handwriting changes
- Dyspnea on exertion
- Subjective fever
- Fatigue
- 10 lbs. weight loss

Very active: stopped daily cardio workouts in favor of yoga
Now uses a cane
Medical History

Past Medical History
- Hypothyroidism
- Asthma

Past Surgical History
- Hysterectomy

Social History
- Noncontributory

Family History
- Noncontributory

Medications
- Levothyroxine 50 mcg by mouth once daily
- Metoprolol succinate 25 mg by mouth once daily
- Montelukast 10 mg by mouth once daily
- Albuterol rescue inhaler

Allergies
- NKDA

Physical Exam

Vital Signs
- Temp: 96.4° F (35.8° C)
- HR: 60 bpm
- BP: 114 mmHg/68 mmHg
- RR: 16 bpm
- Pulse Ox: 95% RA

General: healthy middle aged woman

Neck: supple, no lymphadenopathy noted, no jugular venous distension

Chest: S1, S2, an extra sound noted in diastole over the left 5th intercostal space

Lung: breath sounds were noted to be clear bilaterally without rhonchi or wheezes

Abdomen: soft, non-tender to palpation, bowel sounds auscultated

Neurological Exam

Neuro:
- Alert, oriented to person, place, time, and situation
- CN II-XII intact
- Speech fluent
- Sensation diminished to fine touch distal to left knee, intact in remaining 3 extremities

Strength:
- Plantar flexion: 4/5 bilaterally
- Dorsiflexion: 3/5 bilaterally
- Knee flexion/extension: 4/5 bilaterally
- Hip Flexion: 2/5 bilaterally
- 3/5 strength in bilateral upper extremities
- Unable to stand or ambulate
- Reflexes: 2/4 upper extremities, 3/4 lower extremities
MRI Brain and Spine

Echocardiogram

- Occult Primary Tumor
- CUP (Cancer of Unknown Primary)
- Estimated 30,000 – 50,000 cases per year
- 2% of all cancer diagnoses
**Biopsy:** positive S100 and HMB-45 markers consistent with metastatic melanoma

**Melanoma at Presentation**
- Cutaneous: 91.2%
- Ocular: 5.2%
- Mucosal: 1.3%
- Unknown primary: 2.2%

**Treatment for Metastatic Melanoma**
- Surgical Metastasectomy
- Radiation
  - Palliative therapy
- Immunotherapy
  - Interleukin-2
  - Anti-PD-1, Anti-CTLA-4
- MAPK Inhibition (BRAF)

**Patient Follow Up**
- **Skin Exam:** no abnormal nevi noted
- **Eye Exam:** normal fundal exam
- **Oral, Genital Exam:** no abnormal lesions
- **BRAF mutation:** positive

- Vemurafenib (BRAF inhibitor)
- Palliative Radiation
  - Brain and Spine
- Aggressive Physical Therapy
- 6 month follow-up
  - Ambulating with walker
Response

Presentation 6 Month Follow Up

Response

Presentation 6 Month Follow Up

Review

Unexpected Presentation of Metastatic Melanoma

Evaluation of an Occult Primary Tumor

Melanoma Treatment Modalities
References


NCCN Clinical Practice Guidelines in Oncology: Occult Primary (Cancer of Unknown Primary)/v.3.2014. NCCN.org

Febrile Awhile

Ena Sharma, MD
PGY3 Resident
Texas Tech Internal Medicine Permian Basin

Case Presentation: History

- 65-year-old Hispanic male admitted to outside hospital with 1 week abdominal pain and fevers
- In outside hospital for 1 week: Persistent fever 101–102.5 without chills or night sweats and leukocytosis despite empiric antibiotics
- Transferred to our facility

- PMH/PSH: none
- Family History: one brother has colon and kidney cancer
- Social History: Single, has one dog, no tobacco, alcohol or drug use.
  - 10 years prior: Travel to Iraq
  - 45 years prior: Exposed to Agent–Orange
- ROS: mild arthralgia
Physical Exam

- **Vitals:** Temp 102°F, HR: 96, BP 138/85, RR 20, SaO2 96% on room air
- **HEENT:** No lymphadenopathy
- **Abdomen:** soft, non distended, BS+, mildly tender to palpation in LUQ, mildly tender prostate.
- Rest of physical exam was normal.

Labs

- **WBC:** 24000/μL, 89% PMN, 1% bands
- **Hb:** 12.8, **Platelets:** 592
- **AST:** 136
- **ALT:** 141
- **AP:** 120
- **T. bilirubin:** 0.6
- **LDH:** 217 (115–230)
- Serum electrolytes, renal and thyroid function normal
- Chest X-ray WNL
- CT abdomen/pelvis WNL
- Hepatitis panel negative
- HIV screen negative
- Serum IGRA negative
- RF and ANA negative
- **CRP:** 27.5 (NL<1)
- **ESR:** 64 (NL<20)
- Procalcitonin 0.59 (NL<0.50)
- Peripheral smears normal
Bacterial Infections: abscess, endocarditis, TB
Fungal infections
Malignancy
Viral Syndromes

Differential Diagnosis:
- Bacterial Infections: abscess, endocarditis, TB
- Fungal infections
- Malignancy
- Viral Syndromes

Hospital Course: Day 0—4
- Initial infectious work up negative
- Symptoms persist despite broad spectrum antibiotics
- Serum ferritin: 1870 (20–250 NL)
Hospital Course: Day # 5

- Fever and leukocytosis persist
- Trans-esophageal echocardiogram negative
- Nuclear tagged WBC scan negative
- Blood cultures x4 and fungal panels: all negative

Recap

- Persistent leukocytosis with negative infectious and malignancy workup.
- Persistent, recorded, true fever for 2 weeks.

Fever of Unknown Origin
Differential Dx for FUO

- Infection
- Malignancy
- Rheumatic Disease
  - Vasculitis
  - RA, SLE
- Drugs

Autoinflammatory Disease
- Hyper Ig-D syndrome
- TNF Receptor associated periodic syndrome (TRAPS)
- Schnitzler’s Syndrome
- Sweet syndrome
- Adult Onset Stills Disease

Hospital course day # 7

- Serum ferritin: 2610 ng/mL
- High dose Ibuprofen started
- Fever resolved over 24–36 hours
- Leukocytosis started improve
Temperature graph

Differential Dx for FUO

- **Infection**
  - Tuberculosis
  - Endocarditis
- **Malignancy**
  - Lymphoma
  - Leukemia
- **Autoinflammatory Disease**
  - Hyper Ig-D syndrome
  - TNF Receptor associated periodic syndrome (TRAPS)
  - Schnitzler’s Syndrome
  - Sweet syndrome
  - Adult Onset Stills Disease
- **Systemic-Rheumatic Disease**
  - Vasculitis (Polyarteritis Nodosa; Giant cell Arteritis, GPA etc.)
  - RA, SLE etc.
- **Drugs**
  - Antithyroid drugs
  - NSAIDs
  - Antihypertensives (Hydralazine)
  - Antiarrhythmics (Quinidine)

Adult Onset Still’s Disease

Auto-inflammatory disease of unknown etiology

Currently hypothesized to cause pathologic inflammation by activating innate immune system
Described in children by George Still in 1896

Adult patients (>18yo)
Similar to the systemic juvenile idiopathic arthritis
Does not fulfill criteria for rheumatoid arthritis

**SYMPTOMS:**
- Fever
- Evanescent rash
- Arthritis or arthralgia
- Sore throat
- Lymphadenopathy
- Serositis

**Adult Onset Still’s Disease**
**Inclusion Criteria**

**Adult Onset Still’s Disease**
**Evanescent Salmon Rash**
Adult Onset Still’s Disease

Diagnosis of exclusion

Yamaguchi Criteria for AOSD
- 5 criteria total
- At least 2 must be major criteria

Major criteria (2+)
- Fever >102.2°F ≥1 wk
- Arthralgias/Arthritis ≥2wk
- Non pruritic rash
- Leukocytosis >10,000/μL

Minor Criteria
- Sore throat
- Lymphadenopathy
- Hepatosplenomegaly
- Abnormal LFTs,
- Negative ANA and RF
Adult Onset Still’s Disease

Course of the Disease

- **Monophasic pattern**
  - <1 yr symptoms
  - Systemic features predominate

- **Intermittent pattern**
  - One or more disease flares
  - Complete remissions between episodes (wk—yrs)
  - +/- Articular symptoms

- **Chronic pattern**
  - Persistently active disease
  - Articular symptoms predominate
  - +/- Destructive arthritis

---

Adult Onset Still’s Disease

Etiology unknown
   Both genetic factors and infectious triggers have been suggested

Mechanisms?
   Focus = INNATE IMMUNITY and the role of the inflammatory cytokines:
   - IL-1, TNF, IL-6, 8, 12
   No apparent role for classic humoral or cellular memory immunity

---

Innate Immunity
Innate Immunity

- **Mild disease**: NSAIDs, optional low dose Glucocorticoids
- **Moderate Disease**: Glucocorticoids, DMARDs (MTX, anti-TNFα)
- **Severe Disease**: Glucocorticoids + biologic agent (anti IL-1 or anti IL-6)

Approach to Therapy

- **Mild disease**: NSAIDs, optional low dose Glucocorticoids
- **Moderate Disease**: Glucocorticoids, DMARDs (MTX, anti-TNFα)
- **Severe Disease**: Glucocorticoids + biologic agent (anti IL-1 or anti IL-6)

Adult Onset Still’s Disease

- Biologic Therapeutics
  - Anakinra
  - Tocilizumab

- Inflammatory Cytokines: IL-1, IL-6, IL-8, IL-12, TNF
Patient given Ibuprofen 600mg TID x 3months

At 6 month follow up:

- Patient symptom free, observation continued
- All markers (WBC, Ferritin, Temp) in normal range

It represents a diagnostic challenge because it's a diagnosis of exclusion

The pathogenesis is unclear but revolves around the activation of innate immunity

Drugs that block inflammatory cytokines are therapeutically effective
References

- Efficacy of tocilizumab in conventional treatment-refractory adult-onset Still's disease: multicenter retrospective open-label study of thirty-four patients. Ortiz-Sanjuán F, Blanco R, Chivo Río V. *Arthritis & Rheumatology* (June 2014)

Questions?
Acyclovir Resistant Herpes Simplex Virus Meningo-encephalitis In An Immunocompetent Individual

Anusha Thomas, MD1, Ashley Drews, MD1

1Houston Methodist Hospital, Houston, Texas

CLINICAL PRESENTATION

A 41-year-old woman presents with acute onset of disorientation, slurred speech, and fever.
- Usual state of health till 3 days prior to admission.
- Fever associated with decreased food intake, 2 episodes of non-bloody emesis, lethargy, and chills.
- No improvement with OTC analgesics.
- On the day of admission: altered speech pattern specifically—word-finding difficulty, slurred speech, increased sleepiness and neck soreness.
- On evaluation: dysarthria and aphasia improved; fever, somnolence, generalized weakness persisted.
- "I just do not feel myself."

DEMOGRAPHICS

- Past Medical History: Hypothyroidism; negative PPD 4 years ago.
- Medications: Synthroid, Tylenol.
- Family History: Father—CVA.
- Social History: Denied smoking/alcohol/drug use; no sick contacts; originally from India; moved to the US in 2004; completed her Ph.D. in political science at the University of Alberta; teaches political science at UH; 2 children: 11 and 9 years old.
Review of Systems

GENERAL: subjective fevers, lethargy, gen. weakness and chills.

HEAD, EYES, EARS, NOSE, THROAT: headache, neck discomfort, no syncope, Blackouts, altered mental status, visual changes, dysphagia or sore throat.

RESPIRATORY: positive for cough, no sputum of blood or hemoptysis.

CARDIOVASCULAR: denies chest pain, peripheral edema, exertional dyspnea.

ABDOMINAL: positive for nausea, vomiting, no diarrhea, constipation, abdominal pain.

GENITOURINARY: Denies dysuria, polyuria or changes in urinary habits.

MUSCULOSKELETAL: Denies cyanosis, muscle or joint pain.

HEMATOLOGIC: Denies bleeding or easy bruising.

SKIN: Denies new rashes, ulcers, or pruritus.

NEUROLOGICAL: neck discomfort, disorientation, word finding difficulty and speech alteration as in the HPI.

PSYCHIATRIC: delusions+

Physical Examination

VS: F-max 103.6, T-current 99.1, BP-115/63 HR- 90, RR 19, SpO2 100%

GENERAL: Ill-appearing, no acute distress, resting comfortably.

HEAD: Normocephalic, atraumatic. Pupils were equally round and reactive to light and accommodation. Extraocular movements were intact.

NECK: Neck stiffness+, No tracheal deviation. No thyromegaly. No nuchal rigidity. No Kernig or Brudzinski signs.

RESPIRATORY: Clear to auscultation bilaterally. No wheezes, no rhonchi, no rales.

CARDIOVASCULAR: Regular rate and rhythm, S1, S2. No murmurs, rubs, or gallops.

ABDOMEN: Soft abdomen, normal bowel sounds. No hepatomegaly or splenomegaly.

MUSCULOSKELETAL: Normal tone and bulk.

NEUROLOGIC: Alert and oriented x3. Cranial nerves II through XII grossly intact. No focal deficits were noted. NIHSS 0

Laboratory Values

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<td>135</td>
<td>97</td>
<td>9</td>
<td>122</td>
<td>12.9</td>
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<tr>
<td>3.8</td>
<td>27</td>
<td>0.6</td>
<td>8</td>
<td>38.8</td>
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ANA- not detected
RF-<20
CRP- 0.75
ESR-15
UA- 6 RBCs, 2 WBCs, mod. bacteria, 1+ ketones, 1+ protein, 2 epi cells

11/3/2015
CT Head WO contrast:

- Small acute cortical infarct in the parasagittal aspect of the left frontal lobe.
- Two small nodular hyperdensities in the superior aspect of the cerebellum on either side, most suggestive of cavernous malformations.

Imaging Studies

Lumbar puncture

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<tr>
<td>Color</td>
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<tr>
<td>Appearance</td>
<td>Clear</td>
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<tr>
<td>RBC</td>
<td>104</td>
</tr>
<tr>
<td>WBC</td>
<td>123</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>89%</td>
</tr>
<tr>
<td>Monocytes</td>
<td>11%</td>
</tr>
<tr>
<td>Glucose</td>
<td>51</td>
</tr>
<tr>
<td>Protein</td>
<td>45</td>
</tr>
<tr>
<td>VDRL</td>
<td>Non reactive</td>
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</tbody>
</table>
CSF studies

- Herpes Simplex Virus (HSV) PCR- positive
- VZV PCR negative
- Toxoplasma PCR- negative
- CMV negative
- EBV negative
- West Nile PCR- negative
- Borrelia CSF Ab- negative

She is placed on Acyclovir (ACV) but continues to spike high grade fevers and have worsening headache and nausea!!

MRI W/WO contrast:
Imaging

MRI W/WO contrast:
- Multiple foci of abnormal signal in the cerebellum, left thalamus and left frontal lobe, some of which are hemorrhagic.
- Concerning for atypical infection, metastatic disease, vasculitis or less likely inflammatory/demyelinating process.

Abnormal EEG

- Discharges of slow waves, much more on the left than the right with occasional epileptiform morphology.
- May represent anatomic brain regions, suggesting primarily left temporal lobe.
- Possible that this represents an epileptogenic focus, but there is no clear seizure.
- Abnormal EEG due to 1) generalized slowing and rhythmic delta waves. This is a nonspecific finding indicating generalized cerebral dysfunction. 2) Left temporal epileptiform discharges that are potentially epileptogenic. No frank seizure.

She remains febrile with no clinical improvement. Can this be from septic emboli due to infective endocarditis or a cerebral vasculitis?
11/3/2015

**Imaging**

- **TEE**: Small soft looking "mass" on atrial aspect of mitral valve that may represent a vegetation but is most likely an artifact. TEE may be warranted for further evaluation.
- **TEE**: No evidence of endocarditis

**Imaging - Cerebral angiogram**

- **Negative** cerebral arteriogram with no evidence of vasculitis.
- No evidence of aneurysm, arteriovenous malformation or fistula.

**Lumbar puncture**

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<td>Sugar, CSF</td>
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<td>APV CSF screen</td>
<td>10</td>
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<tr>
<td>CSF WBC</td>
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<td>CSF Lymphocytes</td>
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<td>CSF Glucose</td>
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<tr>
<td>CSF Opening Pressure</td>
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<tr>
<td>CSF Pleura Cell</td>
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**HSV PCR**: positive
She is placed on Foscarnet and demonstrates a significant clinical improvement and a fever curve that begins to trend down.

Herpes simplex virus

- Alpha herpesvirus family
- Short replicative cycle
- Lysis of host cell
- Latency in sensory ganglia
- HSV1: orofacial lesions
- HSV2: genital herpes
- HSV encephalitis: HSV1 (90%)

Laboratory values

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<tr>
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<td>Glucose Level, CSF</td>
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<td>10,000 &lt;br&gt; 344</td>
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<td>0.9 &lt;br&gt; 0.9</td>
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<td>CSF Monocyte</td>
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<td>7 &lt;br&gt; 7 &lt;br&gt; 7 &lt;br&gt; 7</td>
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<td>CSF Plasma Cell</td>
<td>4 &lt;br&gt; 4 &lt;br&gt; 4 &lt;br&gt; 4</td>
<td></td>
</tr>
</tbody>
</table>

Whitley RJ, Roizman B. Herpes simplex virus infections. Lancet 2001;357:1513-1518
Who is at risk of ACV resistance?

