The Northwest Ohio Osteopathic Association

In Partnership with

The University of Toledo, Center for Continuing Medical Education

Present the:

9TH ANNUAL PRIMARY CARE UPDATE 2014

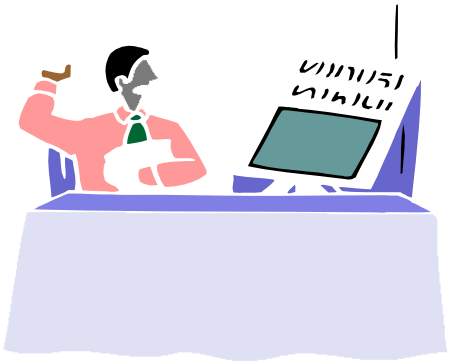
Friday, November 14 – Sunday November 16, 2014

Kalahari Resort and Conference Center
7000 Kalahari Dr
Sandusky, OH 44870

NWOOA
NORTHWEST OHIO OSTEOPATHIC ASSOCIATION
Treating our families and yours

THE UNIVERSITY OF TOLEDO
1872

Please be sure to visit our exhibitor booths:



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Matthew C. Petznick, D.O.
Northern Ohio Medical Specialists, Sandusky, OH

Richard G. Schuster, D.O.
Chair, Primary Care, Marian University College of Osteopathic Medicine, Indianapolis, IN

DISCLOSURES

FACULTY DISCLOSURES

Dr. Alo discloses he is on the Speakers bureau for Astra Zeneca.

Dr. Baxter discloses she is on the Speakers Bureau for NWOOA.

Dr. Evans discloses he is on the Speakers Bureau for Astra Zeneca and Boehringer Ingelheim

Mr. Gipe discloses he is the Founder of Elevation Healthcare Consulting and Agil IT.

Dr. Nagele discloses he is Founder and Chief Scientific Officer and Stockholder of Durin Technologies Inc., and Beren Technologies Inc. He receives funding from Michael J Fox Foundation, Alzheimer's Association, Osteopathic Heritage Foundation, Foundation Venture Capital Group, Boye Foundation, GlaxoSmithKline.

Dr. Nazzal discloses he is on the Speakers Bureau for Medtronic.

Drs. Karen Asher and Thomas Asher, Blank, DeVries, Eyman, Friedhoff, Hensley, Kerger, Kollarits, Kralovic, Mabry, O'Neal Hooker, Peron, Allison Petznik and Matthew Petznik, Schuster, and David Degnan, Wesley Gipe, John King, Mark Nadaud do not have any financial interest or other relationship with any manufacturer of commercial product or service to disclose.

PLANNERS

Dr. Baxter discloses she is on the Speakers Bureau for NWOOA.

Drs. Davis, Espinoza, Lindbloom, Pfleghaar, Rooney and Joy Studer have no financial interest or other relationship with any manufacturer of commercial product or service to disclose.

ACCREDITATIONS

A total of up to 21.5 Category 1A credits will be requested from the American Osteopathic Association. The NWOOA certifies credit hours in conjunction with the OOA, directly to the AOA with the requirements and policies of the AOA.

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the University of Toledo and Northwest Ohio Osteopathic Association. The University of Toledo is accredited by ACCME to provide continuing medical education for physicians. The University of Toledo designates this live activity for a maximum of *21.5 AMA PRA Category 1 Credits*^{TM}. Physicians should claim only credit commensurate with the extent of their participation in the activity.

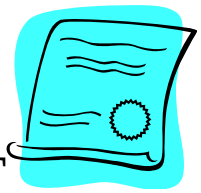
This Live activity, NWOOA 9th Annual Primary care Update 2014, with a beginning date of 11/14/2014, has been reviewed and is acceptable for up to 20.50 Prescribed credit(s) by the American Academy of Family Physicians. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

The Ohio Board of Nursing will accept, at face value, the number of hours awarded for an educational activity that has been approved for CE, provided it was approved by a nationally accredited system of CE approval.

The AAPA accepts certificates of participation for educational activities, certified for Category 1 credit from AOACCME, Prescribed credit from AAFP, and *AMA PRA Category 1 Credit*^{TM} *from* organizations accredited by ACCME or a recognized state medical society.

EVALUATION/CERTIFICATE

Evaluation is an important component of continuing education programs. In addition to providing feedback to the program planners and faculty, it provides information to improve future programs. The evaluation is an integral part of your participation in this meeting.