- Immunocompromised hosts: 3.5-10%
- Bone marrow/Allogeneic HSC transplant recipients (25%)
- ACV prophylaxis
- Immuno-competent hosts <1%
- Immune privileged sites

Mechanism of action of antivirals

- Guanosine analogue
- Alterations in viral thymidine kinase (TK) gene (UL23) and/or nucleotide substitutions in the viral DNA polymerase gene (UL30)
  - TK altered
  - TK negative
  - TK partial
- Laboratory diagnosis:
  - Susceptibility of viral isolate to antivirals (phenotyping)
  - Genetic mutations linked to drug resistance (genotyping)
- Alternative therapy: Foscarnet/Cidofovir/immiquimod

Mechanisms of ACV drug resistance
Mechanism of drug resistance

- HSV helicase-primase complex inhibitor (HPI) (UL5, UL52, UL8 genes)
  - Amenavir
  - Pritelivir
  - Antiviral peptides?
- Viral attachment to host cell receptors
- Inhibit replication complex formation
- Interfere with protein-protein interactions/complex dissociation

**Key points**

- HSV drug resistance should be considered in both immunocompromised and immunocompetent individuals especially during involvement of "immune-privileged sites".
- Research platforms that provide rapid typing of drug resistance are necessary to guide clinicians in their treatment decisions.
- Therapy of drug resistant HSV disease should benefit from the development of novel antivirals.
References

"Calcium... it’s elementary my dear Watson"

By: Miraie Wardi, DO

History of Present Illness

A 43 year old Caucasian female with a past medical history of diabetes mellitus and Hepatitis C presented with a 2 week history of nausea and vomiting; associated with:

• poor appetite
• moments of confusion

Remainder of review of systems negative

Past Medical History:
• Hepatitis C
• Diabetes Mellitus

Family History:
• Father: renal cancer
• Mother: breast cancer

Past Surgical History:
• Hysterectomy
• Tonsillectomy
• Right breast lumpectomy - benign

Medications:
• Ribavirin
• Interferon
• Lantus 25 units

Social History:
• Tobacco: ½ pack per day x 20 years
• Alcohol: discontinued
• Intravenous drug abuse: heroin, last use 5 years prior
Vital signs:
Temperature: 36.7 C oral
Pulse: 79 beats/minute
Blood pressure: 118/59 mmHg
Respirations: 17 breaths/minute
SpO2: 98% 2L nasal cannula

Abdominal: soft, non-tender, non-distended, bowel sounds柔和 and bowel movements normal

Skin: plaque like, scaly red lesions around areas of old track marks on bilateral arms

Physical Examination

Cardiovascular: normal S1 and S2, no murmur or gallop

Respiratory: clear to auscultation bilaterally

Neurologic: awake, alert and oriented x 3, no motor or sensory deficits

Skin: plaque like, scaly red lesions around areas of old track marks on bilateral arms

Laboratory findings:
- White blood cell count: 5.63 x 10^3 cells/UL
- Hemoglobin: 15.6 g/dL
- Hematocrit: 45.5%
- Platelets: 329 x 10^3 cells/UL
- Blood urea nitrogen: 38 mg/dL
- Creatinine: 3.01 mg/dL
- Liver panel: normal
- Serum albumin: 4.0 g/dL

Initial Work-Up

- Elevated serum calcium
- Ionized Ca: 1.95 mmol/L
- 25OHD: 37 pg/mL (18-72)
- 25D: 16 ng/mL (30-100)
- IPTH: 20 pg/mL (14-37)
- PTHrP: 20 pg/mL (14-37)
- Vit D metabolites
- PTHrP and Vit D metabolites
- Non-PTH related mechanism

Calcium… it's elementary my dear Watson
Father has a history of renal cell cancer
Mother has a history of breast cancer
Breast examination revealed mass at 1 o'clock position of the right breast

"Calcium... it's elementary my dear Watson": Miraie Wardi, DO

Has an extensive history of smoking
Skin: plaque like, scaly, red lesions around areas of old track marks

Biopsy Results

Breast biopsy: negative for malignancy
Lung biopsy: negative for malignancy
Skin biopsy: negative for malignancy

"Calcium... it's elementary my dear Watson": Miraie Wardi, DO

ACE: 132 U/L (9-67)
Interferon Induced Sarcoidosis

Incidence 10-20 of 100,000

First reported case: Maximilien Robespierre

Common adverse reactions are non-specific

Respiratory complications secondary to interferon therapy are rare
Interferon-induced Sarcoidosis

Management consists of discontinuation of interferon +/- immunosuppressive therapy

Good prognosis after discontinuation of therapy

What was unique?

Usually occurs in African American women between 25 and 40 years of age

Rare pulmonary complication of interferon

Uncommon cause of hypercalcemia
Back to the Victim

- Patient initially admitted to the intensive care unit on intravenous fluids
- Initial work up for hypercalcemia failed to elucidate source
- Further workup suggestive of sarcoidosis
- Interferon discontinued and patient improved; calcium normalized
- Started on prednisone 20 mg daily for 6 weeks with taper; respiratory complaints and skin lesions resolved

“Quite elementary my dear Watson...”

Acknowledgements

Hasan Salameh, MD
Sarmad Said, MD
<table>
<thead>
<tr>
<th>References</th>
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<tbody>
<tr>
<td><a href="http://www.bio.davidson.edu/courses/immunology/students/spring2005/v_alvarez/ifn-gamma.html">http://www.bio.davidson.edu/courses/immunology/students/spring2005/v_alvarez/ifn-gamma.html</a></td>
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<td>King, TE, Jr. MD. Clinical manifestations and diagnosis of pulmonary sarcoidosis. <a href="http://www.uptodate.com">www.uptodate.com</a></td>
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</tr>
</tbody>
</table>
ACP Celebrates Centennial

In honor of ACP’s 100-year anniversary, a series of articles and events are being offered throughout 2015 to celebrate ACP’s commitment to excellence and its dedication to internal medicine and patient care.

- An online timeline featuring historical facts, images, and anecdotes about the organization in a decade-by-decade format, and two inspiring videos.
- Articles in Annals of Internal Medicine and ACP Internist.

http://www.acponline.org/about_acp/history/

ACP’s Mission & Goals

Mission: To enhance the quality and effectiveness of health care by fostering excellence and professionalism in the practice of medicine.

Goals:

- To establish and promote the highest clinical standards and ethical ideals
- To be the foremost comprehensive education and information resource for all internists
- To advocate responsible positions on individual health and on public policy relating to health care for the benefit of the public, our patients, the medical profession, and our members
- To serve the professional needs of the membership, support healthy lives for physicians, and advance internal medicine as a career
- To promote and conduct research to enhance the quality of practice, the education and continuing education of internists, and the attractiveness of internal medicine to physicians and the public
- To recognize excellence and distinguished contributions to internal medicine
- To unify the many voices of internal medicine and its subspecialties for the benefit of our patients, our members, and our profession
### 2015-16 Priority Initiatives

- Increase the number and engagement of ACP members through expanded outreach.
- Advocate for reform of the American Board of Internal Medicine’s (ABIM) Maintenance of Certification (MOC) process. BOR approved new statements on professional accountability and CPO and is MOC agnostic.
- Help ACP members experience more fulfillment and satisfaction in their professional lives—Mark Linzer and Chris Simsky leading these initiatives.
- Increase ACP’s visibility in academic centers/institutions.
- Facilitate transitions to value based payment and delivery models.
- Redesign ACP’s approach to setting clinical standards—harmonize Clinical Guidelines, Performance Measurement, Informatics to inform the evaluation and payment systems.

### Our interests at ACP are to further . . .

- the science of medicine (e.g., *Annals of Internal Medicine*)
- the clinical practice of medicine (e.g., clinical standards, guidelines)
- the education and professional development of physicians (e.g., MKSAP, meetings and courses)
- the ‘triple aim’ of healthcare (better care, better health, lower per capita costs)
- the future of medicine (students, residents, fellows)
- professional satisfaction (e.g., payment reform, practice redesign)

### Why join ACP?

- Evidence-based Clinical Information and Educational Resources
- Board Certification and Maintenance of Certification (MOC) resources
  - MKSAP, review courses, resources and opportunities for MOC points, MOC Navigator
- CME
  - Earn CME by attending live meetings, working online, or watching course recordings on your own schedule
- Influential Advocacy
- Practice Support
  - Tools and resources for Quality Improvement and Practice Transformation
- Professional Development
Annals of Internal Medicine

Ranked one of the top four peer-reviewed medical journals; current, evidence-based science at your fingertips

- **New:** Beyond the Guidelines, a multimedia educational series, focuses on the care of patients who “fall between the cracks” in available evidence and whom the optimal clinical management is unclear.
- Interactive Virtual Patient cases test the physician’s decision-making skills through examination, diagnosis, and treatment of a virtual patient.
- The Consult Guys Videos, a series of educational videos that use humor to address and solve clinical problems.

Download the updated App for Annals iPad edition and take the journal wherever you go.

MKSAP ® 17

The gold-standard of physician self-assessment for more than 45 years; discounted for ACP members

- Use for board preparation, recertification (MOC) preparation and credit, and updating medical knowledge
- Covers general internal medicine and 11 internal medicine subspecialties
- 1,200 multiple-choice questions; answers and critiques included
- Available for pre-order in both print and digital formats.

IM Essentials

Updated, and integrated suite of educational materials for clerkship directors and students

- Collaboration between ACP and the Clerkship Directors in Internal Medicine
- Help third-year medical students care for patients, prepare for clinical rounds, and study for the end-of-rotation and USMLE Step 2 examinations
- Combines self-assessment questions (formerly in MKSAP for Students) and textbook content of Internal Medicine Essentials for Students in a single suite of educational materials with new enhancements for clerkship directors and students
- **IM Essentials Text** (formerly Internal Medicine Essentials for Students)
- **IM Essentials Questions** (formerly MKSAP for Students)
- **IM Essentials Online** (the next version of MKSAP for Students)
Internal Medicine In-Training Examination (IM-ITE)

Web-based program designed for self-assessment and program evaluation
- Developed by ACP in collaboration with Alliance for Academic Internal Medicine
- Gives residents an opportunity for self-assessment
- Allows program directors the chance to evaluate their programs
- Identifies individual resident knowledge gaps to guide learning

Maintenance of Certification (MOC) Navigator

Interactive tool to help guide ACP members through ABIM's MOC process
- Provides easy-to-use, step-by-step interface to make physicians make decisions about participating in the program, learn more about program enrollment, understand requirements, and earn points
- Offers recommendations for ways for physicians to meet the requirements that fit best with a physician's specific preferences and professional situation
- Discover resources to earn points and select ways to meet requirements

Evidence-based Clinical Guidance

ACP's Clinical Practice Guidelines, Guidance Statements and Best Practice Advice papers are rigorously reviewed based on the best evidence prior to publication.

Recent Clinical Policies and Recommendations:
- Screening for Cancer (May 2015)
- Cervical Cancer Screening (April 2015)
- Risk Assessment and Prevention of Pressure Ulcers (March 2015)
- Treatment of Pressure Ulcers (March 2015)
High Value Care Initiative

Resources to help physicians provide the best patient care while reducing costs to the health care system
- Evidence-based recommendations
- High Value Care teaching curriculum
- High Value Care Coordination Toolkit
- Practice resources
- Public policy papers
- Patient education materials
- Videos

www.acponline.org/hvc

High Value Care Curriculum & Online Cases

For Educator, Residents, and Students
ACP’s High Value Care Curriculum, created by ACP and the Alliance for Academic Internal Medicine (AAIM), features six, one-hour interactive modules.

For Medical Students
A High Value Care Course designed specifically for students to help them evaluate the benefits, harms, and costs of tests and treatment options so they can make High Value Care a reality in clinical practice.

High Value Care Online Cases
ACP’s HVC cases offer clinicians the opportunity to earn FREE CME credits and ABIM Medical Knowledge MOC points.

Smart Testing
A collaboration with Cleveland Clinical Journal of Medicine, presents clinical scenarios in which diagnostic tests are commonly ordered in the absence of supporting data.

DynaMed Plus™

Clinical content that is current, concise, and easy to search
- Enhanced version of the leading evidence-based point-of-care reference tool from EBSCO Health
- Includes overviews and recommendations for more than 750 topics, 2,500 searchable images, and numerous calculators
- Free access for members beginning August 3, 2015
- Mobile apps available for Android and iOS
- ACP Smart Medicine is discontinued as of August 3, 2015
Additional Clinical Resources

Monthly print publications - ACP Internist and ACP Hospitalist provide news and in-depth analysis of issues for inpatient and outpatient internists.


Books - Fenway Guide to Lesbian, Gay, Bisexual, and Transgender Health

Internal Medicine Meeting 2016:
ACP’s Annual Scientific Meeting

Save the Date:
May 5-7, 2016
Washington, D.C.

- Over 200 educational, interactive workshops
- Case-based sessions and feedback on challenging patient management problems

ACP Membership Categories

- Medical Student Member
- Resident/Fellow Member
- Internal medicine residents and subspecialty fellows-in-training

- Member
- Internists and internal medicine subspecialists who meet ACP credentialing standards

- Fellow
- Internists with notable accomplishments recognized by their peers

- Physician Affiliate Member
- Physicians who are not trained in or practice in internal medicine

- Non-Physician Affiliate Member (available in the U.S. only)
- Physician assistants, nurse practitioners and other healthcare professionals
Become an ACP Fellow

Election to Fellowship recognizes excellence in the practice of internal medicine and is achieved through professional accomplishments within one, or across multiple pathways:

- Published Academician - author of at least two published articles in medical journals
- Commitment to continuing education - multiple certifications, recertification, or MKSAP for score
- Active involvement in ACP - at least 5 years of membership and participation in College activities including national or local committees/councils
- Senior Physician - distinguished career in internal medicine

www.acponline.org/FACP

ACP Membership Continues to Grow

- Effective June 30, 2015, total membership is 145,000 and international membership is 13,014.
- ACP has 67 domestic chapters/regions and 17 international chapters.

International Representation

- 17 International ACP Chapters:
  - Brazil, Canada (6 chapters), Central America, Chile, Colombia, Gulf, India, Japan, Mexico, Saudi Arabia, Southwest Asia, Venezuela

  New: 17th international chapter, the ACP Gulf Chapter, was established in July 2015. This chapter includes Bahrain, Kuwait, Oman, Qatar, and the United Arab Emirates.
Resources for Board Certification

ACP members enjoy free, or substantially discounted resources to help with MOC:

- **MKSAP 17**
  - 1,200 new self-assessment questions
  - Used by over 90% of residents for board preparation
- **Board Basics 3**
  - Dozens of classic images, core content and tips on how to take the ABIM exam
- **MOC Navigator**
  - Free interactive tool to help guide ACP members through ABIM’s MOC process
- **Courses**
  - MOC Exam Prep Courses, and Internal Medicine Board Review Courses
  - Live review courses and recordings
- **Virtual Dx**
  - Online image-based study program to prepare for the ABIM recertification exams
- **MOC Special Interest Group**
  - Online discussion group

Practice Resources

- **Physician & Practice Timeline**: Online tool that helps track deadlines for a variety of regulatory, payment, educational, and delivery system changes and requirements. Members can sign up for text alerts from the Timeline by texting ACPtimeline (no space) to 313131 from mobile phones.
- **ICD-10**: Free tools and resources to help physicians understand and implement updated ICD-10 codes, which begins October 1, 2015
- **ACP Practice Advisor**: Online tool to help practices analyze and improve patient care, organization, and workflow
- **ACP Quality Connect**: Quality improvement resources, from point-of-care tools to a national QI network linked to the Physician Quality Reporting System (PQRS), that help physicians improve patient care and gain MOC practice assessment points

Center for Patient Partnership in Healthcare (CPPH)

Formed in 2013, the Center’s primary focus is to promote patient-and family-centered care principles and develop patient partnership tools and resources.

- **Current Initiatives**:
  - STEP – Stopping Stroke Through Engaged Patients program - video, patient guide and shared decision-making worksheets
  - New patient education series, Patient FACTS (Patients & Families: Advice for Conditions, Treatments, and Symptoms) on over 50 topics to be released Fall 2015
  - “In the Patient’s Voice” and patient-centered educational sessions at Internal Medicine Meeting 2016
  - Developing survey to measure patient- and family-centeredness in ambulatory practice
  - Developing set of patient-and family-centered care principles for ACP membership
Quality Improvement

- ACP Quality Connect Immunization Resources
  - An initiative to help physicians promote and implement adult immunizations
- ACP Practice Assessment Tools
  - Free, web-based products that physicians can use to earn both CME credit and ABIM MOC Practice Assessment points
- Near Miss Registry
  - Resources for residency programs and hospitals to identify safety risks and reduce medical errors, using a survey tool
- ACP Genesis Registry
  - A quality reporting service to help physicians meet Meaningful Use requirements and improve patient care
- Diabetes Registry
  - Clinical registry aimed at tracking and improving the quality of diabetes and cardiometabolic care across the primary and specialty care continuum

ACP Public Policy & Advocacy

Your advocate for Internal Medicine on Capitol Hill

ACP’s advocacy priorities:

- Ensuring successful implementation of Physician Payment Reforms in MACRA
- Extending Medicare Primary Care Incentive Program
- Reestablishing Medicaid Primary Care Pay Parity
- Supporting Vital Health Programs (like Primary Care Physician Training) through Appropriations
- Advancing Medical Liability Reforms
- Addressing Administrative Complexities

www.acponline.org/advocacy

Recent ACP Policy Papers

- The Integration of Care for Mental Health, Substance Abuse and Other Behavioral Health Conditions into Primary Care (June 2015)
- Firearm-Related Injury and Death in the United States: A Call to Action from 8 Health Professional Organizations and the American Bar Association (February 2015)
Upcoming Papers/Position Statements/Initiatives

- Direct Patient Contracting Practices
- Elimination of Non-Medical Exemptions from State Immunization Laws
- MACRA Implementation
- America's Health Insurance Plans (AHIP) Core Quality Measures Collaborative: Core Measures Set for ACOs and PCMHs

Advocates for Internal Medicine

- Grassroots advocacy network
- Join ACP’s network and contact your Senators and Representatives about issues important to internists

www.acponline.org/advocacy/aimn/

Professional Development

- ACP Leadership Academy
- Ethics Manual & Case Studies
- Mentoring and networking
  - at the chapter and national levels
- ACP Associate Poster Competition
- ACP Special Interest Groups
- Career Connection
  - a comprehensive listing of career opportunities for physicians
Professional & Personal Benefits

- **Mercer Consumer**: Offering personal insurance options including life, disability, long-term care, and auto/homeowners through leading insurance companies
- **Bank of America**: Offering BankAmericard Cash Rewards™ Visa Signature® with low introductory APR and no annual fee, and including 24/7 complimentary concierge service, shopping protection and travel assistance/protecting

Recruit-a-Colleague

- Recruit one colleague and receive a $100 credit toward your 2016-17 annual dues*
- Recruit two colleagues and receive a $200 credit toward your 2016-17 annual dues*
- Recruit three colleagues and receive a $300 credit toward your 2016-17 annual dues*
- Recruit four colleagues and enjoy free annual dues in 2016-17*
  *US only
  www.acponline.org/rec

Support the Next Generation of IM

- Encourage a young person to understand the rewards of internal medicine as a career
- Convince a medical student to see the bright future of internal medicine
- Recommend general internal medicine to a resident
- Invite another internist to become an ACP member
- Sponsor a qualified ACP Member for Fellowship (FACP)
ACP . . . Connected and Mobile

- **Social Media**
  ACP and Annals of Internal Medicine are using social media more than ever to communicate and share information relevant to internal medicine.

- **Special Interest Groups**
  ACP’s online communities offer physicians an opportunity to share experiences, questions, and solutions with their peers.

- **Mobile Access**
  ACP now offers mobile versions of Annals and MKSAP and Apps for several ACP products.

Visit ACP Online

www.acponline.org

A quick and easy way to find all that you need!

Thank you . . .

for your continued support of ACP and your commitment to internal medicine.
Do you currently screen your patients for lung cancer?

A. Yes
B. No
Does CMS cover lung cancer screening?

A. Yes
B. No
Table 1
Characteristics of the Ideal Screening Program

Features of the disease
• Significant impact on public health
• Asymptomatic period during which detections is possible
• Outcomes improved by treatment during asymptomatic period

Features of the test
• Sufficiently sensitive to detect disease during asymptomatic period
• Sufficiently specific to minimize false-positive test results
• Acceptable to patients

Features of the screened population
• Sufficiently high prevalence of the disease to justify screening
• Relevant medical care is accessible
• Patients willing to comply with further work-up and treatment

Table 2
Measures of Screening Effectiveness

• Relative risk and relative risk reduction
• Gain in life expectancy
• Cost per case detected
• Cost per life saved
• Gain in quality-adjusted life years (QALYs)
• Number needed to screen (NNS)
Bias in the Evaluation of Screening Tests

- Screening bias
- Lead-time bias
- Length bias

**Lead-Time Bias**

<table>
<thead>
<tr>
<th>Natural history</th>
<th>Diagnosis based on clinical presentation</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>4 years</td>
<td>3 years</td>
</tr>
<tr>
<td>Asymptomatic period</td>
<td>Clinical trials</td>
<td></td>
</tr>
</tbody>
</table>

**Unscreened population**

<table>
<thead>
<tr>
<th>Diagnosis based on clinical presentation</th>
<th>3 years</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>4 years</td>
<td></td>
</tr>
</tbody>
</table>

**Screened population**

<table>
<thead>
<tr>
<th>Clinical symptoms</th>
<th>2 years</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>4 years</td>
<td></td>
</tr>
</tbody>
</table>

**FIGURE 1.**

* Schematic representation of lead-time bias. Assuming a fatal disease with an average survival of three years from the time of clinical presentation, the screened population will appear to have better outcomes in terms of earlier survival. In reality, these patients are not actually living longer than the unscreened population but simply being detected at an earlier point in the natural history.