TO OBTAIN YOUR CME CREDIT

Evaluation Form will be readily available immediately following the program. Certificates will be available on Monday, November 17, 2014 after 12 noon. Follow the instructions below:

- Go to website **cme.utoledo.edu**
- Click on **Direct Link to Login**
- **Login:** lastnamefirstname (no commas, no spaces)

  Password: zip code (unless you have changed in our system previously)

- Immediately following the program: sign-in (using information above). You will be directed to the "Online Forms Inbox". Click the evaluation and complete in entirety. Hit "Submit". Certificate will not be available until Monday. So you will need to sign in Monday, then chose "Credit Transcript" in the left margin. Next to the program title will be certificate icon to click and print.

OR

- Wait until Monday Afternoon: sign-in(using information above).. You will be directed to the "Online Forms Inbox". Click the evaluation and complete in entirety. Hit "Submit". You will then be prompted to print your certificate immediately.

FRIDAY, NOVEMBER 14, 2014 8 hours

7:00 a.m.	Registration
7:30 a.m. – 9:00 a.m.	Breakfast Buffet Served - ***West Pathway***
7:50a.m.-8:00 a.m.	Opening Remarks **- *Orange/Nile Rooms*** *Nicholas J. Pfleghaar, D.O.*
8:00 a.m.-9:00 a.m.	Bariatric Surgery Update *Craig M. Eyman, D.O., FACOS*
9:00 a.m.-10:00 a.m.	The Specialized Youth Athlete and Avoiding Burnout *George J. Friedhoff, D.O.*
10:00-10:30 a.m.	Break/View Exhibits - ***West Pathway***
10:30-11:30 a.m.	Return to Work Issues for the Primary Care Providers *L. Bruce Hensley, D.O.*
11:30 a.m.-12:30 p.m.	Medical Clearance of the Psychiatric Patient *Michael C. Carlisle, D.O.*
12:30 p.m.-12:45 p.m.	Lunch Buffet Line
12:45 p.m.-1:45 p.m.	Physician Employment: How to Fly Solo/Start or Restart A Private Practice *Mark J. Nadaud, CPA/ABV & John J. King, CPA*
1:45 p.m.-2:15 p.m.	Break /View Exhibits-***West Pathway***
2:15 p.m.-3:15 p.m.	International Volunteer Work: The Perils and Pearls *Karen L. Asher, D.O. & Thomas E. Asher, D.O.*
3:15 p.m.-4:15 p.m.	Ocular Complications of Diabetes: New Trends in Management *Carol R. Kollarits, M.D.*
4:15 p.m.-5:15 p.m.	Autism Spectrum Disorders and the DSM 5: What does it all mean? *Shanna K. Kralovic, D.O.*

Resident/Student
Poster Exhibition Contest

Sponsored by the Ohio University Heritage College of Medicine

Saturday, November 14, 2014

AM

North End of The West Pathway

SATURDAY, NOVEMBER 15, 2014 8.5 hours

7:00 a.m.	Registration
7:00 a.m.-9:00 a.m.	Breakfast Buffet Served - ***West Pathway***
7:50 a.m.-8:00 a.m.	Opening Remarks - ***Orange/Nile Rooms*** *Nicholas G. Espinoza, D.O.*
8:00 a.m.-9:00 a.m.	*Advancement in Medical Weight Loss: Diet and Drugs* *Mohamed S. Alo, D.O.*
9:00 a.m.-10:00 a.m.	Wound Care Update *Munier M. Nazzal, M.D., FRCS, FACS, RVT, RPVI*
10:00 a.m.-10:30 a.m.	Break /View Exhibits - ***West Pathway***
10:30 a.m.-11:30 a.m.	The Dizzy Patient: An Approach to the Work UP and Management of Vertigo *Ellen L. Baxter, D.O.*
11:30 a.m.-12:30 p.m.	New Anti-Coagulant Guidelines *Daniel J. Evans, D.O., FACC, FACOI*
12:30 p.m.-12:45 p.m.	Lunch Buffet Line
12:45 p.m.-1:45 p.m.	Authentic Leadership: Why Leadership That Matters Begins With You. *Wesley B. Gipe*
1:45 p.m.-3:15 p.m.	Alzheimer's Disease Mechanisms and Early Diagnosis at Mild Cognitive Impairment *Robert G. Nagele, PhD*
3:15 p.m.-3:30 p.m.	Break/View Exhibits – ***West Pathway***
3:30 p.m.-5:30 p.m.	Osteopathic Ground Game *Sean R. Kerger, D.O., FAOASM* *& Richard G. Schuster, D.O.*
Or ***Aloeswood Room***	
3:30 p.m.-4:30 p.m.	E-Cigarettes: The Good, The Bad and The Ugly *Tracey O'Neal Hooker, D.O., MHA*
4:30 p.m.-5:30 p.m.	Benign Prostatic Hyperplasia Update *Salvador E. Peron, M.D.*

COME AND JOIN US FOR A PIZZA PARTY

SPONSORED BY THE:

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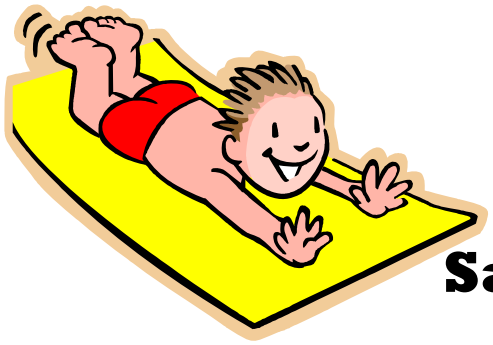
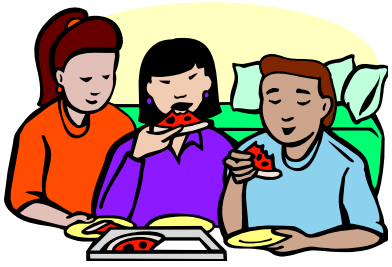


Saturday, November 15, 2014

BEGINNING AT 6:30 PM

IN ZAMBESI ROOM



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7:50 a.m.-8:00 a.m.	Opening Remarks - ***Orange/Nile Rooms***
8:00 a.m.-9:00 a.m.	Improving Adherence in Type 2 Diabetes Mellitus Allison M. Petznick, D.O.
9:00 a.m.-10:00 a.m.	Advancements in Concussion Management *Matthew C. Petznick, D.O.*
10:00 a.m.-11:00 a.m.	Skin and Soft Tissue Infections *Michael S. Blank, M.D.*
11:00 a.m.-12:00 p.m.	Breast Cancer Update 2014 *Helen Mabry, M.D.*

Or

8:00 a.m.-1:00 p.m.	ACLS/BLS Recertification - ***Aloeswood Room*** *Brent C. DeVries, D.O. & Dave Degnan, Fire Chief*

FRIDAY, NOVEMBER 14, 2014 8 hours

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Bariatric Surgery Update

Craig M. Eyman D.O., FACOS

Learning Objective:

Discuss updates in surgical treatment for obesity.

Discuss who are candidates for surgical treatment.

Discuss complications to look for after bariatric surgery.

NOTES

The Specialized Youth Athlete and Avoiding Burnout

George J. Friedhoff, D.O.

Learning Objective:

Define sports specialization.

Recognize and interpret overuse syndrome.

Identify high risk injuries.

Develop a prevention plan.

THE SPECIALIZED YOUTH ATHLETE AND AVOIDING BURNOUT

George Friedhoff D.O.
St. Vincent Charity
Spine and Ortho Group

19 y/o lacrosse player p/w with 3 days of persistent axillary pain and swelling especially with weight-lifting. Pain remains despite reduction in overhead training but still practices lacrosse. PE- localized swelling with tenderness and firmness over left axilla. Supine there is prominent venous structures with left UE > right. Which of the following is the presumed diagnosis?

a) Superficial phlebitis
b) Pectoralis major tear
c) Labral tear
d) Effort induced thrombosis
e) Lymphangitis

Objectives

I. Define Sports Specialization

II. Recognize and Interpret Overuse Syndrome

III. Identify High Risk Injuries

IV. Develop Prevention Plan

D.O.'s Do It Better

Osteopaths(D.O.s)

- 60% Primary Care
- Back Pain
  - 84% of providers
- Foot Pain
  - 41% of providers

Allopaths(M.D.'s)

- 35% Primary Care
- Back Pain
  - 31% of providers
- Foot Pain
  - 10% of providers

Youth Participation

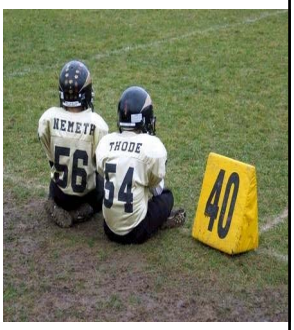
- 27 million youth between 6 to 18 y/o in team sports
- National Council of Youth Sports
  - 60 million participate in some form of organized sports
- Less than 6 y/o in organized sports
  - 1997: 6%
  - 2008: 12%

Defining Sport Specialization

- Intense year round training with exclusion of other sports?
  - Hours spent in Sport A > Sport B & Sport C
- Not a “single focus” but also training time
- Starting sooner & sooner(Age Limit)
- Multiple teams during single season