THOMAS J. GATES, M.D., Lancaster General Hospital, Lancaster, Pennsylvania

**Length Bias**

<table>
<thead>
<tr>
<th>Aggressive disease</th>
<th>Simple diagnosis</th>
<th>Clinical presentation</th>
<th>1 year of survival</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Clinical presentation</td>
<td>1 year of survival</td>
<td>Death</td>
<td></td>
</tr>
</tbody>
</table>

**FIGURE 2.**

* Schematic representation of length or length-time bias. In the case of cancer, patients with aggressive tumors have at least a 50 percent change of diagnosis on annual screening. By contrast, less aggressive tumors, with long asymptomatic periods, will almost certainly be detected at annual screening. Thus, a screening program can appear to improve survival when it has only selected subgroups with the least prognosis.

THOMAS J. GATES, M.D., Lancaster General Hospital, Lancaster, Pennsylvania
Background
The aggressive and heterogeneous nature of lung cancer has thwarted efforts to reduce mortality from this cancer through the use of screening. The advent of low-dose helical computed tomography (CT) altered the landscape of lung-cancer screening, with studies indicating that low-dose CT detects many tumors at early stages. The National Lung Screening Trial (NLST) was conducted to determine whether screening with low-dose CT could reduce mortality from lung cancer.

Participant Eligibility
• Between 55–74 years of age
• History of cigarette smoking of at least 30 pack years
• If former smokers had quit within the previous 15 years
• Must be asymptomatic
Conclusions

Screening with the use of low-dose CT reduces mortality from lung cancer. (Funded by the National Cancer Institute; National Lung Screening Trial ClinicalTrials.gov number, NCT00047385.)
Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 2004 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for lung cancer.

Methods: The USPSTF reviewed the evidence on the efficacy of low-dose computed tomography, chest radiography, and sputum cytologic evaluation for lung cancer screening in asymptomatic persons who are at average or high risk for lung cancer (current or former smokers) and the benefits and harms of these screening tests and of surgical resection of early-stage non–small cell lung cancer. The USPSTF also commissioned modeling studies to provide information about the optimum age at which to begin and end screening, the optimum screening interval, and the relative benefits and harms of different screening strategies.

Population: This recommendation applies to asymptomatic adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

Recommendation: The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. (B recommendation)


For author affiliation, see end of text.

* For a list of the members of the USPSTF, see the Appendix (available at www.annals.org).

This article was published online first at www.annals.org on 31 December 2013.
Decision Memo for Screening for Lung Cancer with Low Dose Computed Tomography (LDCT) (CAG-00439N)
February 2015

Decision Summary
The Centers for Medicare & Medicaid Services (CMS) has determined that the evidence is sufficient to add a lung cancer screening counseling and shared decision making visit, and for appropriate beneficiaries, annual screening for lung cancer with low dose computed tomography (LDCT), as an additional preventive service benefit under the Medicare program only if all of the following criteria are met:

Beneficiary eligibility criteria:
- Age 55-77 years;
- Asymptomatic (no signs or symptoms of lung cancer);
- Tobacco smoking history of at least 30 pack-years (one pack-year = smoking one pack per day for one year; 1 pack = 20 cigarettes);
- Current smoker or one who has quit smoking within the last 15 years; and
- Receives a written order for LDCT lung cancer screening that meets the following criteria:

For the initial LDCT lung cancer screening service: a beneficiary must receive a written order for LDCT lung cancer screening during a lung cancer screening counseling and shared decision making visit, furnished by a physician (as defined in Section §1861(r)(1) of the Social Security Act) or qualified non-physician practitioner (meaning a physician assistant, nurse practitioner, or clinical nurse specialist as defined in 1861(aa)(5) of the Social Security Act). A lung cancer screening counseling and shared decision making visit includes the following elements (and is appropriately documented in the beneficiary’s medical records):

- Determination of beneficiary eligibility including age, absence of signs or symptoms of lung cancer; a specific calculation of cigarette smoking pack-years; and if a former smoker, the number of years since quitting;
- Shared decision making, including the use of one or more decision aids, to include benefits and harms of screening, follow-up diagnostic testing, over-diagnosis, false positive rate, and total radiation exposure;
- Counseling on the importance of adherence to annual lung cancer LDCT screening, impact of comorbidities and ability or willingness to undergo diagnosis and treatment;
- Counseling on the importance of maintaining cigarette smoking abstinence if former smoker; or the importance of smoking cessation if current smoker and, if appropriate, furnishing of information about tobacco cessation interventions; and
- If appropriate, the furnishing of a written order for lung cancer screening with LDCT.

For subsequent LDCT lung cancer screenings: The beneficiary must receive a written order for LDCT lung cancer screening, which may be furnished during any appropriate visit with a physician (as defined in Section 1861(r)(1) of the Social Security Act). If a physician or qualified non-physician practitioner elects to provide a lung cancer screening counseling and shared decision making visit for subsequent lung cancer screenings with LDCT, the visit must meet the criteria described above for a counseling and shared decision making visit. Written orders for both initial and subsequent LDCT lung cancer screenings must contain the following information, which must also be appropriately documented in the beneficiary’s medical records:

- Beneficiary date of birth;
- Actual pack – year smoking history (number);
- Current smoking status, and for former smokers, the number of years since quitting smoking;
- Statement that the beneficiary is asymptomatic (no signs or symptoms of lung cancer); and
- National Provider Identifier (NPI) of the ordering practitioner.
Cost-Effectiveness of CT Screening in the National Lung Screening Trial

William C. Black, M.D., Laura F. Cuzick, Ph.D., Sarah S. Sama, Ph.D., Jedrzej K. Galyk, M.S., Kristin B. Koler, Ph.D., Dennis R. Aberle, M.D., John N. Sensenbrenner, M.D., Timothy R. Church, Ph.D., Gerard A. Shuster, M.D., Jeremy Gierach, Ph.D., and Constantine Gartos, Ph.D., for the National Lung Screening Trial Research Team

Abstract

The National Lung Screening Trial (NLST) showed that screening with low-dose computed tomography (CT) as compared with chest radiography reduced lung cancer mortality. We examined the cost-effectiveness of screening with low-dose CT in the NLST.

Conclusions

We estimated that screening for lung cancer with low-dose CT would cost $6,000 per QALY gained, but we also determined that modest changes in our assumptions would greatly affect this figure. The determination of whether screening outside the trial will be cost-effective will depend on how screening is implemented. (Funded by the National Cancer Institute; NLTCTrittals.gov number, NCT00947315.)

Clinical Guideline

Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia M. Morris, M.S., M.P.H., chair of the U.S. Preventive Services Task Force

Description: Squad of the 2009 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for lung cancer.

Methods: The USPSTF reviewed the evidence on the efficacy and harms of lung cancer screening using chest radiography, non-contrast helical computed tomography (CT), high-resolution CT, and/or volumetric CT for current or former smokers who are at least 55 years old and who have a smoking history of at least 30 pack-years. Smoking histories were defined as a history of smoking 30 pack-years or more in a lifetime, or a history of smoking 15 pack-years or more in the past 5 years.

Recommendation: The USPSTF recommends screening for lung cancer with low-dose CT in adults age 55 to 80 years who are current smokers or former smokers with a smoking history of at least 30 pack-years and at least 5 years of follow-up since quitting.

Population: This recommendation applies to asymptomatic adults aged 55 to 80 years who are current smokers or former smokers with a smoking history of at least 30 pack-years and at least 5 years of follow-up since quitting.
Conroversy?
You bet!

Evidence Lacking to Support or Oppose Low-dose CT Screening for Lung Cancer, Says AAFP

Inability to Make Harms/Benefits Comparison Precludes Definitive Recommendation

January 13, 2014 04:50 pm Cindy Borgmeyer—Citing a paucity of high-quality evidence on which to base a comparison of relative harms and benefits, the AAFP today released an “I” recommendation regarding the routine use of low-dose CT scans in screening high-risk, older smokers for lung cancer.

The Academy’s action puts it at odds with a recommendation issued last month (www.uspreventiveservicestaskforce.org) by the U.S. Preventive Services Task Force (USPSTF).
Summary
Lung Cancer Screening

• United States Preventive Task Force recommends lung cancer screening with low-dose CT scan.
• Recommendation strength is B
• Qualifications for screening
  • 55-77 years of age
  • Smoking history of at least a 30 pack-years
  • Asymptomatic
  • Currently smoke or have quit within 15 years

• Medicare (CMS) will cover this screening recommendation and
  – Counseling visit for shared decision making
  – Imaging centers are required to collect data on each screening and submit it to a CMS-approved registry.
• Controversy in screening recommendations
  – AAFP
A 65 y/o patient presented to your office for information regarding his risk of lung cancer. He had a 60 pk/yr tobacco history however he quit smoking 10 years ago. Should you enroll this patient in yearly low dose chest CT scans for lung cancer screening?

A. Yes  
B. No  
C. Maybe
SPIRITUALITY AND FAITH IN SERIOUS ILLNESS: A PRIMER FOR CLINICIANS, TEXAS ACP, 11/8/15

"Nothing in life is more wonderful than faith -- the one great moving force which we can neither weigh in the balance nor test in the crucible...mysterious, indefinable, known only by its effects, faith pours out an unflagging stream of energy while abating neither jot nor tittle of its potency."


Robert L. Fine, MD, FACP, FAAHPM
Clinical Director, Office of Clinical Ethics and Palliative Care
Baylor Scott & White

LEARNING OBJECTIVES

• Learners will be able to:
  - Define spirituality, religion, and the relationship between them.
  - Outline the impact of religious and/or spiritual practices on illness and health.
  - Define serious illness and relate spiritual and religious thinking to coping with serious illness.
  - Use simple questions to learn about a patient's spirituality and faith.
  - Use the unique religious or spiritual world view of each patient or family in a respectful manner to better care for the patient at life's end, obviate medical futility disputes and honor our ethical obligation towards true beneficence and stewardship.

SPIRITUALITY

• "of, relating to, or affecting the human spirit or soul as opposed to material or physical things." OED

• Spirituality reflects our individual, unique and subjective response to our quest for meaning and clarity in life -- about the path we are on or our place in the universe.
SPIRITUALITY

• Spirituality comes to the forefront of our consciousness in numinous, moral, or life-and-death experiences.

SPIRITUALITY

• Spiritual experience is often considered mystical – i.e. not the stuff of the material world of science, but “Mystical experience is biologically, observably, and scientifically real.”
  - Brain Science and the Biology of Belief: Why God Won't Go Away. Andrew Newberg MD and Eugene D’Aquili MD.

RELIGION AND RELIGIOUS FAITH

• Religion may be understood as a social structure of beliefs, relationships, practices, and institutions designed to shape a spiritual practice.

• Although derived by faith, it is not necessarily an endeavor without intellectual reason.
  - “Religious thinking... is a source of cognitive insight into the ultimate issues of human existence.”
  - Rabbi Abraham Joshua Heschel.
SPIRITUALITY ↔ RELIGION

• Spiritual/Mystical aspects of life are often, although not always, expressed in relationship to a deity or deities.
• Functional brain studies of meditating (spiritual) or praying (religious) patients who report mystical experience show similar brain activity patterns, distinct from non-meditative or non-praying states.
• Buddhists who meditate (no God) and Catholic nuns who pray (to God) show the same brain images during meditation or prayer but
  - Buddhists describe feeling at one with the universe,
  - Nuns describe feeling at one with God.

SPIRITUALITY ↔ RELIGION/FAITH

WHAT DO SPIRITUALITY AND RELIGION HAVE TO DO WITH DISEASE/ILLNESS?

• “Disease forges an especially close link between G-d and man; the Divine Presence Itself ... rests on the head of the sick bed.” —Rabbi Immanuel Jakobovits, Former Chief Rabbi of the British Commonwealth
• Disease leads to suffering, but “Man is not destroyed by suffering, he is destroyed by suffering without meaning.” —Dr. Viktor Frankl, Man’s Search for Meaning
• Spirituality and religion provide a framework of meaning.
• Illness attacks that framework, causing not only physical suffering, but spiritual suffering by challenging our sense of meaning with questions of ‘why?’
• Spiritual suffering is not answered by medical science!
WHO ARE WE RELIGIOUSLY?

- American Religious Identification Survey (ARIS 2008)²
  - 54,461 English or Spanish language respondents
  - 70% report belief in a personal God
    - 50% non-Catholic Christian, 25% Catholic, 15% Jews, Muslims, Mormons, Hindus, other minority faiths.
  - 24% report no belief in a personal God
    - Half Agnostic or Atheist, half Deist

- Pew Religious Landscape Study (2014)³
  - 71% Christian, 6% non-Christian faiths
  - 23% no religion

WHAT ABOUT PHYSICIANS?

- 76% of physicians report a belief in God, but
  - Physicians compartmentalize and are less likely to carry that belief into all aspects of life.
  - Twice as likely as the general population to cope with problems without relying on God.
  - Caveat: a number of minority religions are over-represented in medicine. In this survey compared to the general population there were: 20 x Hindus, 7 x Jews, 6 x Buddhists, 5 x Muslims.

DOES RELIGIOUS PARTICIPATION IMPACT HEALTH?

- Among those who attend church more than once a week compared to those who never attend church:
  - 7 years longer life expectancy and for Blacks 14 years longer.

- Among acutely ill hospitalized men who draw on their religious faith for strength and comfort:
  - A lower rates of depression
  - A wider network of supportive friends, but
  - The same mortality rates as the less religious.
DOES RELIGIOUS PARTICIPATION IMPACT HEALTH?

• Religious participation associated with worse health:
  - Those who abstain from blood may die unnecessarily young (Jehovah's Witness).
  - Fundamentalist beliefs such as “If a person prays about cancer, God will heal it…” are associated with delays in treatment.
  - 83% of children with easily treatable conditions such as dehydration, diabetes, pneumonia, or appendicitis not treated due to religiously motivated medical neglect died.

SHOULD WE ASK PATIENTS/FAMILIES ABOUT RELIGIOUS BELIEFS?

• YES!
• 94% of patients believe doctors should ask religious questions in the face of serious illness.

ARE THERE OTHER REASONS WHY WE SHOULD ASK?

FAITH AND MEDICAL DECISIONS

• Cancer patients
  - Faith is second only to oncologist opinion as influence on patient treatment decisions.
  - 88% of advanced cancer patients say religion and spirituality important in coping with the cancer.
• Trauma patients
  - 68% of families of trauma patients state religious beliefs guide their medical decisions and 57% believe God can heal even when physicians say it is futile.
• You don't know if you don't ask!
FAITH IMPACTS EOL DECISIONS

- High levels of positive religious coping associated with greater likelihood of ICU use at life's end.12
- But spiritual support from physicians makes a huge difference.13

<table>
<thead>
<tr>
<th>HIGH RELIGIOUS COPING</th>
<th>Odds Ratio Aggressive EOL Rx</th>
<th>Odds Ratio Death in the ICU</th>
<th>Odds Ratio Hospice Enrollment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spiritual Support from personal faith community</td>
<td>2.62</td>
<td>5.22</td>
<td>0.37</td>
</tr>
</tbody>
</table>

CAVEAT! WHAT ABOUT DEISTS, AGNOSTICS, AND ATHEISTS?

- Spirituality is a loaded term and must be used carefully with atheists and/or agnostics.
  - May be acceptable if focused on self-acceptance, personal growth, interpersonal relations, connection to nature.
- Atheists more likely to want strong scientific support for treatment, less likely to request futile treatments.
- Respect for beliefs by caregivers and avoiding references to God or prayer are very important in this setting.14

SERIOUS ILLNESS
SERIOUS ILLNESS

• Serious illness confronts patient, family and physician with bad or sad news.
  - Serious illnesses typically adversely and/or negatively affects the patient's view of his or her future. Families affected as well.
  - Confronting a serious illness often leads to cognitive, behavioral, or emotional changes that persist for long periods of time — including post remission or cure of the serious illness.
  - Even physician cognition, behaviors, and emotions may change for the worse in the face of treating seriously ill patients!

THE SERIOUS ILLNESS POPULATION

• Sickest 5% of population, Chronic (organ failures, metastatic cancer) > Acute
• High risk of mortality within next several years. If not terminal this year, they may well be next year or the year after
• High cost
• High suffering – physical, emotional, social, and spiritual

SUPPORTIVE AND PALLIATIVE CARE

Years of Care

HOSPICE

Months of Care

The less than 1% of population who dies annually but about 5% of those on Medicare.

80% of suffering**
60% of health care costs*
Sickest 5% of population

WHAT DO THE SERIOUSLY ILL WANT?

• Cure!
• Remission!
• Life extension!
• But this desire is not unlimited!!!
WHAT DO THE SERIOUSLY ILL WANT IN THE ABSENCE OF CURE?

• Faced with a hypothetical terminal illness\(^\text{15}\)
  - 40% fear too little and 45% fear too much treatment
  - 86% prefer last days at home (but 80% die in hospital or NH)
  - 87% would not want ventilator to gain 1 week of life
  - 77% would not want ventilator to gain 1 month of life

• 340 seriously ill patients ranked 44 attributes of quality care near the end of life\(^\text{16}\)
  1. Freedom from pain
  2. Peace with God
  3. Other top preferences: presence of family, mental awareness, treatment choices followed, finances in order, feel life was meaningful, resolve conflicts, die at home.

WHAT DO SERIOUSLY ILL PATIENTS GET FROM US?

• Non-beneficial (futile) treatment prior to death!
  - Last 6 months of life: Hospital days vary 3x and ICU days vary 6x\(^\text{17,18}\)

• Unnecessary suffering!
  - Severe pain in over 50% of hospital patients in last 3 days of life\(^\text{19}\)
  - Emotional suffering of patients, families, and professionals.

• Unsustainable cost to patients and society!
  - 43% of patients have expenditures in last 5 years of life exceeding non-housing assets, 25% have expenditures exceeding total assets\(^\text{20}\)
  - 28% of MC expenditures in last year of life, 14% in last 2 months\(^\text{21}\)
    - 2013 $163 billion and $81.5 billion
    - 2013 NIH $29 billion, NCI $4.75 billion
    - US spends 4 x what Western Europeans spend at EOL, and this is primarily among elders\(^\text{22}\)

COSTS BY AGE: US v Europe

[Graph showing costs by age for US vs Europe]
SERIOUS ILLNESS: THE INEVITABLE SETTING FOR MEDICAL FUTILITY

HOW TO DEFINE FUTILITY?

- Ancient cultural wisdom
  - Greek mythology: the Danaides and Sisyphus
  - Ecclesiastes: “Futility of futilities, all is futility…”
- Medical concepts
  - Hippocrates: “Refuse to treat those overmastered by illness…”
  - Physiologic vs. qualitative (Younger, 1988)
  - Quantitative (Schneiderman, 1990)
  - Benefit whole persons, not parts (Shorter, 1992)
- Alternative terminology
  - Non-beneficial, medically inadvisable, medically inappropriate

SUBWAY MAP OF SERIOUS ILLNESS!
HOW TO DEFINE FUTILITY?

• We know it when we see it!
• How do we see it?
• STOP THE LINE! MIND THE GAP! LOOK AND LISTEN!
• Ask yourself: Am I restoring health or prolonging dying?