Introduction To Overuse

- Centers For Disease Control and Prevention
  - > 5 million children suffer sport-related injury annually
- Year-Round Specialized Training
- Safe Kids Survey
  - 9 out 10 parents underestimate length of recovery
- 25% of adult athletes



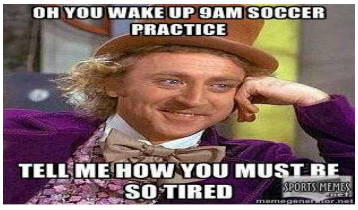
Burnout & Overtraining Syndrome

- Open Access Journal of Sports
  - 80% of youths quit by age 15
- Non-functional overreaching
- Overtraining Syndrome
  - Series of psychological, physiological and hormonal changes that result in decreased performance
  - Fatigue
  - Lack of Enthusiasm

TABLE 5. Factors Related to Burnout in Young Athletes[184,187,188]

Environmental Factors
Extremely high training volumes
Extremely high time demands
Demanding performance expectations (imposed by self or significant other)
Frequent intense competition
Inconsistent coaching practices
Little personal control in sport decision making
Negative performance evaluations (critical instead of supportive)
Personal Characteristics
Perfectionism
Need to please others
Nonassertiveness
Unidimensional self-conceptualization (focusing only on one's athletic involvement)
Low self-esteem
High perception of stress (high anxiety)

Preventing Overtraining/Burnout



- 1) Keep practice fun
- 2) Take 1-2 days off per week
- 3) Permit longer scheduled breaks from training & competition focusing on cross-training
- 4) Be in tune with their bodies
- Organizations
  - National Youth Sports & Safety Institute(www.NYHSI.org)

Who Is Responsible?

- 1-Coaches
- 2-Parents

10-Child

Clinical Presentation

TABLE 6. Symptoms of Overtraining Syndrome/Burnout[180,187,188]

Fatigue	Insomnia	Loss of appetite
Depression	Irritability	Weight loss
Bradycardia or tachycardia	Agitation	Lack of mental concentration
Loss of motivation or interest	Decreased self-confidence	Heavy, sore, stiff muscles
Hypertension	Anxiety	Restlessness
Sleep disturbances	Nausea	Frequent illness

TABLE 7. Diagnosis of Overtraining Syndrome/Burnout[180,1

History

- Decreased performance persisting despite weeks to months of recovery
- Disturbances in mood
- Lack of signs/symptoms or diagnosis of other possible causes of underperformance
- Lack of enjoyment participating in sport
- Inadequate nutritional and hydration intake

Presence of potential triggers: (a) increased training load with adequate recovery, (b) monotony of training, (c) excessive number of competition (d) sleep disturbance, (e) stressors in family life (parental pressure), (f) stressors in sporting life (coaching pressure and travel demands), (g) previous illness.

Testing (if indicated by history)

- Consider laboratory studies: complete blood count, comprehensive metabolic panel, erythrocyte sedimentation rate, C-reactive protein, iro studies, creatine kinase, thyroid studies, cytomegalovirus and Ebstein-Barr virus titers.
- Profile of Mood States (POMS): A psychometric tool for a global measu of mood, tension, depression, anger, vigor, fatigue, and confusion.[169]

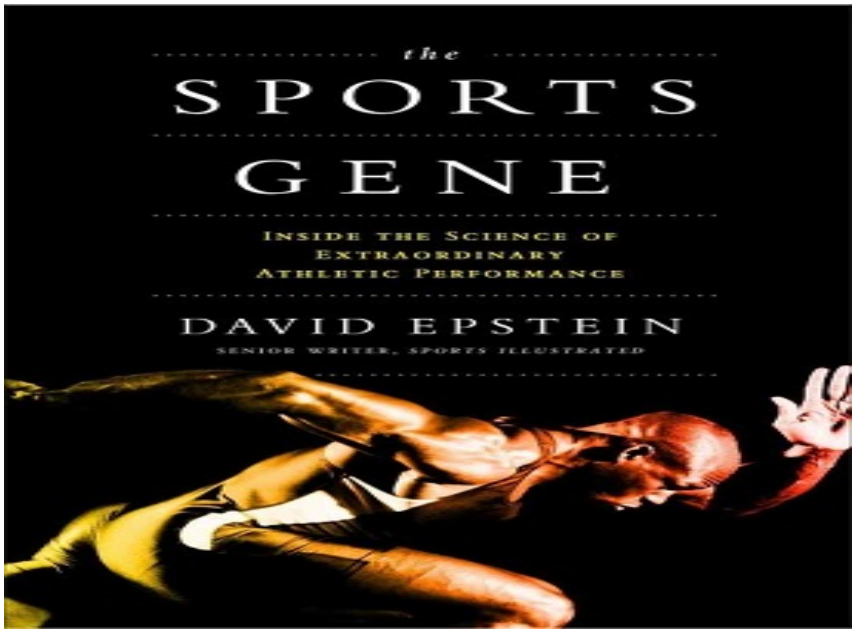
Early specialization — Early diversification

Ericsson	Cote
10,000 hours of deliberate practice to achieve expertise	More diverse range of skills developed through variety of sports
Strong correlation between performance level & training hours	Promotes development of intrinsic motivation, increased self-involvement
Problems – elite performers don't always attain 10,000 hours	Talent transfer across sports (cognitive and physical)
Evidence of higher attrition & negative health outcomes	Evidence from tennis (age 15), but still compile enough hours

Trends In Sports Specialization

- Children 6 Years Or Younger
  - 9% in 1997
  - 12% in 2008
- 77% of HS AD's Notice Trend
- ↑ USTA (70% by 14 & 95% by 18)

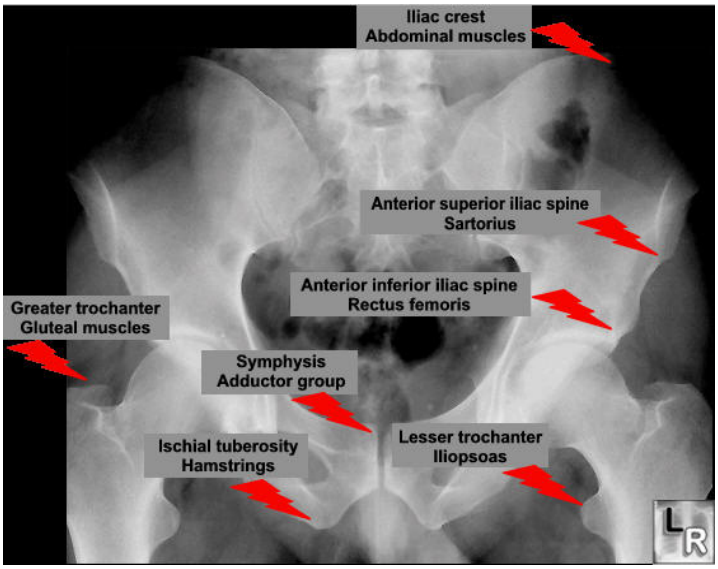
- Growing Number of Travel Leagues

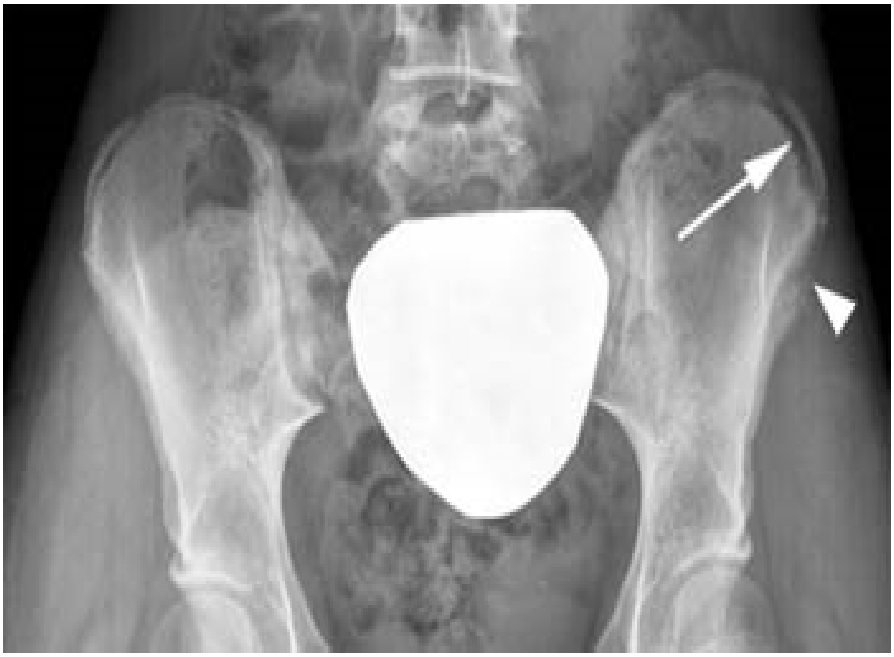


Risk Factors For Overuse Injury

- Intrinsic Risk Factors
  - Growth-Related Factors
    - Susceptibility of growth cartilage to repetitive stress
    - Adolescent growth spurt
  - Previous injury
  - Previous level of conditioning
  - Anatomic factors
  - Menstrual dysfunction
  - Psychological and developmental factors—athlete specific
- Extrinsic Risk Factors
  - Training workload (rate, intensity, and progression)
  - Training and competition schedules
  - Equipment/footwear
  - Environment
  - Sport technique
  - Psychological factors—adult and peer influences