FUTILITY AS CLINICAL CONCEPT

• The clinical concept futility embodies cannot be reduced to its parts and transcends isolated physiologic, qualitative and quantitative notions.
• Patient centered element: If a treatment cannot meet the patient’s goal of treatment, it should be considered futile from a patient centered perspective.
• Most requests for futile interventions come from families, not patients.

“Futility cannot be eradicated from medicine as long as patients are mortal.”
E. Pellegrino, Former Chair, President’s Bioethics Commission, 2007

THE LAST QUESTION!

• How can you utilize knowledge of spirituality and religion to support those with serious illness and lessen the demand for medically futile interventions?
RULE 1: SUFFERING AND DEATH ARE NOT ALWAYS MEDICAL PROBLEMS TO BE SOLVED, THEY ARE SPIRITUAL PROBLEMS TO BE FACED.

RULE 2: SUPPORT THE PATIENT AND FAMILY WHERE THEY ARE!

- How do you know where they are? Ask the FICA questions.
  - Faith
  - Importance/Investment
  - Community
  - Address (What can we do to help address any faith concerns?)
- If they talk God, you need to talk God.
  - Don’t talk God if they don’t, but look for their spiritual side
- If your patient talks God and you can’t or you don’t have the time, get someone who can!
  - Multidisciplinary Palliative Care teams
  - Pastoral care if Palliative Care not available in your facility

RULE 3. OPEN A SPIRITUAL DOOR

- Tell me about your journey with this illness so far?
- Where do you see this going?
- What is it like to be you right now?
- How are you coping? Where does your strength come from?
- What would give you peace of mind?
- What are you hoping for?
- Is your sense of spirituality helping? How?
- Is your faith helping you? How?
- Have you been praying? What are you praying for?
- Do you feel your prayers are being answered?
- May I keep you in my prayers?
SUMMARY AND CONCLUSIONS

• Spirituality is biologically real and is molded for many by religion.
• Serious illness confronts spiritual well being as much as physical well being!
• Patients confront spiritual questions when facing serious illness and expect us to ask about that part of their life.
• You can’t solve a patient/family spiritual problem talking about surgical margins, lymph nodes and physiologic parameters!
• Failure to address spiritual concerns in the seriously ill contributes to multifocal consultopathy and futile interventions associated with high suffering and high costs.
• You can help improve the deficits in treatment and care near life’s end by paying attention to the spiritual dimensions of your patient’s life … and your life as well!

WE ARE NOT HUMAN BEINGS HAVING A SPIRITUAL EXPERIENCE, WE ARE SPIRITUAL BEINGS HAVING A HUMAN EXPERIENCE.

PIERRE TEILHARD DE CHARDIN

References
Case Presentation – January 2015

- 40 yr old male presents to PCP with 2-day h/o
  - Cough
  - Conjunctivitis
  - Coryza
  - Fever
- Reports recent travel to Illinois
- Rapid Flu test negative; Dx viral syndrome, Rx supportive care
- Hospitalized 1 day later with seizure, fever 105.7°F
- Pneumonia
- Further history: Travels in USA. Corporate sales rep for Soccer equipment. Meets with adolescent players / parents
  - Recent trip 10 days prior to onset of symptoms, met with players in Illinois
Additional Physical Exam Finding:

1-3 mm whitish elevation on an erythematous base on buccal mucosa opposite the molar tooth. Can appear on labial mucosa and hard/soft palate as well.
Measles: Signs and Symptoms

- Fever
- Cough
- Coryza
- Conjunctivitis
- Koplik spots
- Malaise
- Rash: Starts about 14 days after exposure
  - Begins on face, then spreads to body
  - Lasts 5-6 days

Measles - Complications

- Dehydration
- Pneumonia
- Croup
- Blindness
- Encephalitis
- Death

Measles Transmission

- Spread by coughing, sneezing, close personal contact, with infected oro-pharyngeal secretions
- Virus remains active and contagious in the air or on infected surfaces for up to 2 hours
- Can be transmitted by an infected person from 4 days prior to the rash to 4 days after onset of rash
- Incubation period from exposure to fever is about 10 days (range 7-12 days)
Measles

**Diagnosis:**
- Serologic testing – IgM, IgG
- Isolation of virus
- PCR testing – Blood, throat, nasopharyngeal, urine

**Treatment:**
- No specific treatment
- Supportive care: IVF, antibiotics for PNA/otitis, seizure meds
- Ribavirin has in vitro activity
- Vitamin A deficiency contributes to complications

Measles

- Highly contagious – 90% of susceptible contacts will become infected
- Paramyxovirus
- Still a big problem in some areas:
  - Western Europe
  - Pakistan
  - Vietnam
  - Philippines
- Consider measles in DDx of patients with fever and rash
  - Ask about international travel or venues frequented by international travelers

2015 Measles Cases in the U.S.

January 1 to February 20, 2015

*Cases*:
- < 3
- 1-4
- 5-19
- 20+
Measles (Rubeola)
- One of the leading causes of death worldwide in young children
- Vaccination efforts: 75% drop in measles deaths (2000 – 2013) worldwide
  - In 2013:
    - There were 145,700 deaths globally
    - 84% of children received 1 dose of vaccine at age 12-15 months
Measles Prevention
- Vaccination with MMR (live virus)
- Adults born before 1957 are considered immune to Measles (and Mumps)
- Adults born in 1957 or later should be vaccinated now, unless:
  - Documentation of 1 or more lifetime doses of MMR
  - Serologic evidence of immunity for those without documentation
  - Contraindications: immunosuppression, pregnancy
- Single dose adequate for most persons
- Second dose (minimum 28 days after 1st dose):
  - College students
  - Healthcare workers
  - International travel

Measles in U.S.
- 88% of cases 2000-2011 originated from countries outside of US
- 2014: 644 cases from 27 states; worst since 1994
- 2015: Over 133 cases from Disneyland outbreak
  - Majority of cases were unvaccinated or unknown status (85%)
  - Multiple states involved
  - 1 death in Washington State due to Pneumonia
    - 1st Measles death since 2003 in USA
  - Airborne spread in crowded locations
    - E.D. waiting rooms
    - Airport terminals

Measles in California
- Parts of California are anti-vaccine
- 8% of kindergarten kids have exemptions
- Some schools with exemption rates as high as 43%
- Usually upper/middle class, well educated parents
- Other states have high exemption rates-CO, PA, AR, KS - 11 states worse than CA
- In Texas, Denton ISD account for 10% of state's exemptions
Measles Vaccine Exemptions

- Exemptions
  - Religious
  - Medical
  - School
  - Data not available

**Never inject them.**
There are NO safe vaccines!

- Shaken Baby Syndrome
- Chronic Ear Infections
- Death
- SIDS
- Seizures
- Autism
- Allergies
- Asthma
- Differen

immunization action coalition

IAC
immunize.org
Case Presentation

- 64 yr old female presents with fever, chills, hypotension, sepsis
- Recent workup for biliary obstruction
  - Had ERCP done
- Admit now to ICU
- Started on empiric treatment with:
  - Vancomycin, Meropenem

Micro lab calls:

- Blood cultures x 2 reported as:
  - Klebsiella pneumoniae
  - Resistant to all Carbapenems, Penicillins, Cephalosporins
- Patient is on pressors, febrile

- What is your preferred treatment option?

CRE

- Increasingly recognized in U.S.
- First major outbreaks in Asia

- Timeline of resistant GNR's:
  - 1960's: Beta-Lactamases
  - 1980's: Extended Spectrum Beta-Lactamases (ESBL)
  - 2000's: Carbapenemases
### Recommended Treatment for MDR Organisms

<table>
<thead>
<tr>
<th>Type of Resistance</th>
<th>Common Organisms</th>
<th>Recommended Treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>AmpC beta-lactamase</td>
<td>Enterobacteriaceae, etc.</td>
<td>Any carbapenem or tigecycline, (see above)</td>
<td></td>
</tr>
<tr>
<td>ESBL</td>
<td>Klebsiella pneumoniae, etc.</td>
<td>Any carbapenem</td>
<td></td>
</tr>
<tr>
<td>Carbapenemase</td>
<td>Klebsiella pneumoniae, etc.</td>
<td>Ceftazidime-avibactam, Meropenem, tigecycline, colistin, AG (combination therapy)</td>
<td></td>
</tr>
<tr>
<td>Altered PBP</td>
<td>MRSA</td>
<td>Vancomycin</td>
<td>Daptomycin, Linezolid, TMP-SMX, ceftazoline</td>
</tr>
<tr>
<td>Mutated DNA gyrase</td>
<td>CRE</td>
<td>Daptomycin/linezolid, Tigecycline</td>
<td></td>
</tr>
<tr>
<td>Decreased permeability</td>
<td>Pseudomonas, Acinetobacter</td>
<td>Ceftolozane-tazobactam, Tigecycline</td>
<td></td>
</tr>
<tr>
<td>AG-modifying enzyme</td>
<td>Pseudomonas, Acinetobacter</td>
<td>Meropenem, imipenem, Pip-Tazo, Ceftazime</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Infectious Diseases Special Edition Fall 2015

### Case follow-up

- Patient treated with combination therapy
  - Tigecycline
  - Colistin
- Cleared bacteremia
- Contact isolation
Case Presentation

- 21 yr old male presents with 1 day h/o Urethral discharge
- 3 recent sexual partners in past 2 weeks
- Male and Female
- Last STD testing over 1 year ago
- Prior episode of Urethritis
- No PMH, No medications, NKDA

Management

- Urethritis
  - Treated with Ceftriaxone 250 mg IM + Azithromycin 1000 mg PO
  - Recent partners treated for contact with case
- Full STD testing done:
  - HIV, Syphilis, GC (all exposed sites), HSV serology, Hepatitis
- Prevention:
  - Counseling re: Risk reduction, Condoms
  - Screening every 3 months : HIV, Syphilis, GC
  - HAV/ HBV vaccination
  - PrEP ?
Estimated Number of AIDS Cases and Deaths Among US Adults and Adolescents (1985-2013)

PrEP
- **Pre-**Exposure Prophylaxis = PrEP
  - Daily 3-drug ART for duration of risk
  - Highly effective, > 95%
  - Truvada (Tenofovir + emtricitabine)
  - FDA requires close monitoring at least every 3 months
  - Can stop if risk abates
- **Post-**Exposure Prophylaxis = PEP
  - 28 days of 3-drug ART starting ASAP after risky exposure
  - Guidelines suggest Truvada + Isentress (raltegravir)

PROUD Study: Results
- Significantly fewer new HIV infections with immediate versus deferred PrEP (3 versus 19 cases)
  - 86% reduction (P=0.002)
- Number needed to treat to prevent 1 HIV infection 13
- PEP used by 31% in deferred arm
- Preliminary analysis found that risk behaviors were similar between the 2 arms

HIV Incidence
- Deferred (n=269)
  - 86% reduction (P=0.002)
- Immediate (n=276)
  - 1.3 (0.4-3.0)
- PEP: post-exposure prophylaxis.

Chronic HIV in the US: Underdiagnosed and Undertreated

- Number of individuals with HIV:
  - Prevalence: 1,196,000 - 1,300,000
  - Diagnosed: 874,056 - 960,000
  - Treated: 437,028 - 489,600
  - Viral Suppression: ~80%

- 20%-30% of All HIV-Infected Are HIV RNA <50 copies/mL

- Diagnosed: ~40% Treated: ~20% Unaware of Infection


CDC Recommendations for HIV Testing in Healthcare Settings

- Routine voluntary testing for patients ages 13 to 64 years in healthcare settings
  - Not based on patient risk
- Opt-out testing
  - No separate consent for HIV
  - Pretest counseling not required
  - Repeat HIV testing left to discretion of provider
  - Based on patient risk

**CDC and APHL: Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens**

- **Perform HIV-1/2 Antigen/Antibody Combination Immunoassay**
- **Perform HIV-1/2 Antibody Differentiation Immunoassay**
  - HIV-1 (+), HIV-2 (-): HIV-1 Antibodies Detected
  - HIV-1 (-), HIV-2 (+): HIV-2 Antibodies Detected
  - HIV-1 (+), HIV-2 (+): HIV Antibodies Detected
- HIV-1 (-) or Indeterminate HIV-2 (-)
- Perform HIV-1 Nucleic Acid Test

**Note:** New algorithm may not be uniformly adopted in all settings. If a rapid 3rd generation test is used with a positive result, confirmation is needed with a more specific test (e.g., Western Blot).

---


- PrEP is recommended as one prevention option for:
  - MSM at substantial risk of HIV acquisition
  - Heterosexual women and men whose partners are at substantial risk of HIV acquisition
  - Adult IDUs at substantial risk of HIV acquisition
  - Heterosexually active discordant couples
- PrEP should be discussed as one of several options to protect the uninfected partner during conception and pregnancy.


**Who should prescribe PrEP?**

- Refer patients to an experienced provider
- Many HIV treaters are offering PrEP now
- Requires counseling/monitoring
- Most insurance companies provide coverage for PrEP
- Patient access program
HIV Treatment: Recommended Regimens

Regardless of Baseline HIV RNA Level or CD4 Count

<table>
<thead>
<tr>
<th>INSTI</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Raltegravir + emtricitabine/tenofovir DF</td>
</tr>
<tr>
<td></td>
<td>Elvitegravir/cobicistat/emtricitabine/tenofovir DF*</td>
</tr>
<tr>
<td></td>
<td>Dolutegravir/abacavir/lamivudine*</td>
</tr>
<tr>
<td></td>
<td>Dolutegravir + emtricitabine/tenofovir DF</td>
</tr>
<tr>
<td>PI</td>
<td>Darunavir + ritonavir (qd) + emtricitabine/tenofovir DF</td>
</tr>
</tbody>
</table>

*Available as a once-daily, single-tablet regimen.

Notes:
- Lamivudine may substitute for emtricitabine or vice versa.
- Tenofovir DF: use with caution in patients with renal insufficiency.
- Elvitegravir/cobicistat/emtricitabine/tenofovir DF: only for patients with pre-ART creatinine clearance >70 mL/min.
- Dolutegravir/abacavir/lamivudine: only for patients who are HLA-B*5701 negative.

Regardless of Baseline HIV RNA Level or CD4 Count

**Most HIV+ patients will be treated with 1-pill once daily regimen**


Most HIV+ patients will be treated with 1-pill once daily regimen

---

**Case Presentation**
- 45-year-old male presents to E.D. in Abilene, TX, in Spring 2015 with 4-day illness:
  - Fever
  - Rhinorrhea
  - Dry cough
  - Dyspnea
- No PMH. No medications. Non-smoker.
- CXR: **RUL infiltrate**
  - Workup:
    - Normal/Negative: WBC, d-Dimer, troponin, BNP, Rapid flu, HIV antibody, ECG
    - **Abnormal**: Temp: 101.2°F, Creatinine: 1.6. Mild lymphopenia. Pulse ox: 91%
Hospital course
- Admit to 23-hour observation for CAP.
- Dx: Routine vs. Atypical vs. Viral
- Required supplemental O2.
- Chest CT: Bilateral patchy infiltrates, no P.E./cavities, nodes < 1 cm
- All Micro negative, including Blood cultures, Sputum Gm stain/ cx, UAT
- Additional history: Patient traveled from Saudi Arabia to London to DFW airport 3 days prior to admission; took bus to Abilene, TX
- Dx: ____ confirmed by PCR from sputum, NP/OP swab, and serum

Question
- How did the patient most likely acquire this infection?
  A. Close contact (i.e., household) with another human with this infection
  B. Close contact with an animal with this infection
  C. Brief contact (i.e., airplane travel) with a human with this infection
  D. Consumption of food product from an infected animal

MERS:
- How did the patient most likely acquire this infection?
  A. Close contact (i.e., household) with another human with this infection
  B. Close contact with an animal with this infection
  C. Brief contact (i.e., airplane travel) with a human with this infection
  D. Consumption of food product from an infected animal

Inpatient Prevention of MERS Transmission:
- Standard
- Contact
- Airborne
General Public Prevention:
- Handwashing
- Avoid camels, including drinking raw camel milk or camel urine

Middle East Respiratory Syndrome (MERS)
- First reported in Jordan in 2012
- 1042 cases, Males 62%
- Caused by a corona virus; “cousin” of SARS
- Fatality Rates – men 52%; women 23%
- Arabian peninsula: Saudi Arabia, UAE, Qatar, Oman, Jordan, Kuwait, Yemen
- Surge of 67 cases in February 2015 in Saudi Arabia
- Recent case in the Philippines
  - Healthcare-associated cases in Korea, 2015

Middle East Respiratory Syndrome (MERS)
- Cases reported in 23 countries
- 2 U.S. cases- HCW’s who returned home
- Fever and respiratory symptoms with 14 days of travel to endemic area
- Can survive for 2 days on hospital surfaces
- May be related to contact with camels
  - Bats are also probable reservoirs
- Can spread from person to person
  - Nosocomial spread noted
MERS Clinical Features

- Incubation period – 2-13 days (mean = 5)
- Acute respiratory illness:
  - F/C, Dry cough, Dyspnea, Myalgias
  - N/V/D, Sore throat, Abdominal pain, Dizziness
- Range from Asymptomatic → Mild Illness → Rapid progressive:
  - Pneumonia: Unilateral, Bilateral, Interstitial, Effusion
  - Leukopenia, Thrombocytopenia, Elevated LDH
  - Respiratory failure
  - Septic shock
  - Multi-organ failure

MERS Diagnosis: PCR of Upper & Lower Respiratory tract, and Blood

- Treatment: Supportive care

- Isolation: Standard, contact, airborne isolation
  - Korea, summer 2015:
    - Single Korean traveler to Middle East
    - 191 cases confirmed
    - 36 deaths
    - 16,693 contacts placed in Quarantine
    - Linked to healthcare facilities where MERS patients were treated
Original case report from Saudi Arabia 2012: 60 year old man died after 11 days in hospital. Progressive Renal and Respiratory failure.

Air Supply on Commercial Jetliners
- Fresh air pulled into cabin from outside through jet engine compressors
- Cooled air reaches you through overhead ducts
- Air leaves through grills along sidewalls and floor
- When air is pulled into grills, half is expelled from the plane and half is recycled through HEPA filters
- Total exchange of air occurs every 2-3 minutes
- Air flow is divided in sections, thereby limiting spread of infections
What is the Risk of Communicable Diseases on an Airplane?