Physes Vs. Apophyses





Classification of Overuse Injuries

1) Pain In Affected Area After Physical Activity
2) Pain Without Restricting Performance
3) Pain With Restricting Performance
4) Chronic Pain Even At Rest

Overuse Injuries:Predisposing Factors

Extrinsic Factors

- Training Errors
  - Excessive Volume
  - Excessive Intensity
  - Rapid Increase
  - Sudden Change in Type
  - Inadequate Recovery
  - Faulty Technique
- Equipment
- Psychological Factors
- Environmental Conditions
- Inadequate Nutrition

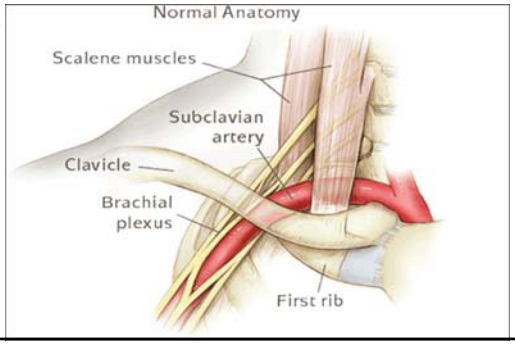
Intrinsic Factors

- Malalignment
- Muscle Weakness
- Muscle Imbalance
- Lack of Flexibility
- Sex
- Size
- Body Composition
- Other
  - Genetic Factors
  - Endocrine Factors
  - Metabolic Conditions

Location	High Risk	Low Risk
Hip/Pelvis	Femoral neck (tension-sided)	Femoral shaft stress fracture
Back (lumbar spine)	Pars interarticularis stress fracture	Congenital spondylolysis, pedicle stress fracture
Leg	Anterior cortical tibial stress fracture	Medial tibial stress fracture, fibular shaft stress fracture
Ankle	Medial malleollar stress fracture, talar dome osteochondral defect, talar neck stress fracture	Distal fibular stress fracture
Foot	Tarsal navicular stress fracture, fifth metatarsal proximal diaphyseal stress fracture, sesamoid stress fracture	Second, third, fourth metatarsal stress fractures, cuboid
Knee	Patellar stress fracture, osteochondritis dissecans of femoral condyle or patella	Tibial tubercle and inferior patellar pole apophysitis
Shoulder/arm	Effort thrombosis	Proximal humeral physeal stress fracture
Elbow	Osteochondral dissecans capitellum, apophyseal non-union of medial epicondyle	Medial epicondyle apophysitis
Wrist	Distal radial physeal stress injury	

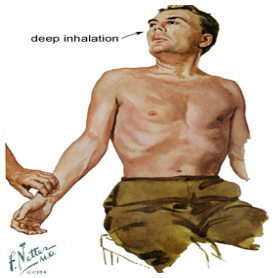
Thoracic Outlet Syndrome

- Costoclavicular space-clavicle and 1st rib
- Hyperabduction syndrome
- Overhead sportspeople
  - Poor posture-scapular protraction
  - Scapular dyskinesis
  - Anterior tilt



Thoracic Outlet Syndrome Presentation

- Symptoms-pain, numbness & weakness
- Venous engorgement
- Clinical tests
  - Adson's test-enhances sensitivity with doppler flow
  - Roos test-most sensitive

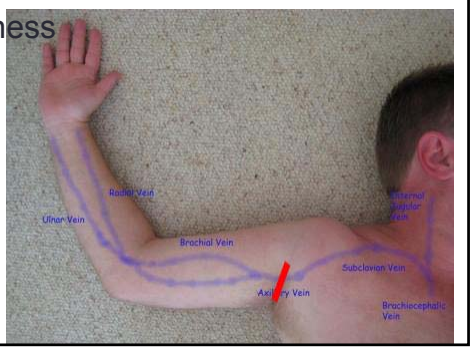


Thoracic Outlet Syndrome Management

- Physical Therapy
  - Pectoral and scalene stretching
  - Joint mobilization of 1st rib
  - Scapular and scapulothoracic mobilization
  - Thoracic extension and brachial plexus exercises
  - 3 to 6 months
- Anticoagulation & thrombolysis
- Thoracic outlet decompression
  - Unresponsive neurogenic
  - Vascular compromise