- Research has shown very little risk
- HEPA filters remove dust, bacteria, fungi and viruses
- Transmission between passengers in same area:
  - As a result of coughing, sneezing or by touch
- Greatest risk: +/- 2 rows from index patient
- You are no more likely to contract a disease during a flight than you are sitting in a movie theater

Transmission of Infectious Diseases on an Airplane

- Most likely transmission occurs when airplane ventilation system is not working
- Transmission can occur in all sections of the passenger cabin when ventilation system is non-operational
- When aircraft is on the ground, ventilation system may not be turned on; fresh air is not pulled in
- Evidence of spread of disease in aircraft on the ground
Case Presentation

- 28-year-old female presents to E.D. with a 5 day history of:
  - Fever
  - Headache
  - Muscle aches
  - Joint pain
  - Increasing pain → unable to walk, unrelieved by nonsteroids.
- Returned 10 days ago from vacation in Bora Bora.
- Physical examination:
  - Temperature: 103°F, BP 110/60, P=120
  - Symmetric warmth, swelling, erythema, and tenderness of ankles, wrists, and fingers
  - Fine erythematous maculopapular rash is noted on the trunk and extremities.
- DDx = ______
Chikungunya Virus

- **History**
  - First described/identified by viral cultures in Tanzania in 1952
  - Case reports of similar illnesses trace back to 18th century in sailors to Africa and the West Indies
  - Name originates from “kungunyala” in the Kimakonde language – “to become contorted”

**Epidemiology**

- Endemic sylvatic cycle – Africa
  - Three genetically different lineages/sublineages
    - Asian lineage (Central/West African sublineages)
      - First major urban outbreak in 1958 – Bangkok
      - 1962 – urban areas India
      - 1958-1973 – sporadic outbreaks SE Asia, Indonesia
      - October 2013 – Caribbean, Brazil
    - Indian Ocean lineage
      - 2004 – urban outbreak coastal Kenya
      - 2005-2013 – various urban outbreaks on Indian Ocean islands, India, Southeast Asia
      - 2007 – urban outbreak Venice
      - 2010 – SE France

**CKV in the Americas**

Locations with reported local transmission by month

- Last updated February 9, 2013. Updates will be made monthly.
  - Chikungunya data: Pan American Health Organization
Laboratory-Confirmed US Chikungunya Cases, 2014

Travel-associated cases: 2,481
Texas: 8(1%)
Locally-acquired cases: Florida: 11
Laboratory-Confirmed US Chikungunya Cases, 2015

Total = 542
Texas = 32
(6% of total cases)

Countries with Documented Local Transmission

Human-to-human transmission of CKV via bites of infected mosquito –
- Aedes aegypti - chikungunya
- Aedes albopictus - Asian tiger
- Ochlerotatus - chikungunya
- Culex - yellow fever
- Anopheles - malaria

Occupational - documented; transfusion, transplantation (including corneal) - theoretical
Vertical/perinatal - documented
• Since early 1990's in eastern Texas
• Daytime biter
**Virology**
- CKV: single-stranded RNA virus
  - Genus: Alphavirus
  - Family: Togaviridae
- Genetic mutation in the envelope protein (A226)
- Enhances susceptibility of *Aedes albopictus* to infection, facilitates replication and dissemination to mosquito salivary glands
- Requires lower level of human viremia for effective transmission

**CKV Clinical Manifestations**
- Incubation: 2-4 days (up to 14 days)
- Acute illness: 7-10 days
  - High fever (40°C) 3-5 days
  - 2-5 days after onset of fever:
    - Polyarthralgia/arthritis
    - 10 or more joints
    - Symmetric - mimics seronegative
    - Hands (50-76%)
    - Wrists (29-81%)
    - Ankles (41-60%)
    - Axial skeleton involved (34-52%)
CKV Clinical Manifestations
3 days after onset of fever:
- Rash (40-75%) –
  - Trunk and extremities, including palms/soles
  - Pruritic
  - Patchy
  - Erythematous
  - Macular/maculopapular
  - Occasionally bullous
  - Rarely hemorrhagic

Headache
Myalgia (though joint complaints predominate)
Nausea, vomiting, diarrhea
Conjunctivitis
Peripheral lymphadenopathy (particularly cervical)
Lab: Lymphopenia, thrombocytopenia, elevated LFTs

CKV Clinical Manifestations
Persistent/relapsing symptoms:
- Arthritis, arthralgias
- Morning pain/stiffness
- Severe tenosynovitis/carpal tunnel
- Occasional TMJ/SCJ involvement
- Raynaud’s phenomenon (20%)
- Cryoglobulinemia present in up to 90% of patients with persistent symptoms
- Duration – up to 3 years post acute infection
CKV Management

- Diagnosis
  - Serum CHV RNA by RT-PCR if within first 5 days of illness (more sensitive/specific than viral culture)
  - CKV IgM is detectable an average of 5 days after onset of illness (range 1-12 days) and persist up to 3 months; if initial results negative and CKV still suspected, recheck IgM > 7 days after onset
  - CKV IgG is detectable ~ 2 weeks after onset of illness and persists for years, confers immunity

- Therapy
  - Supportive care
  - Ribavirin active in vitro
  - No vaccine available
  - Reportable disease

Prevention

- Air conditioning or window/door screens
- Empty standing water from containers where mosquitoes can breed
- Long-sleeved shirts and long pants
- Insect repellents containing DEET, picaridin, IR3535, oil of lemon eucalyptus or para-menthane-3, 8-diol
- Permethrin-treated clothing
Differential Diagnosis
- Dengue
- Malaria
- Rickettsial illness
- Enteric fever
- Leptospirosis
- Relapsing fever
- Ross River virus
- Measles, rubella
- EBV
- Meningococcal infection

CKGV vs. DENV

**CKGV**
- Fever
- Headache
- Rash (erythematous)
- Arthralgias
- Arthritis
- Thrombocytopenia (mild)
- Elevated LFTs (mild)
- Mild-moderate disease

**DENV**
- Fever
- Headache
- Retroorbital pain
- Rash (may be hemorrhagic)
- Arthralgias
- Myalgias
- Thrombocytopenia (marked)
- Elevated LFTs (marked)
- Severe disease

THINK CO-INFECTION
Case Presentation

- 32 yo female traveled to Cook Islands for vacation
- Returned to Plano, Tx with c/o:
  - Fever
  - Arthralgia (without arthritis)
  - Myalgia
  - Headache
  - Maculopapular rash
  - Conjunctivitis
  - Diarrhea

DDx = ?

- Dengue
- Chikungunya
- Malaria
- Rickettsial infection
- Leptospirosis
- Typhoid
- Measles
- Rubella
- Yellow Fever
- WNV
- Japanese Encephalitis

Zika virus infection

- ssRNA flavivirus
- Mosquito vector
- Aedes aegypti
- First isolated in 1947
- Zika forest, Uganda
- 2007 outbreak on Yap island
- Micronesia
Other ID News 2015

- New drugs:
  - Avycaz (ceftaz + avibactam)
  - Dalvane (dalbavancin)
  - Oxtav (oxtavancin)
  - Sivextro (tedizolid)
  - Zerbaxa (ceftolozane + tazobactam)
- C Diff
- Vaccines:
  - Prexar-13
  - Mening B
  - HPV
  - Varicella Zoster

- Shigella resistance
- Ebola
- HCV drugs
- Ocular syphilis
- STD guidelines
- Isolation precautions
- Cellular therapy
- MALDI-TOF
- Microbiome

Thank You
Adult Survivors of Childhood Cancer

Hilary Suzawa, MD, MS
Assistant Professor
Baylor College of Medicine
Texas Children’s Cancer Center

Who?

• Childhood cancer survivor
  – Diagnosed with cancer at age <18 years
  – Completed therapy and in remission
  – Off therapy at least 2 years

• ~300,000 childhood cancer survivors in the U.S.
  – Most between the ages 20-34 years

Seehusen et al. American Family Physician 2010

Desired Outcome

• Increase awareness of clinical recommendations for adult survivors of childhood cancer

• Where do I find clinical recommendations?

• What information do I need about the patient?
Resource

What is the best resource for recommended follow-up of childhood cancer survivors?

A. American Cancer Society (ACS)
B. National Comprehensive Cancer Network (NCCN)
C. Pediatric Oncology Group (POG)
D. Children’s Oncology Group (COG)

Resource

Answer D. Children’s Oncology Group
www.childrensoncologygroup.org

Clinical Recommendations

Follow-up recommendations are primarily based on what patient information?

A. Diagnosis (cancer type)
B. Age at diagnosis
C. Cancer treatment (chemotherapy, XRT)
D. Time off therapy
Clinical Recommendations

Answer C. Cancer treatment
- Surgery, Chemotherapy, Radiation, Transplant
- Exposures

A. Diagnosis (cancer type)—eg ALL SR vs HR, T-cell, infant ALL
B. Age at diagnosis—may affect risk, <1 yr
D. Time off therapy—no “safe” time

Case 1: Hodgkin’s Disease

- 30 yo F with h/o Hodgkin’s Disease dx at 17 yrs
- Surgery—biopsy of supraclavicular LN
- Chemotherapy

<table>
<thead>
<tr>
<th>Bleomycin</th>
<th>Prednisone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Vincristine</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>VP-16</td>
</tr>
</tbody>
</table>
- Radiation—21 Gy to mantle field
- Off therapy 12 years

Case 1: Hodgkin’s Disease

Which of the following is the patient LEAST likely to need?

A. Echocardiogram
B. DEXA bone density
C. Pulmonary Function Tests (PFTs)
D. CT chest
Case 1: Hodgkin’s Disease

Answer D. CT Chest
- Imaging for surveillance of cancer
- Road map

A. Echocardiogram—Doxorubicin + XRT
B. DEXA bone density—Prednisone
C. Pulmonary Function Tests (PFTs)—Bleomycin + XRT

Case 1: Hodgkin’s Disease

What BEST describes recommendations for breast cancer screening in this patient?

A. Same as general population
B. Early screening at age 35 with mammogram
C. Early screening at age 25 with breast ultrasound
D. Early screening at age 25 with breast MRI

Case 1: Hodgkin’s Disease

Answer D.
Early screening at age 25 with breast MRI

- Children’s Oncology Group Guideline
- >20 Gy to the Chest
- Mammogram and Breast MRI
- Yearly
- Beginning 8 years after radiation or at age 25, whichever occurs last
Breast Cancer Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>Cumulative incidence of breast cancer by age 50 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRCA 1</td>
<td>31%</td>
</tr>
<tr>
<td>BRCA 2</td>
<td>10%</td>
</tr>
<tr>
<td>Hodgkin’s Lymphoma Survivors</td>
<td>35%</td>
</tr>
<tr>
<td>Other childhood cancer survivors</td>
<td>15% (by age 45 years)</td>
</tr>
</tbody>
</table>

Moskowitz C et al. Journal of Clinical Oncology 2014

---

Case 2: Osteosarcoma

- 22 yo M with Osteosarcoma dx at age 4 yrs
- Surgery: Femur bone biopsy, right AKA
- Chemotherapy
  - Cisplatin
  - Doxorubicin
  - Ifosfamide
- No XRT
- Off therapy 16 years

---

Case 2: Osteosarcoma

Which of the following chemotherapy agents is MOST likely to affect fertility?

A. Doxorubicin
B. Ifosfamide
C. Methotrexate
D. VP-16
Case 2: Osteosarcoma

- Answer B. Ifosfamide

- Alkylating Agents

<table>
<thead>
<tr>
<th>Substance</th>
<th>Abbreviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Busulfan</td>
<td>Busem</td>
</tr>
<tr>
<td>Carmustine (BCNU), Lomustine (CCNU)</td>
<td>Melphalan</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>Procarbazine</td>
</tr>
<tr>
<td>Cyclophosphamide, Ifosfamide</td>
<td>Thiopeta</td>
</tr>
</tbody>
</table>

- Heavy Metals: Carboplatin, Cisplatin
- Non-Classical Alkylators: Dacarbazine (DTIC), Temozolomide

Case 2: Osteosarcoma

- Fertility—2 types of testing

  - Hypogonadism
    - LH, FSH, testosterone—baseline at age 14
    - 8 AM labs
    - Refer to Endocrine
  - Sperm analysis testing
    - Refer to Urology (Fertility Specialist)
    - Sperm banking prior to testosterone therapy

Case 2: Osteosarcoma

Patient returns 5 years later. He is newly married and they want to have kids. What should you tell him?

A. Offspring are at higher risk of having cancer
B. Offspring are at higher risk of having birth defect
C. Parents should see a genetic counselor
D. There are no special recommendations
Case 2: Osteosarcoma

• Answer D. 
There are no special recommendations

• For offspring of childhood cancer survivors there is no identified increased risk of cancer or birth defects compared to the general population
  – Childhood Cancer Survivor Study (CCSS)
• Exception: Genetic/Hereditary cancer types

Passport for Care

• Internet resource
  – Collaboration TXCH, BCM, CCIT, COG
• Uses the COG guidelines to generate an individualized treatment summary and clinical follow-up recommendations for specific patient
• Two versions: Clinician and Patient
• http://txch.org/cancer-center/long-term-survivor-program/passport-for-care/

PFC Clinician 
Breast Cancer Screening
Passport for Care Patient Website

• If you have an eligible patient who is interested in signing up for Passport for Care Patient Website, please contact
  
- Help Desk: svp-helpdesk@bcm.edu

- Ellen: exshohet@txch.org
References


References

- Children’s Oncology Group
  - http://childrensoncologygroup.org
  - http://www.survivorshipguidelines.org
- Passport for Care
  - https://www.passportforcare.org/
2015 - Back to the Future with Adult Congenital Heart Disease?

Wilson Lam, MD
November 8th, 2015
Texas ACP
Dallas, Texas

NO DISCLOSURES

Goals and Objectives

• To review recommendations and guidelines about adult congenital heart disease training and expertise

• To examine follow-up for common lesions and lifelong care

• To address common questions on SBE prophylaxis, pregnancy, and implantable devices
Well-known ACHD patients...

Epidemiology

- CHD affects 8 out of every 1000 live births
  - In the U.S.: 32,000 infants born/year have CHD
- 20,000 open heart operations/year for CHD
- 40% are operated on during 1st year of life
- Surgical mortality rate is about 2 in 100
- U.S. population of adults with CHD now exceeds 1,000,000

Prevalence of Congenital Heart Disease (CHD)

- Prevalence in US: approximately 1.8 million
  - 6/1000 general population
- More patients living to adulthood
  - ~85% with CHD survive to adulthood due to medical and surgical advancements
  - Median age of CHD patient: 17 in 2000 vs 11 in 1985
**Question 1**
A new patient with Tetralogy of Fallot is scheduled to see you but hasn’t seen a doctor in 20 years. You call your local general cardiologist for consultation. They have an interventional cardiologist and an EP in the group as well. They all trained in the COCATS 3 era (Core Cardiovascular Training Statement - requirements for cardiology) and all achieved Level 1 (basic) training. Which of the following statements about cardiology training in the United States is TRUE?

A) COCATS 3 required 12 hours of lectures regarding ACHD care  
B) COCATS 4 does not support Level 2 (intermediate) training  
C) COCATS 4 requires a month rotation on ACHD service  
D) 1 year of advanced ACHD training is required for Level 3 (expert) COCATS 4 certification and ABIM board eligibility
Training in ACHD:

- 6 hours of lectures
- Keep a patient log
- Hopefully once a month case discussion
- ACHD service recommended

Adult Congenital Heart Centers in the U.S. 2015

http://www.achaheart.org/home/clinic-directory.aspx

Trained ACHD Cardiologists
Question 2

You are reviewing the reports from the Texas Adult Congenital Heart Center. You are aware of the Choosing Wisely campaign to reduce unnecessary testing. Regarding your patients and their families, which of the following pairs is NOT matched correctly?

A) 25 yo with coarctation: routine MR angiogram of the head
B) 35 yo older brother of your 26 yo pt with bicuspid AoV: echo
C) 18 yo with confirmed Loeys-Dietz syndrome: MR angiogram c/a/p
D) 30 yo asymptomatic daughter of 55 yo with HCM: annual echo
Question 2

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C) 18 yo with confirmed Loeys-Dietz syndrome: MR angiogram cl/p
D) 30 yo asymptomatic daughter of 55 yo with HCM: annual echo

5. Recommendations for Genetic Syndromes

Class I

1. An echocardiogram is recommended at the time of diagnosis of Marfan syndrome to determine the aortic root and ascending aortic diameters (see Figure 5) and in months thereafter to determine the rate of enlargement of the aorta. (Level of Evidence: C)

2. Annual imaging is recommended for patients with Marfan syndrome if unsplitting of the aortic diameter is documented. If the aortic diameter is 4.5 cm or greater, or if the aortic diameter shows significant growth from baseline, more frequent imaging should be considered. (Level of Evidence: C)

3. Patients with Loeys-Dietz syndrome should undergo complete aortic imaging at initial diagnosis and 6 months thereafter to establish if enlargement is occurring. (Level of Evidence: C)

4. Patients with Loeys-Dietz syndrome should have yearly magnetic resonance imaging from the area of arteriovenous fistula to the pelvis. (Level of Evidence: B)

Table: Recommended Clinical Practices for Adults

<table>
<thead>
<tr>
<th>Recommended Clinical Practices for Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access To Care</td>
</tr>
<tr>
<td>Code Red: The Critical Care in Texas</td>
</tr>
<tr>
<td>Access For Change</td>
</tr>
</tbody>
</table>

11/3/2015
Question 3

A 28 yo with cleft mitral valve becomes severely regurgitant. She has a mechanical valve replacement and has an INR of 3.1 on Coumadin 4 mg daily. She is 7 weeks pregnant. Which of the following statements regarding management is **TRUE** for her case?

A) Warfarin is preferred in the first two trimesters
B) First trimester anticoagulation of choice is enoxaparin
C) Pregnancy is contraindicated; advise termination
D) WHO pregnancy category is II, trimesterly visits are recommended
Question 4

Your local dentist is about to do teeth cleaning on several of your patients with adult congenital heart disease. Which of the following patients does NOT require SBE prophylaxis per 2007 guidelines?

A) 37 yo Fontan with saturation 89% and echo evidence of fenestration
B) 25 yo TOF with transannular patch repair and mod Pulm Regurg
C) 52 yo with transcatheter ASD closure 4 weeks ago
D) 18 yo VSD closure with residual patch leak

Question 5

A 42 yo with d-TGA and Mustard procedure has a systemic RV with severely depressed systolic function and was told he needs to have a defibrillator implanted. He has never been resuscitated for sudden death. Which of the following statements about cardiac implantable defibrillators in congenital heart disease is TRUE?

A) Primary prevention ICD implantation for systemic RVs is a class I indication and compares favorable to primary prevention for ICMP/NICMP
B) Subcutaneous ICDs are contraindicated in congenital heart disease
C) Evidence to support primary prevention ICD implantation in systemic RV is level C (expert opinion)
D) Antitachycardia pacing in CHD shows similar negative effects as seen in the MADIT-RIT trial
Question 5

A 42 yo with d-TGA and Mustard procedure has a systemic RV with severely depressed systolic function and was told he needs to have a defibrillator implanted. He has never been resuscitated for sudden death. Which of the following statements about cardiac implantable defibrillators in congenital heart disease is TRUE?

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C) Evidence to support primary prevention ICD implantation in systemic RV is level C (expert opinion)
D) Antitachycardia pacing in CHD shows similar negative effects as seen in the MADIT-RIT trial
Less is more... MADIT


Summary

- Training in ACHD is being redefined
  - Importance of access to care
    - Palliation + cure
  - SBE prophylaxis changed in 2007
    - Are infections on the rise?
    - Most ACHD patients can get pregnant
      - Some conditions require closer monitoring
  - Device therapies are gaining momentum
    - Despite low-level evidence
THE END
Hydroxyurea in the Young Adult with Sickle Cell Disease

Alecia Nero, M.D.
Assistant Professor
Division of Hematology-Oncology
Departments of Internal Medicine and Pediatrics
UT Southwestern Medical Center, Dallas, TX

CASE #1

An 18 y/o male with hemoglobin SC disease presents to establish care. His sickle cell disease has been complicated by several hospital admissions for pain during pediatric care and thus started on hydroxyurea 1000 mg daily. He has been maintained on this stable dose for the last 2 years prior to his current transfer from pediatric to adult-centered care with perfect medication and laboratory compliance. He plans to attend college out of the city but has frequent trips planned to return home for visits as his university is within driving distance.

CASE #1 (cont’d)

At this point you recommend which of the following:
A. Refill his hydroxyurea and advise him to find a provider near his college campus to monitor.
B. Coordinate with his local resources and you monitor his laboratory counts and hydroxyurea refills.
C. Tell the patient he should stop taking hydroxyurea and see if he still needs this medication as he has been well for the past 2 years and this drug will give him cancer.
CASE #2

A 20 year old male with hemoglobin SS disease presents to establish care. He reports that he has not had any hospital admissions or Emergency Department visits. He has pain about twice per week for which he takes prescribed oral opioid pain medication at home. His baseline total hemoglobin is 6.5 g/dL. He reports experiencing some DOE but no SOB at rest. He does take naps in the daytime after classes due to chronic fatigue. He does not participate in any extracurricular physical activities as it makes him feel very tired.

CASE #2 (cont'd)

You provide the following management plan for this patient:
A. You order a type and crossmatch to begin packed red blood cell transfusion protocol.
B. You tell the patient he is addicted to prescription pain drugs and offer referral to addiction medicine.
C. You educate patient on hydroxyurea and recommend this as the potential therapeutic option.
D. You tell the patient he is doing well and can continue the current regimen as it seems to be working.

HYDROXYUREA

First used in 1970’s to treat polycythemia vera

Studied in sickle cell disease (SCD) in mid-1980’s as oral agent that increases Hb F (Fetal hemoglobin)

Small uncontrolled studies in late 1980’s and early 1990’s showed promise

The only FDA-approved drug for sickle cell disease
HYDROXYUREA

• Nomenclature
  o Hydroxyurea (HU) = Hydroxycarbamide
  o Brand Names: Droxia®, Hydrea®

• Drug category
  o Antimetabolite

• Ribonucleotide reductase inhibitor that inhibits DNA synthesis

• Cellular effects
  o Induce fetal hemoglobin
  o Reduce neutrophil/retic counts
  o Decrease hemolysis and adhesiveness
  o Increase NO availability

HYDROXYUREA

• Clinical consequences
  o Decrease pain crises
  o Decrease hospitalizations
  o Decrease need for blood transfusions
  o Decrease episodes of acute chest syndrome
  o Decrease in mortality
HYDROXYUREA

- Adverse Effects:
  - Myelosuppression (excessive)
  - Mild GI upset
  - Skin/nail discoloration, rash
  - Dose reduce with renal dysfunction to minimize toxicity
  - Elevated LFTs
  - Contraindicated with anti-retroviral
  - Potential teratogen/ lower sperm counts

UNDERUTILIZATION OF HYDROXYUREA

- 4 Levels of Barriers:
  - Patient: lack of knowledge about the drug, lack of understanding how the drug works/discordant expectations, concerns of being part of an experiment, need for monitoring, poor adherence
  - Parent/Family/Caregiver: fears (cancer, infertility, long-term unknown effects), lack of knowledge, difficulty communicating with patient about the medication

UNDERUTILIZATION OF HYDROXYUREA

- Barriers (cont’d):
  - Provider: fears of drug effects, lack of knowledge/understanding specifically in sickle cell disease, provider bias and negative attitudes, unfamiliar with regimen/underdosing; limited access to SCD experts; not engaging family/caregiver in discussion
  - System: under-/uninsured, geographic location, lack of coordination between academic and community providers, limited access to comprehensive centers, inadequate support for SCD, slow development/promotion of SCD, cultural/language barriers, inadequate IT to support long-term care of people with SCD

CASE #1

An 18 y/o male with hemoglobin SC disease presents to establish care for his sickle cell disease. His disease has been complicated by several hospital admissions for pain during pediatric care and thus started on hydroxyurea 1000 mg daily and has been maintained on stable dose for the last 2 years before his pediatric transfer. He plans to attend college out of the city but has been perfect in medication/laboratory compliance and has frequent trips planned to return home for visits as his university is within driving distance.

ANSWER: B
Coordinate with his local resources and you monitor his laboratory counts and hydroxyurea refills.

CASE #2

A 20 year old male with hemoglobin SS disease presents to establish care. He reports that he has not had any hospital admissions or Emergency Department visits. He has pain about twice per week for which he takes prescribed oral opioid pain medication at home. His baseline total hemoglobin is 6.5 g/dL. He reports experiencing some DOE but no SOB at rest. He does take naps in the daytime after classes due to chronic fatigue. He does not participate in any extracurricular physical activities as it makes him feel very tired.

ANSWER: C
You educate patient on hydroxyurea and recommend this as the potential therapeutic option.

RESOURCE

Evidence-Based Management of Sickle Cell Disease
Expert Panel Report, 2014

I have no disclosures of any kind

This lecture is intended to inform, and to advocate neither for nor against the described practice.

I do not want to die. But I am dying. And I want to die on my own terms. I would not tell anyone else that he or she should choose death with dignity. My question is: Who has the right to tell me that I don’t deserve this choice? That I deserve to suffer for weeks or months in tremendous amounts of physical and emotional pain? Why should anyone have the right to make that choice for me?

Slide courtesy of Robert Fine - used with permission
Patients' Rights Movement

Loss of institutional trust

New technology, new questions

1967 - Living Will invented
1990 - Cruzan case: right to refuse medical treatment
1997: IOM Report

History and Definitions

Brittany Maynard
 Died November 3, 2014

Definitions

Euthanasia - the act or practice of killing someone who is very sick or injured in order to prevent any more suffering

Suicide - the act of killing oneself because of a desire not to continue living

Physician Aid in Dying: The act whereby a qualified terminally ill patient self-administers life-ending medication provided by a physician. Unlike suicide, the person is going to die and curative treatment is not available.
ACP Position Paper: 2001

In summary, the ACP–ASIM does not support the legalization of physician-assisted suicide. Its practice would raise serious ethical and other concerns, as outlined above. Physicians cannot give to individuals the control over the manner and timing of death that some seek. But, throughout patients’ lives, including as patients face death, medicine must strive to give patients the care, compassion, and comfort they need and deserve.

Snyder & Sulmasy, Annals of Int Med 2001

Current Consensus

Decision to forgo life-sustaining treatment is NOT equivalent to PAD or euthanasia

morally

legally

clinically

Patients have a right to refuse unwanted medical treatment

Patients have a right to aggressive symptom management, even if treatment inadvertently hastens death


Safeguards

Concerns about capacity to Psychiatric capacity and Psychiatry & Medicine

2 Witnesses to written request

Pt. reminded can rescind at anytime

Pt. is asked to contact NOK about request

Figure 1: DWA prescription recipients and deaths*, by year, Oregon, 1998-2012

Figure 2: Summary of DWA prescriptions written and medications ingested in 2014, as of February 2, 2015

673 patients died using PAD since 1997

1997
15 Years of DWDA

Table 1. Characteristics and end-of-life care of 673 DWDA patients who have died from ingesting a lethal dose of medication as of January 14, 2013, by year, Oregon, 1998-2012

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>2012 (N=77)</th>
<th>1998-2011 (N=596)</th>
<th>Total (N=673)</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of life concerns</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Losing autonomy (%)</td>
<td>72 (93.5)</td>
<td>538 (90.9)</td>
<td>610 (91.2)</td>
</tr>
<tr>
<td>Less able to engage in activities making life enjoyable (%)</td>
<td>71 (92.2)</td>
<td>523 (88.3)</td>
<td>594 (88.8)</td>
</tr>
<tr>
<td>Loss of dignity (%)</td>
<td>60 (77.9)</td>
<td>386 (62.7)</td>
<td>446 (66.2)</td>
</tr>
<tr>
<td>Losing control of bodily functions (%)</td>
<td>27 (35.3)</td>
<td>318 (53.7)</td>
<td>345 (51.6)</td>
</tr>
<tr>
<td>Burden on family, friends/caregivers (%)</td>
<td>44 (57.1)</td>
<td>214 (36.1)</td>
<td>258 (38.6)</td>
</tr>
<tr>
<td>Inadequate pain control or concern about it (%)</td>
<td>23 (29.9)</td>
<td>134 (22.6)</td>
<td>157 (23.5)</td>
</tr>
<tr>
<td>Financial implications of treatment (%)</td>
<td>3 (3.9)</td>
<td>15 (2.3)</td>
<td>18 (2.7)</td>
</tr>
</tbody>
</table>


Characteristics of 673 DWDA patients who died after ingesting lethal dose of medication:

- 51.6% male
- Median age of 71 (range 25 - 96)
- 97.6% white (81% of Oregon residents are white)
- 45% married, 23% divorced
- 71% had at least some college education
- 64.6% had private insurance.
- The primary diagnosis was cancer (80.3%)
- 95% died at home


Role of Palliative Care and Hospice in the era of PAD

Table 1. Characteristics and end-of-life care of 673 DWDA patients who have died from ingesting a lethal dose of medication as of January 14, 2013, by year, Oregon, 1998-2012

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>2012 (N=77)</th>
<th>1998-2011 (N=596)</th>
<th>Total (N=673)</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of life care</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospice</td>
<td>64 (87.0)</td>
<td>522 (88.7)</td>
<td>586 (88.4)</td>
</tr>
<tr>
<td>Not enrolled (%)</td>
<td>2 (2.8)</td>
<td>60 (10.3)</td>
<td>62 (9.3)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Patient died at</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home (patient, family or friend) (%)</td>
<td>94 (89.5)</td>
<td>726 (93.1)</td>
<td>819 (86.6)</td>
</tr>
<tr>
<td>Long term care, assisted living or foster care facility (%)</td>
<td>8 (7.6)</td>
<td>29 (4.3)</td>
<td>37 (4.3)</td>
</tr>
<tr>
<td>Hospital (%)</td>
<td>0 (0.0)</td>
<td>1 (0.1)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Other (%)</td>
<td>0 (0.0)</td>
<td>1 (0.1)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>


Who is requesting PAD?

Seekers tend to be:
- Active, independent/anti-dependent types
- Long-time believers in self-determination
- Pragmatic, take-charge people
- Less interested in quantity of life than in quality of life

- Seekers seem greatly palliated by knowing that the option is accessible on demand.

Motivation is:
- Desire to control circumstances of death
- Die at home
- Maintain independence
- Avoid future physical symptoms

Ganzini L et al. Oregonians' reasons for requesting MD
Arch Intern Med 2009;169:
Hopelessness, Depression, or Lack of self-deception?

- I look forward to the future with hope and enthusiasm.
- I have enough time to accomplish the things I most want to do.
- In the future I expect to succeed in what concerns me most.
- My future seems dark to me.
- I just don’t get the breaks, and there’s no reason to believe that I will in the future.
- My past experiences have prepared me well for my future.
- All I can see ahead of me is unpleasantness rather than pleasantness.
- I don’t expect to get what I really want.
- When I look ahead to the future I expect I will be happier than I am now.

Beck Hopelessness Scale

“A recent study using a sample of physically healthy psychiatric inpatients and nonpsychiatric community-based individuals found that higher BHS hopelessness scores were correlated with lower scores on a measure of unconscious self-deception.”

Smith et al. J Pain Sympt Mgmt 2015

Spirituality and PAD Requests

Characteristics associated with request for PAD were depression, hopelessness, dismissive attachment and low levels of spirituality.


15 Years of DWDA

Process remains tightly regulated and monitored - almost 100% compliance with requirements.

No evidence of slipping down the slope to include euthanasia, voluntary or otherwise.

Good Palliative Care did not eliminate desire for PAD


PAD and Depression

About 50% of those with persistent desire for PAD have some evidence of clinical depression.

17% of the patients approved for a prescription met criteria for depression and ingested lethal medication, none evaluated by psychiatry.

“whether the depressive disorder influenced the judgment of the three individuals who received PAD is unknown.”

Only 2% of patients who received prescription were referred for psychiatric evaluation.


Moral Traditions

Sanctity of human life
Value of struggle and suffering

Questions Answered
Vulnerable populations not at increased risk
Requests not a barrier to Palliative Care
Requests are not driven by poor pain management or primarily by financial concerns
Untreated depression may be an issue or may represent lack of self-deception

Hippocratic Oath

Hippocratic oath precludes euthanasia and assisted suicide: “I will apply dietetic measure for the benefit of the sick according to my ability and judgment; I will keep them from harm and injustice. I will neither give a deadly drug to anybody if asked for it, nor will I make a suggestion to this effect. Similarly I will not give a woman an abortive remedy. In purity and in holiness I will guard my life and my art.”

“I will not give a lethal drug to anyone if I am asked.” Historical context: in ancient Greece, doctors were sometimes used as skilled political assassins. There was thus a legitimate fear of the physician as a poisoner. Oath was not rediscovered until 1590. Asks participant to swear to Apollo, treat teacher as equal to parent (and offspring as siblings), and train other physicians for free.

PAD undermines the integrity of the profession
Failure to provide PAD undermines integrity of the profession.

The Debate

Beneficence
“Human life is sacred, but only to the extent that it contributes to the joy and happiness of the one possessing it, and to those about him, . . . and it ought to be the privilege of every human being to cross the River Styx in the boat of his own choosing, when further human agony cannot be justified by the hope of future health and happiness.”  - Eugene Debs

Concerns NOT addressed by the Oregon Data

Oregon is different from other places
PAD undermines the integrity of the profession
PAD undermines patient/physician relationship
Prognostic accuracy of physician estimates not monitored - errors?

Autonomy

The right to self governance is absolute
This right must include the ultimate autonomous act of choosing when and how to die
Competent people should have right to choose the timing and manner of death.

Not all voluntary acts are themselves justified by autonomy (as a society we prevent dueling or the selling of oneself into slavery).

Not all agree that autonomy is absolute, arguing that we belong to either God or our community.
Genuine tragedies in the world are not conflicts between right and wrong. They are conflicts between two rights.

Georg Wilhelm Friedrich Hegel

The View from the Edge

Death is messy. Even the best Palliative Care cannot change the reality that dying is scary both physically and existentially.

Suffering can be tremendous.

Spiritual and emotional growth can be substantial.

Stance on PAD is about how you balance the right of the patient to avoid "unnecessary suffering" and physician right not to cause death

In the end, PAD is a distraction from the real problem: fear of death, and lack of a reassuring medical structure to care for the dying

Benficience

In the face of unmitigated suffering, the most beneficent act is to kill the patient.

The most beneficent act in the face of suffering is good palliative care.

Rare cases of unmitigated suffering do not justify changing medicine’s historic rules

Intent Vs. Effect

End result is death with PAD or without it. How we get there is not important.

Morally, intent and action are what matter. The intent of withdrawal is to allow nature to take its course.

It is disingenuous to argue that death is not the intent in cases of withdrawal, withholding or terminal sedation.
Thanks

Bob Fine and Michael Rubin
Ethicists

UT Southwestern Palliative Care Teams

Parkland: Sigy Chathanatt, Nadine Semer, Ramona Rhodes, Reeni Abraham, Betsy Porter, Porsche Jones, Eileen McMenemey, Virginia Buschardt, Michael Smith, Abigale O’Reilly, Carol Chamberlain, Kimberly Williams, Horacio Gutierrez, Flor Perez, Latisha Blair, Janice Jones, Karen Jones, Veronica Saucedo

Thanks

UT Southwestern Palliative Care

CUH: Sunitha John, Tamara McGregor, Desi Carozza, Chidimma Nguma, Melissa Mayer, Mary Gill, Steven Leach, Jack Hamilton

VA: Elizabeth Polanco, Guna Raj, David Hales

CMC: Donald Cochran, Heather Patterson, Stacy Smith

If I spend all my time worrying about the lottery I will never win, what am I not doing?

We do not maintain hope by maintaining false hope. We propagate fear, and distract from the real work to be done.

We respect autonomy, beneficence and correct intention when we help patients stop playing a lottery they can never win.

Dying in America
Inspiring Quality and Honesty in End-of-Life Care

COMPONENT
- Frequent assessment of the patient’s physical, emotional, social, and spiritual needs
- Management of emotional distress
- Management of pain and other symptoms
- Counseling of patient and family
- Family caregiver support
- Attention to the patient’s spiritual and religious needs

RATIONAL
- Interventions and assistance must be based on accurately identified needs
- All decisions should be able to identify distress and direct the initial and basic management. This is part of the definition of palliative care, a basic component of hospice, and clearly of fundamental importance.
- People with palliative needs beyond those that are provided by non-specialist level clinicians deserve access to appropriate level care.
- People who meet the hospice eligibility criteria deserve access to services designed to meet their end-of-life needs.
- Care of people with serious illness may require specialized level palliative care physician and corresponding physician management requires direct examination, contact, and communication.
- All decisions should be able to identify and direct the physical, emotional, social and spiritual management of pain and other symptoms. This is part of the definition of palliative care, a basic component of hospice, and clearly of fundamental importance.
- A focus on the family is part of the definition of palliative care, family members and caregivers both participate in the patient’s care and require assistance themselves.
- Person-centered care requires awareness of patients’ perspectives on their social environment and of their needs for social support, including at the time of death. Compassion at the bedside or in time of death may depend on understanding the medical, social, and spiritual aspects of end of life care for some individuals.

The final phrase of life often has a spiritual and religious component and research shows that spiritual care is associated with quality of care. Care must be person-centered and fit current circumstances, which may mean that not all of the above components will be important or desirable in all cases.
A Case of a GI Motility Disorder

Richard W. McCallum, MD, FACP, FRACP (AUST.), FACG, AGAF
Professor and Founding Chair of Medicine, Director of Center for Neurogastroenterology and GI Motility
Texas Tech University Health Sciences Center, Paul L. Foster School of Medicine, El Paso, TX

Case Presentation

- A 33-year-old woman
- Chief complaint:
  - nausea and vomiting of 8 months duration
- PMH:
  - 20-year history of type I diabetes mellitus with retinopathy and peripheral neuropathy.
  - Her glycemic control is suboptimal; hemoglobin A1c = 9.8%.
  - Symptoms begin about 30 minutes after a meal and are characterized by early satiety, nausea, epigastric fullness, bloating, and pain as well as degrees of heartburn and GE reflux. In addition, there is increase in gas and bloating and irregular episodes of diarrhea, including nocturnal.
  - Vomiting is less frequent (2–3 days/week); however, when it does occur, it is usually 2 to 4 hours after eating and on several occasions she has identified food in the vomitus that she consumed the previous day. She also lost 9 kg in this timeframe.
  - Her nausea and vomiting have led to 6 emergency department visits and 4 hospitalizations in the past year.
  - She is not able to work and take care of her family because of these symptoms.
- Medications:
  - Insulin, Lisinopril

Physical Exam:

- Her weight was 50 kg and height: 158 cm (body mass index: 20 kg/m²).
- Her abdominal examination revealed epigastric fullness and tenderness.
- A succussion splash was able to be induced.
- Peripheral neuropathy in the distal extremities was detected.
- Labs & Diagnostic tests:
  - Complete blood count, comprehensive metabolic panel: Alb: 2.9, normal renal function, thyroid function tests (thyroid stimulating hormone, 2 mIU/L; free T4, 6 mg/dL), and random cortisol levels (18 mg/dL) were normal.
  - An abdominal ultrasound, small-bowel series, and upper gastrointestinal endoscopy did not show any abnormalities (gastric ulcer, pyloric obstruction) including negative biopsies for sprue and H. pylori.
  - A Glucose Breath Test was positive for Small Intestinal Bacterial Overgrowth (SIBO) and treated with Rifaximin and then Probiotics which resolved her diarrhea, gas and bloating.

Clinical Course:

- Patient started on PPI Therapy (Nexium 20 mg/day) for heartburn and epigastric pain, antihistaminics (Phenergan, Zolmet PRN) and Tramadol PRN for abdominal pain.

Case Continued-
• What is the next test recommended to make the diagnosis for her nausea and vomiting?