Axillary Vein Thrombosis "effort thrombosis"

- Paget-von Schrotter Syndrome
- Compression
  - Costoclavicular Space
  - Clavicle & 1st rib
  - Subclavian Muscle & 1st rib
- Presentation-fatigue & heaviness
- Physical Exam
  - Superficial veins prominent
- Venography
- Rest and Anticoagulation

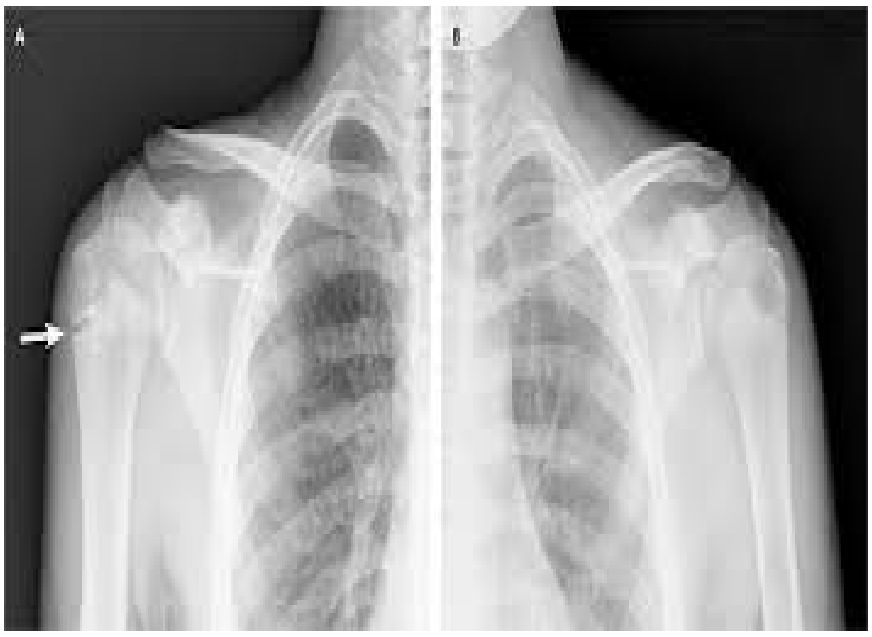


Little Leaguer's Shoulder

- Olsen et al.
  - 6 innings with 7.9 months versus 4innings with 5.5 months
- 11-13 years of age
- Proximal humeral physis
  - Repetitive rotational stress

TABLE 1. Little League Baseball Pitch Count Regulations

Age (y)	Maximum Pitches Per Game
7-8	50
9-10	75
11-12	85
13-16	95
17-18	105



Little Leaguer's Shoulder Management

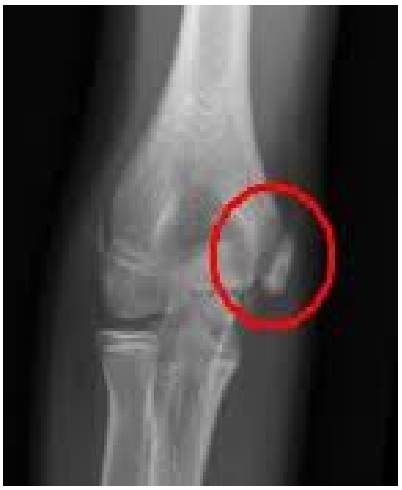
- Radiographs-Gasser & Carson
  - Widening
  - Sclerosis
  - Cystic changes
- Treatment
  - Progressive throwing program
  - Proper mechanics
  - 3 months

TABLE 2. Little League Baseball Rest Requirements for Pitchers Age 16 Years and Under

Pitches	Days Rest
1-20	No calendar day
21-40	1 calendar day
41-60	2 calendar days
>61	3 calendar days

Little League Elbow

- Humeral origin of UCL
- 8-15 years of age
- Medial elbow pain with throwing
- Widening of apophysis
- Rest & biomechanical assessment



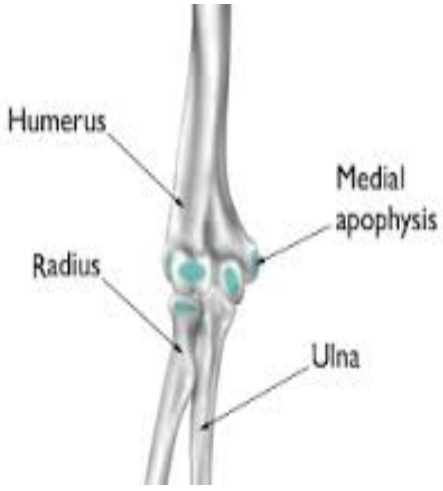


TABLE.