• 1) Abdominal CT Scan
• 2) Gastric Emptying Test
• 3) Colonoscopy
• 4) Brain MRI

Normal 4-hour standardized Scintigraphic Gastric Emptying

Gold Standard Meal:
- 120 g 99mTc-labeled egg substitute (Eggbeater)
- 2 slices of bread
- 30 g strawberry jam
- 120 ml water
- 255 kcal, 2% fat

A 4-hour standardized gastric emptying study showed 40% retention of the meal at the end of 4 hours (normal, <10% retention).
Management Continued-

- Based on the results of the gastric emptying test, dietary modification was instituted (small frequent meals and a low-roughage diet).
- Metoclopramide orally at 10 mg 4 times/day and Promethazine at 25 mg orally every 4 hours as needed.
- Recommendations also were made to better control her blood sugars.

Course:
- Although she noticed some improvement in symptoms initially with these therapeutic measures, the response seemed to wane over the next few months.
- The patient wants relief from nausea, which she regards as the most disabling symptom, and seeks further consultation.

What are other treatment options that are available for this patient?

- 1) Other Prokinetic Agents
- 2) CNS Modifying Agents
- 3) Pyloric sphincter Botox injection
- 4) Feeding Jejunostomy and antral biopsy
- 5) All of the above
Treatment Strategies:
Escalating the Intensity of Therapy

- **Mild Gastroparesis**
  - Not daily symptoms, no hospitalizations, no impact on work and family functioning
    - Recommended: diet modifications—smaller meals, mechanical soft, low fiber, low fat, caloric supplements as needed
  - Antiemetics prn, review of medications and glucose control

- **Moderate Gastroparesis**
  - Daily symptoms, not continuous, occasional hospitalization, interfering with work and family functioning
    - Recommended: diet modifications, prokinetics, one or more antiemetics and glucose control, also address pain and psychological aspects

- **Severe Gastroparesis**
  - Daily, continuous symptoms, multiple ED/hospitalizations, not able to work and function
    - Recommended, combining prokinetics, multiple antiemetics, nutrition and enteral support
    - 25-30% of gastroparetic patients will fail these medical therapies.
    - Gastric stimulator and surgical options then required

Medical Management of Gastroparesis

**Standard of treatment includes:**

- **Antiemetics**
  - Compazine (Prochlorperazine)
  - Phenergan® (Promethazine)
  - Zofran® (Ondansentron)
  - Emend (Aprepitant)
  - Scopolamine patch
  - Marinol

- **Prokinetics**
  - Erythromycin (Motilin agonist)
  - Reglan® (Metoclopramide)
  - Motilium® (Domperidone)
  - Mestinon (Pyridostigmine)
  - [Acetylcholineesterase Inhibitor]
  - For Abdominal Pain (Neuromodulators); e.g. Gabapentin, Lyrica, Duloxetine (Cymbalta)

**Recommendation Regarding Initiating Reglan Therapy from Medico-legal Standpoint**

- Discuss with patient, available family members & with a nurse present all the side effects expected with Reglan.
  - Emphasize initial first day namely “muscle spasm” type immediate reactions (1-5% range)
  - The early onset side effects (within first week) namely anxiety – akathisia, insomnia or excessive sleep or fatigue (20% range)
  - Long term side effects namely depression, Parkinsonism, prolactin related & rare tardive dyskinesia (1-5% range)

- Overall side effects could be in to excess of 30%

- Document all this discussion in the office chart or medical record or in a specifically designed informed consent which patient and/or nurse also sign.
Clinical course continued-

- Under an IND protocol, Domperidone was started 10 mg 4 times a day and metoclopramide stopped.
- Domperidone was increased over one month to 30 mg qid along with monitoring of the QT interval on ECG.
- In addition, patient received transdermal scopolamine patch 1.5 mg every 3 days (behind the ear) and nortriptyline 20 mg at bedtime increasing slowly each two weeks to reach 80 mg after 3 months as tolerated.
- The patient did well for about 4 months with improvement in symptoms and reduced need for hospitalization.
- Within 6 months her symptoms started worsening again and more weight loss occurred.

Feeding Tubes in Gastroparesis

- No role for a PEG for nutrition or decompression, and limited role for PEG-PEJ (temporary trial of tolerance for jejunal feedings).
- TPN not appropriate with intact small bowel
- Jejunostomy tube – Surgical, Radiological, or Endoscopic placement – is the choice for both nutrition and medications
- Resting the Stomach: Nocturnal J-tube feeding while slowly reintroducing oral intake during the day and giving medications via J-tube
- Maximizing Glucose control, Psychological Support, Pain Control and reassessing vomiting characteristics to rule out Rumination Syndrome.
- Antral smooth muscle biopsy can also be obtained while surgically placing J-tube.
Enteric Nervous System and Interstitial Cells of Cajal (ICC) in Gastroparesis

C-Kit Staining of antral smooth muscle for ICC

Normal (>10 ICC/HPF)  Gastroparesis

Working Hypotheses to explain Gastroparesis

In addition, Pyloric Dysfunctions ??
Clinical Course Continued-

- Jejunostomy tube (J-Tube) was placed surgically and the biopsy of gastric smooth muscle was taken.
- Antral biopsy showed depletion of ICC: less than 10 ICC/high power field
- After 3 months of j-tube feeding, the patient had not been able to sustain oral intake during the day and her weight was being maintained by J-tube feeding at night.

What is the next step?

1) TPN
2) Gastric electrical stimulation
3) Pyloroplasty
4) Total gastrectomy

Gastric Electrical Stimulation

Enterra® Therapy

- Indicated for the treatment of chronic, intractable nausea and vomiting secondary to diabetic, idiopathic gastroparesis
- Humanitarian Device Exemption (HDE)

• System
  - Implantable neurostimulator: Medtronic Itrel3 (model 7425G)
  - Neuromuscular leads (2): Medtronic model 4351
  - Stimulation Parameters
    - Amplitude: 5 milliamps
    - Pulse Width: 330 µsec
    - Rate: 14 Hz
    - Cycle On Time: 0.1 sec
    - Cycle Off Time: 5.0 sec

- System includes:
  - Implantable neurostimulator: Medtronic Model 7425G or 3116
  - Neuromuscular leads (2): Medtronic Model 4351
  - Stimulation Parameters
    - Amplitude: 5 milliamps
    - Pulse Width: 330 µsec
    - Rate: 14 Hz
    - Cycle On Time: 0.1 sec
    - Cycle Off Time: 5.0 sec
Clinical outcomes-10 year Follow-up:

- 221 GP patients: 142 DM, 48 ID and 31 P; 164 (74%) were F
- Median age of 38 y (18-70).
- Median duration of GP 3.5 years (1-33)
- Median duration of DM 18 years (1-41)

- 60% of patients with DM had > 50% reduction in TSS
- Mean HbA1c levels in DM Enterra patients with available results beyond 1 year (n=37) were reduced from 8.5% to 7.8% at last follow-up

The weight in all patients (n=124) significantly increased from 149 ± 41 lbs at baseline to 162 ± 43 lbs (p<0.05) as well as within each group

Enterra therapy resulted in 89% of patients discontinuing J-tube use and was associated with a significant increase in weight in severe gastroparetic patients who had failed all medical treatments.

Enterra therapy resulted in 89% of patients discontinuing J-tube use and was associated with a significant increase in weight in severe gastroparetic patients who had failed all medical treatments.

GET was not improved

Factors Influencing Enterra Outcome

- **Negative**
  - Abdominal pain
  - Role of narcotics
  - Migraine headaches, Menstrual cycles
  - Anorexia/Bulimia
  - Conditioned vomiting, rumination syndrome
  - Cyclic vomiting syndrome
  - Marked dyssrhythmias (tachygastria) which could be a marker for loss of interstitial cells of Cajal and the severity of gastroparesis.
  - Approximately, 40% of patients refractory to medical therapy and requiring GES therapy have depletion of ICC.
  - Idiopathic etiology (heterogeneous group)

- **Positive**
  - Diabetes mellitus (known pathophysiology – homogeneous group)


Mechanisms of Action of Enterra System:

1) Centrally acting anti-emetic
2) Increased vagal activity
3) It does not change gastric emptying or electrical dyssrhythmias
4) Abdominal pain is not a target
Evolving role for the Pylorus In Gastroparesis

GES improves GP symptoms, but there is a minimal or no effect on acceleration of GET

Clinical Course Continued-

- Patient agreed to proceed with GES implantation and pyloroplasty with backup feeding jejunostomy tube.
- At 6 months follow up, she graded herself as >75% improvement of symptoms, HbA1C: 7.5% and GET showed 8% retention at 4 hours (Normal), regained weight and J-tube removed.
- The symptom response has been sustained now for 1 year and she stopped all prokinetics, TCA, uses occasional backup antiemetic and body weight is stable.
- She is now being considered for future pancreatic transplant since there is no vomiting to interfere with absorption of antirejection medications.
The Role of “Rescue” Total Gastrectomy

A) Gastroparesis following either Billroth I or Billroth II gastric surgeries.

B) With Intact Stomach
<25% improved after GES and pyloroplasty with admissions to hospital related to substantial ongoing narcotic use.
-Less than 5% of post-GES/Pyloroplasty patients will require total gastrectomy.


Unmet needs being addressed by the NIH funded Gastroparesis Research Consortium

- Further characterize the molecular events in the pathogenesis of gastroparesis: How to prevent ICC depletion and loss of nNOS in gastric smooth muscle?

- More investigation of pyloric dysfunction as a contributor to the pathophysiology and provide new therapeutic direction.

- What are the genetic risk factors for gastroparesis?

- Future Therapies:
  - Prokinetics: “Ghrelin agonists, 5-HT4 agonists”
  - Antiemetics: NK1 antagonists (Aprepitant; Emend)
  - Devices: gastric pacemaker

Texas Tech University Neurogastroenterology and GI Motility Center

Endoscopy  Surgery  Nutrition

Nuclear Medicine  Research  Pathology  Diet

Research  Referral
Update in hepatitis C

James F. Trotter, MD
Baylor University Medical Center

Hepatitis C - overview

- screening
  - new recommendations from the CDC
- evaluation
  - new non-invasive staging technique
- treatment
  - all-oral, non-interferon, > 90% cure

Who becomes infected with hepatitis C?
**Question**

Which of the following patients should be screened for hepatitis C?

a. 27 yo history of IV drug abuse

b. 56 yo office administrator, no risk factors

c. both “a” and “b”

---

**Hepatitis C**

- 2 % of US population HCV antibody positive
- risk factors
  - IV drug use
  - hx of blood products pre-1989
  - spouse w/ HCV
  - hemodialysis
  - transplant recipient
- CDC screening recommendations

**Hepatitis C – screening**

- about ½ infected with HCV report exposure risk
- 45% – 85% of 3 M with HCV unaware of infection
- 1945 – 1965 birth cohort accounts for > % of HCV
Hepatitis C – screening

Adults born during 1945–1965 should receive one-time testing for HCV without prior ascertainment of HCV risk

(Strong Recommendation, Moderate Quality of Evidence)

CDC, 2012

What are the consequences once you become infected?

Question

Most patients infected with hepatitis C will develop cirrhosis in their lifetime?

a. true

b. false
Hepatitis C - presentation

• asymptomatic

• elevated LFT’s

• end-stage liver disease
  – ascites, jaundice, encephalopathy, bleeding

• hepatoma (liver cancer)

Spectrum of disease

- Acute HCV Infection
  - Recovery: 15%-30%
  - Chronic HCV Infection: 70%-85%

- Chronic Hepatitis C
  - Mild, Moderate, Severe

- Cirrhosis: 20%

- End-Stage Liver Disease
- Hepatocellular Carcinoma
- Liver Transplantation
- Death

HCV: hepatocellular carcinoma

The risk of hepatocellular carcinoma in cirrhosis with HCV
How are patients evaluated for hepatitis C?

Question
Which test proves active infection, versus prior exposure, with hepatitis C?

a. hepatitis C antibody

b. hepatitis C RNA (viral load)
Hepatitis C – initial evaluation

• history/physical
  – other medical problems
  – signs of chronic liver disease
    • spider angiomas
    • palmar erythema
    • large left hepatic lobe
    • splenomegaly
    • ascites
    • edema

Hepatitis C – initial evaluation

• laboratories/imaging
  – CBC, LFT’s
  – HCV Ab (proves exposure, not infection)
  – HCV-RNA (proves infection)
  – genotype (strain of virus)
  – other serologies (ferritin, HBV, AMA, ANA, ASMA, a1AT)
  – liver ultrasound or CT

Question

Liver biopsy is currently the preferred test for staging liver damage in patients infected with hepatitis C.

a. true

b. false
Hepatitis C – assessment of stage

• historically
  – done with liver biopsy
  – treat patients with advanced fibrosis
  – follow patient with minimal disease
  – treatment worse than disease (interferon)

Hepatitis C – assessment of stage

• current
  – done with non-invasive elastography
  – treat patients with advanced fibrosis
  – treat patient with minimal disease
  – treatment is easy

Hepatitis C – assessment of stage

• current
  – done with non-invasive elastography
  – cirrhosis vs. no cirrhosis

  cirrhosis = risk of disease progression
treatment duration
risk of hepatocellular cancer
The risk of hepatocellular carcinoma in cirrhosis with HCV

Hepatic elastography
non-invasive
vibrates tissue
US platform
estimates fibrosis - stiff liver = fibrosis

US hepatic elastography
FDA approved for assessment
of hepatic fibrosis
Liver Stiffness Correlates with Fibrosis Stage

Liver Stiffness (kPa)

Ultrasound elastography

US elastography
What are the treatment options for hepatitis C?

Question
Can hepatitis C be cured with therapy and, if so, what is the cure rate?

a. no, 0 %
b. yes, 50 %
c. yes, 75 %
d. yes, 99 %

Advances in therapy

<table>
<thead>
<tr>
<th>Year</th>
<th>Treatment</th>
<th>Sustained virologic response rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991</td>
<td>IFN (6 months)</td>
<td>50%</td>
</tr>
<tr>
<td>1998</td>
<td>IFN (12 months)</td>
<td>50%</td>
</tr>
<tr>
<td>2000</td>
<td>Peginterferon + ribavirin (12 months)</td>
<td>70%</td>
</tr>
<tr>
<td>2013</td>
<td>90% + direct acting agents</td>
<td>100%</td>
</tr>
</tbody>
</table>
Advances in therapy

Which HCV therapy?
- genotype 1, no cirrhosis, prior treatment failure, Aetna insurance
Currently approved HCV therapies

**genotype 1**
- ledipasvir/sofosbuvir 12 wk
- paritaprevir/ritonavir/ombitasvir/dasabuvir/RB
  12 wk (no cirrhosis) or 24 wk (cirrhosis)*
- sofosbuvir/voxilaprevir/RBV
  12 wk (no cirrhosis) or 24 wk (cirrhosis)
- daclatasvir/sofosbuvir
  12 wk (no cirrhosis) or 24 wk +/-RBV (cirrhosis)

Currently approved HCV therapies

**genotype 2**
- sofosbuvir (400 mg) and RBV for 12 weeks
  16 weeks recommended for cirrhosis
- daclatasvir/sofosbuvir for 12 wk

Currently approved HCV therapies

**genotype 3**
- sofosbuvir and RBV and PEG-IFN for 12 wk
- sofosbuvir and RBV for 24 wk
- daclatasvir/sofosbuvir
  12 wk (no cirrhosis) or 24 wk +/-RBV (cirrhosis)
Advances in therapy

- Harder to treat patient groups
  - genotype 1
  - cirrhosis
  - prior treatment failures

- all of this overcome with new therapies

Question

On HCV therapy (sofosbuvir/ledipasvir), what fraction of patients develops undetectable virus?

- a. 10 %
- b. 50 %
- c. 99 %
- d. 100 %
Cost is $94,000

Drug interactions

- anticonvulsants: carbamazepine, phenytoin, phenobarbital
- rifampin
- herbal supplement: St. John’s wort
- HIV antiretrovirals
- rosvastatin
**Other considerations**

- no meaningful resistance reported
- use in GFR < 30 ml/min?
- ≤ omeprazole 20 mg

**HCV - case**

52 yo WM with hypertension diagnosed with HCV by PCP

PSH – none
PMH – hypertension

Soc hx – married, two grown children, car salesman

<table>
<thead>
<tr>
<th>AST</th>
<th>ALT</th>
<th>AP</th>
<th>TB</th>
<th>WBC</th>
<th>HCT</th>
<th>Cr</th>
<th>INR</th>
<th>HCV viral load</th>
</tr>
</thead>
<tbody>
<tr>
<td>52</td>
<td>83</td>
<td>121</td>
<td>0.9</td>
<td>7.2</td>
<td>42</td>
<td>0.8</td>
<td>1.0</td>
<td>1,397,234</td>
</tr>
</tbody>
</table>

genotype 1

Hepatic elastography

kPa = 10
fibrosis, not cirrhosis
HCV - case

52 yo WM with hypertension diagnosed with HCV by PCP
started on one pill QD ledipasvir/sofosbuvir

HCV - undetectable at EOT
HCV - undetectable 12 wks after EOT = CURED OF HCV

repeat elastography, labs to determine response to therapy.

Hepatitis C – summary

The developments in hepatitis C therapy
are the most important in liver disease ever.

Hepatitis C – summary

Therapy is 8 to 24 weeks,
all oral
minimal side effects
cure rate > 90 %
Hepatitis C – summary

Therefore, identification of patients with hepatitis C is more important that ever before.
Screening

<table>
<thead>
<tr>
<th>BMI ≥ 25kg/m² or ≥ 23kg/m² in Asian Americans + 1 of the following</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical inactivity</td>
<td>HTN (≥ 140/90 or on therapy)</td>
</tr>
<tr>
<td>First degree relative with diabetes</td>
<td>HDL &lt; 35mg/dL and/or TG &gt;250 mg/dL</td>
</tr>
<tr>
<td>African American, Latino, Native American, Asian American, Pacific Islander</td>
<td>Women with PCOS</td>
</tr>
<tr>
<td>Women with GDM or baby with birthweight &gt; 9lbs</td>
<td>HbA1c ≥ 5.7%, impaired glucose tolerance, or impaired fasting glucose previously</td>
</tr>
<tr>
<td>Conditions associated with insulin resistance (severe obesity, acanthosis nigricans)</td>
<td>History of CVD</td>
</tr>
</tbody>
</table>

Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>Pre-diabetes</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>HbA1c</td>
<td>5.7-6.4%</td>
<td>≥ 6.5</td>
</tr>
<tr>
<td>Fasting Plasma Glucose</td>
<td>100-125 mg/dL</td>
<td>≥ 126 mg/dL</td>
</tr>
<tr>
<td>Oral glucose tolerance test</td>
<td>140-199 mg/dL</td>
<td>≥ 200 mg/dL (on 2 occasions)</td>
</tr>
<tr>
<td>Random plasma glucose</td>
<td></td>
<td>≥ 200 mg/dL (with classic symptoms of hyperglycemia or hyperglycemic crisis)</td>
</tr>
</tbody>
</table>

Type 1 Diabetes
- Consider screening for hypothyroidism and celiac disease

Common co-morbid conditions
- Obesity
- Obstructive sleep apnea
- Depression
- Vitamin D deficiency
Diabetes self-management education begins at diagnosis but should be re-assessed as throughout a patient’s lifetime. Below is a summary chart of the 4 critical times to assess and refer patients for DSME.

### Goals of Nutrition Therapy

- Attain individualized glycemia, blood pressure, and lipid goals
- Achieve and maintain body weight goals
- Delay or prevent diabetes complications
- Consider personal, cultural preferences as well as health numeracy, literacy, willingness to make changes, barriers to change
- Practical meal-planning

### Physical Activity

- 150 min/wk of moderate intensity aerobic physical activity 3 days/weekly
- Reduce sedentary time to <90 min
- If no contraindication, resistance training 2x/wk

### Psychosocial Assessment

Assess all patients for:
- Depression*** (high priority in elderly)
- Anxiety
- Cognitive impairment
- Eating disorders

### Prediabetes

- Includes impaired glucose tolerance
- Impaired fasting glucose
- Hba1c 5.7-6.4%

---

[Diagram and Chart]

Diabetes Self-management Education and Support for Adults With Type 2 Diabetes: Algorithm of Care

ADA Standards of Medical Care in Diabetes recommends all patients be assessed and referred for:

- Nutrition
  - Registered dietitian for medical nutrition therapy
- Education
  - Diabetes self-management education and support
- Emotional Health
  - Mental health professional, if needed

### Four Critical Times to Assess, Provide, and Adjust Diabetes Self-management Education and Support

<table>
<thead>
<tr>
<th>1 At Diagnosis</th>
<th>2 Annual Assessment of Education, Nutrition, and Emotional Needs</th>
<th>3 When New Complicating Factors Influence Self-management</th>
<th>4 When Transitions in Care Occur</th>
</tr>
</thead>
<tbody>
<tr>
<td>Needs review of knowledge, skills, and behaviors</td>
<td>Needs review of knowledge, skills, and behaviors</td>
<td>Change in medication, activity, or nutritional intake</td>
<td>Change in living situation such as patient or caregiver rehabilitation or move to assisted living facility</td>
</tr>
<tr>
<td>Needs review of knowledge, skills, and behaviors</td>
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<td>Change in medication, activity, or nutritional intake</td>
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<td>Change in medication, activity, or nutritional intake</td>
<td>Change in living situation such as patient or caregiver rehabilitation or move to assisted living facility</td>
</tr>
</tbody>
</table>

---

[Table and Chart Continued]
• Provide diet counseling, encourage physical activity, and behavioral counseling to target 7% body weight loss
• Increase moderate-intensity physical activity to at least 150min/wk
• Metformin in prediabetes, but especially in BMI>35, age <60, and women with hx GDM
• Annual monitoring for diabetes development
• Screening for modifiable risk factors

**Hba1c testing**
• Quarterly in patients with therapy changes or suboptimal control
• All other patients 2x/year

**Hba1c discrepancies**
• Consider hemoglobinopathies
• Altered RBC turnover
• Different timing of self-monitored blood glucose testing or use of a sensor
• Consider fructosamine testing but prognostic significance not as clear as Hba1c

**Hba1c goals**
*General goal: Hba1c <7%; Preprandial blood glucose 80-130 mg/dL; Peak post-prandial blood glucose <180 mg/dL.*

<table>
<thead>
<tr>
<th>&lt;6.5%</th>
<th>&lt;7%</th>
<th>&lt;8%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No significant hypoglycemia</td>
<td>Most patients</td>
<td>History of severe hypoglycemia</td>
</tr>
<tr>
<td>Short duration of diabetes</td>
<td>Long-standing diabetes with inability to reach goal with self-management, appropriate glucose monitoring, effective insulin doses</td>
<td></td>
</tr>
<tr>
<td>Treatment is lifestyle and/or metformin alone</td>
<td>Advanced micro-/macrovascular complications</td>
<td></td>
</tr>
<tr>
<td>Long life expectancy</td>
<td>Limited life expectancy</td>
<td></td>
</tr>
<tr>
<td>No significant CAD</td>
<td>Extensive co-morbid conditions</td>
<td></td>
</tr>
</tbody>
</table>

**Hypoglycemia**
• Rule of 15:
  1. Check blood sugar with symptoms
  2. Eat simple sugars (15-20g)
  3. Re-check blood sugar in 15 minutes
  4. If normal blood glucose, eat a snack; if still low, repeat steps 2 and 3 until blood glucose is normal
  ***Administer glucagon only if patient unable to ingest
• Prolonged hyperglycemia or frequent hypoglycemia can alter hypoglycemia awareness and glucose level at which neuroglycopenic symptoms present
Insulin Pumps

- Considerations for starting an insulin pump
  - **Primary criteria:** Patient on basal-bolus injections and checking at least 4 times daily AND knows how to count carbohydrates
  - **Secondary considerations:**
    - DM1
    - Frequent hypoglycemia
  - Nonadherence to treatment plan is not a reason to use an insulin pump!

---

**Insulin Pump Settings**

- **Basal rate** ➔ **Basal insulin dose**
  - Can have multiple to accommodate for activity

- **Bolus** ➔ **Pre-meal insulin**
  - Input grams of carbohydrates

- **Sensitivity** ➔ **Correction insulin**
  - If blood glucose entered, pump administers correction insulin

---

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability to change basal rate during the day (especially to accommodate activity)</td>
<td>Must know how to count carbohydrates</td>
</tr>
<tr>
<td>Ability to keep “track” of insulin to prevent insulin stacking</td>
<td>Must change out infusion sets every 3 days (potential cost)</td>
</tr>
<tr>
<td>Ability to use half units of insulin</td>
<td>Must order all supplies from the company (not available at local pharmacy)</td>
</tr>
<tr>
<td>Use of special features that allow for prolonged prandial insulin delivery or delayed prandial insulin delivery (for high fat meals, gastroparesis)</td>
<td>Lack of familiarity by health care professionals in many disciplines for after hours assistance</td>
</tr>
</tbody>
</table>

---

**Sensors**

- Checks interstitial blood
- glucose values every 5 min
- Can be used with an insulin
- pump or independently of a pump
- Helps identify wide glucose excursions that could be occurring between glucose checks
- Aids with alarms for hypoglycemia
- Indicated for DM1, DM2, pregnancy, and pediatric patients

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ability to see glucose trends throughout the day and night</td>
<td>Not as accurate as fingerstick blood glucose (10 minute delay in glucose value so up to 20% variability)</td>
</tr>
<tr>
<td>Ability to set alarms for hypo-/hyperglycemia</td>
<td>Sometimes malfunctions with clot at cannula, acetaminophen can interfere with reading</td>
</tr>
<tr>
<td>Each sensor lasts 6-7 days</td>
<td>Must be changed every 6-7 days (cost)</td>
</tr>
<tr>
<td>If patient uses a Medtronic pump, the information can be seen on the pump</td>
<td>Still need to check fingerstick blood glucose and input into pump</td>
</tr>
<tr>
<td>Ability to change lifestyle, make insulin adjustments in “real-time”</td>
<td>Calibrate sensor at least twice daily with fingerstick blood glucose</td>
</tr>
</tbody>
</table>
Use metformin in all patients with DM2 if tolerated and not contraindicated.

Metformin
- Contraindicated (at this time) in male patients with Cr > 1.5 and female patients with Cr > 1.4
- Avoid in patient with liver problems
- Black box warning for lactic acidosis
- Generally not suggested in elderly patients
### DPP-4 Inhibitors

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand Name</th>
<th>Dosing</th>
<th>Renal Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitagliptin</td>
<td>Januvia</td>
<td>Daily</td>
<td>CrCl 30-49: max dose 50mg CrCl &lt;30: max dose 25 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alogliptin</td>
<td>Nesina</td>
<td>Daily</td>
<td>CrCl 30-59: max dose 12.5mg CrCl &lt;30: max dose 6.25 mg</td>
</tr>
<tr>
<td>Saxagliptin</td>
<td>Onglyza</td>
<td>Daily</td>
<td>CrCl&lt;50: max dose 2.5mg</td>
</tr>
<tr>
<td>Linagliptin</td>
<td>Tardjenta</td>
<td>Daily</td>
<td>None</td>
</tr>
</tbody>
</table>

- Class Issues: Caution with pancreatitis hx, latest reports of associated joint pain in some patients
- Recent studies suggest possible renal protective effects
GLP-1 agonists

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Dosing</th>
<th>Renal Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exenatide</td>
<td>Byetta</td>
<td>BID</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CrCl 30-50: caution CrCl &lt;30: avoid use</td>
</tr>
<tr>
<td></td>
<td>Bydureon</td>
<td>Weekly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CrCl 30-50: caution CrCl &lt;30: avoid use</td>
</tr>
<tr>
<td>Albiglutide</td>
<td>Tanzeum</td>
<td>Weekly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Caution with impairment</td>
</tr>
<tr>
<td>Dulaglutide</td>
<td>Trulicity</td>
<td>Weekly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Caution with impairment</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>Victoza</td>
<td>Daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Caution with impairment</td>
</tr>
</tbody>
</table>
- Class Issues: Do not use if history of abdominal pain, pancreatitis, Hx of medullary thyroid cancer (or risk for it)

**SLGT-2 Inhibitors**
<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Dosing</th>
<th>Renal Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dapagliflozin</td>
<td>Farxiga</td>
<td>Daily</td>
</tr>
<tr>
<td>Canagliflozin</td>
<td>Invokana</td>
<td>Daily</td>
</tr>
<tr>
<td>Empagliflozin</td>
<td>Jardiance</td>
<td>Daily</td>
</tr>
</tbody>
</table>

- Class Issues: euglycemic diabetic ketoacidosis, urinary tract infections, vaginal infections
- Canagliflozin: increased fracture risk

![SGLT-2 Inhibitors: Hba1c and Weight change](chart)

**Insulin Therapy**
- Consider adding basal insulin therapy after Hba1c >9
- Consider adding combination insulin after Hba1c >10

**Cardiovascular Risk Reduction**

**Hypertension**

<table>
<thead>
<tr>
<th>Treatment goals</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>All individuals (start agent at this time)</td>
<td>&lt;140</td>
<td>&lt;90</td>
</tr>
<tr>
<td>Maybe for younger individuals or if can be achieved without undue burden of treatment</td>
<td>&lt;130</td>
<td>&lt;80</td>
</tr>
</tbody>
</table>
Lipid Control

ADA recommendations:

- **Four groups likely to benefit**
  - (1) Secondary prevention of established atherosclerotic cardiovascular disease
  - (2) Primary prevention
    - (2) LDL ≥ 190 mg/dl
    - (3) Diabetes age 40-75 with LDL 70-189 mg/dl
    - (4) Age 40-75 with 10-yr ASCVD risk of ≥ 7.5%
- Routine statin initiation not recommended for CHF class 2-4 or patients on hemodialysis

ACC/AHA recommendations for lipid management:

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk factors</th>
<th>Recommended statin dose*</th>
<th>Monitoring with lipid panel</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 years</td>
<td>None</td>
<td>Moderate or high</td>
<td>Annually or as needed to monitor for adherence</td>
</tr>
<tr>
<td></td>
<td>CVD risk factor(s)**</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overt CVD***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>40-75 years</td>
<td>None</td>
<td>Moderate</td>
<td>As needed to monitor adherence</td>
</tr>
<tr>
<td></td>
<td>CVD risk factors</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overt CVD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;75 years</td>
<td>None</td>
<td>Moderate or high</td>
<td>As needed to monitor adherence</td>
</tr>
<tr>
<td></td>
<td>CVD risk factors</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Overt CVD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*In addition to lifestyle therapy.
**CVD risk factors include LDL cholesterol ≥100 mg/dl (2.6 mmol/L), high blood pressure, smoking, and overweight and obesity.
***Overt CVD includes those with previous cardiovascular events or acute coronary syndromes.
Selecting Statin Intensity

<table>
<thead>
<tr>
<th></th>
<th>General</th>
<th>Age &gt; 75</th>
<th>10-yr ASCVD 5 to &lt;7.5%</th>
<th>10-yr ASCVD ≥7.5%</th>
<th>(+) safety concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Established ASCVD</td>
<td>High</td>
<td>Mod</td>
<td></td>
<td></td>
<td>Mod</td>
</tr>
<tr>
<td>LDL ≥ 190 mg/dl (age ≥ 21)</td>
<td>High</td>
<td>Adjust</td>
<td></td>
<td></td>
<td>Adjust</td>
</tr>
<tr>
<td>Age 40-75 with LDL 70-189 mg/dl</td>
<td>Adjust</td>
<td>Mod</td>
<td>High?</td>
<td></td>
<td>Adjust</td>
</tr>
<tr>
<td>Age 40-75 with LDL 70-189 mg/dl plus DIABETES</td>
<td>Adjust</td>
<td>Mod</td>
<td>High</td>
<td></td>
<td>Adjust</td>
</tr>
</tbody>
</table>

Other factors may be considered: LDL-C level 160 mg/dL, family history of premature ASCVD, lifetime ASCVD risk, high-sensitivity C-reactive protein level of 2.0 mg/L, coronary artery calcification score 300 Agatston units, or ankle–brachial index 0.9
AACE guidelines (2012) for patient with DM (AACE does not endorse the AHA guidelines):

- LDL <100mg/dL with no additional risk factors
- LDL <70mg/dL with cardiac risk factors
- Encourage use of statin therapy to attain

Cautions
- Statin + fibrate can increase risk for abnormal transaminases, myositis, rhabdomyolysis (no help with CVD risk above statin alone)
- Statin + niacin can increase risk of stroke

Aspirin therapy
- Start aspirin for primary prevention in all patients with DM, age >50 (in men), age >60 (in women), and at least 1 of the following risk factors:
  - Smoking
  - HTN
  - Albuminuria
  - Family hx of CVD

Microvascular Complications
- Prevention and slowing progression come from tight glycemic, blood pressure, and lipid control

Referral to Nephrology

<table>
<thead>
<tr>
<th>eGFR 45-60 (concern for non-diabetic kidney disease)</th>
<th>eGFR &lt;30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of DM1 &lt;10yrs</td>
<td>refer</td>
</tr>
<tr>
<td>Heavy proteinuria</td>
<td></td>
</tr>
</tbody>
</table>
Abnl renal u/s findings
Resitant HTN
Rapid fall in GFR
Active urinary sediment on urinalysis

ACEI and ARB Therapy
- ACEIs reduce major risk of CVD in patient with albuminuria
- ARBs reduce albuminuria and progression to ESRD but do NOT reduce risk of CVD in DM1 or DM2 patients with normotension
- Combining ACEI and ARB therapy does not provide any additional CVD risk or diabetic nephropathy benefit and only increase risk of adverse events

Nephropathy Management

<table>
<thead>
<tr>
<th>GFR (mL/min/1.73 m²)</th>
<th>Recommended management</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>Yearly measurement of creatinine, urinary albumin excretion, potassium</td>
</tr>
<tr>
<td>45–60</td>
<td>Referral to a nephrologist if possibility for nondiabetic kidney disease exists (duration of type 1 diabetes &lt;10 years, heavy proteinuria, abnormal findings on renal ultrasound, resistant hypertension, rapid fall in GFR, or active urinary sediment on urinalysis)</td>
</tr>
<tr>
<td></td>
<td>Consider need for dose adjustment of medications</td>
</tr>
<tr>
<td></td>
<td>Monitor eGFR every 6 months</td>
</tr>
<tr>
<td></td>
<td>Monitor electrolytes, bicarbonate, hemoglobin, calcium, phosphorus, parathyroid hormone at least yearly</td>
</tr>
<tr>
<td></td>
<td>Assure vitamin D sufficiency</td>
</tr>
<tr>
<td></td>
<td>Consider bone density testing</td>
</tr>
<tr>
<td></td>
<td>Referral for dietary counseling</td>
</tr>
<tr>
<td>30–44</td>
<td>Monitor eGFR every 3 months</td>
</tr>
<tr>
<td></td>
<td>Monitor electrolytes, bicarbonate, calcium, phosphorus, parathyroid hormone, albumin, weight every 3–6 months</td>
</tr>
<tr>
<td></td>
<td>Consider need for dose adjustment of medications</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Referral to a nephrologist</td>
</tr>
</tbody>
</table>

Retinopathy
- In DM1, patients need retinal exam within 5 years of diagnosis and renal screening 5 years after diagnosis
- DM2 at diagnosis

Neuropathy
- Pain control
  - Start with pregabalin, duloxetine, and tapentadol
  - Persistent pain? Consider venlafaxine, amitryptiline, gabapentin, valproate, and opioids
• Independent risk factors for CV mortality in patients with autonomic neuropathy

**Clinical Manifestations**

- Resting tachycardia
- Exercise intolerance
- Orthostatic hypotension
- Gastroparesis
- Constipation
- Erectile dysfunction, retrograde ejaculation
- Autonomic failure in response to hypoglycemia

**Foot care**

**Risk Factors for foot problems**

- Previous amputation
- Prior foot ulcer
- Foot deformity
- PVD
- Peripheral neuropathy
- Poor glycemic control
- Visual impairment
- Smoking

**Key Components of the Foot Exam**

- Inspection of skin integrity, musculoskeletal deformity
- Pedal pulse assessment
- Test for loss of peripheral sensation
  - Perform 2 test annually
  - 1+ abnormal = loss of sensation
  - 2+ normal test rule out loss of sensation
- 10-g monofilament
- 128-Hz tuning fork
- Pinprick sensation
Considerations for older adults

<table>
<thead>
<tr>
<th>Patient characteristics/health status</th>
<th>Rationale</th>
<th>Reasonable A1C goals</th>
<th>Fasting or preprandial glucose (mg/dL)</th>
<th>Bedtime glucose (mg/dL)</th>
<th>Blood pressure (mmHg)</th>
<th>Lipids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy (few coexisting chronic illnesses, intact cognitive and functional status)</td>
<td>Longer remaining life expectancy</td>
<td>&lt;7.5%</td>
<td>90-130</td>
<td>90-150</td>
<td>&lt;140/90</td>
<td>Statin unless contraindicated or not tolerated</td>
</tr>
<tr>
<td>Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild to moderate cognitive impairment)</td>
<td>Intermediate remaining life expectancy, high treatment burden, hyperglycemia vulnerability, fall risk</td>
<td>&lt;8.0%</td>
<td>90-150</td>
<td>100-180</td>
<td>&lt;140/90</td>
<td>Statin unless contraindicated or not tolerated</td>
</tr>
<tr>
<td>Very complex/poor health (long-term care or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL dependencies)</td>
<td>Limited remaining life expectancy makes benefit uncertain</td>
<td>&lt;8.5%†</td>
<td>100-180</td>
<td>110-200</td>
<td>&lt;150/90</td>
<td>Consider likelihood of benefit with statin (secondary prevention more so than primary)</td>
</tr>
</tbody>
</table>

This represents a consensus framework for considering treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes. The patient characteristic categories are general concepts. Not every patient will clearly fall into a particular category. Consideration of patient and caregiver preferences is an important aspect of treatment individualization. Additionally, a patient’s health status and preferences may change over time. ADL, activities of daily living. †A lower A1C goal may be set for an individual if achievable without recurrent or severe hypoglycemia or undue treatment burden.

*Coexisting chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, congestive heart failure, depression, emphysema, falls, hypertension, incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke. By “multiple,” we mean at least three, but many patients may have five or more (Laiteerapong N, Veniuk J, John PM, Laumann EO, Huang ES. Classification of older adults who have diabetes by comorbid conditions, United States, 2005–2006. Prev Chronic Dis 2012;9:E100).

**The presence of a single end-stage chronic illness, such as stage 3–4 congestive heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status and significantly reduce life expectancy.

†A1C of 8.5% equates to an estimated average glucose of ~200 mg/dL. Looser glycemic targets than this may expose patients to acute risks from glycosuria, dehydration, hyperglycemic hyperosmolar syndrome, and poor wound healing.