Little League Baseball Pitch Count Regulations

Age	Limits Per Game	Rest Requirements
17-18 years	105/day	76 or more pitches → 4 days rest 61-75 pitches → 3 days rest 46-60 pitches → 2 days rest 31-45 pitches → 1 day rest 01-20 pitches → 0 days rest
15-16 years	95/day	
13-14 years	95/day	66 or more pitches → 4 days rest 51-65 pitches → 3 days rest 36-50 pitches → 2 days rest 21-35 pitches → 1 day rest 01-20 pitchers → 0 days rest
11-12 years	85/day	
9-10 years	75/day	
7-8 years	50/day	

From The Little League® Pitch Count Regulation Guide for Parents, Coaches and League Officials; with permission.

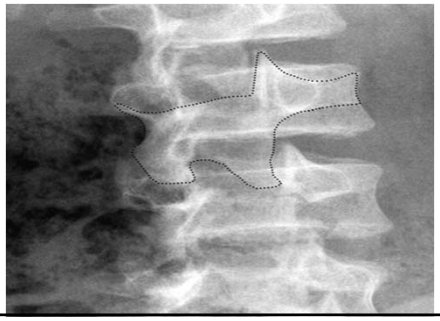
Shoulder Overuse Prevention

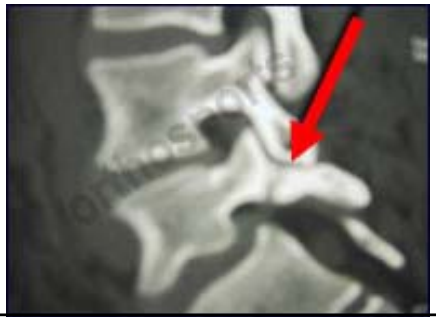
Table 2 General baseball pitching guidelines set forth by the American Sports Medicine Institute [6]

Age (years)	Maximum number of pitches/game	Suggested pitch types
8–10	52	8 years – fastball 10 years – change-up
11–12	68	Fastball, change-up
13–14	76	Fastball, change-up 14 years – curveball
15–16	91	Fastball, change-up 16 years – slider
17–18	106	Fastball, change-up, curveball, slider

Pars Interarticularis

- Insidious Onset
  - 48.5% youth athletes with back pain
  - Progression to non-union-14-70%
- Oblique plain films
  - Scotty Dog





Management

Imaging of Choice

- MRI
  - No radiation
  - 85% & 95%
- SPECT scan
  - Radiation
  - 85%
- MRI vs. SPECT

Treatment Plan

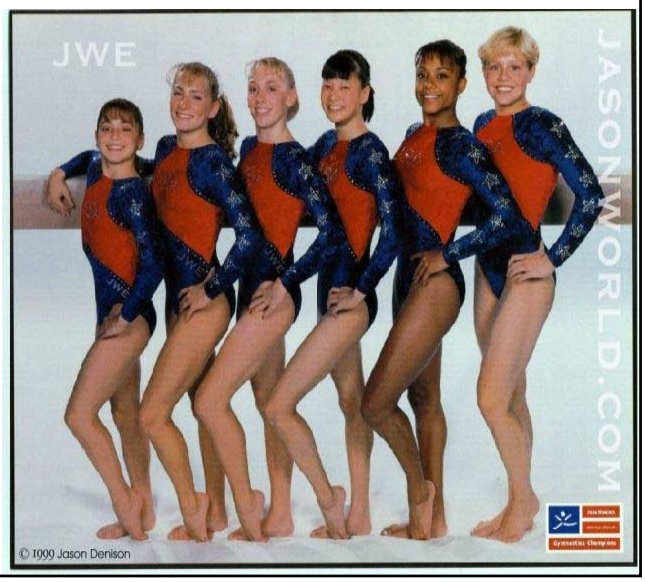
- Goal-Pain Free
- Rest-3 months
  - 57 youth soccer players(optimal results)
- Physical Therapy
- Bracing ?

Endurance Athletes

- American Academy of Pediatrics
  - Triathlons Are Safe
- Marathons
  - 10% Rule
  - Heat Stress
- Nutrition
  - Total Caloric Intake
  - Iron
  - Calcium

Growth And Development

- Menarche
- Amenorrhea
- Pre-Selection
- Female Triad
- Boys vs. Girls



Will Early Specialization Get Me To the Pros?

- 

  - Swimming,diving, gymnastics and figure skating

What is the Goal?

- Pie In The Sky?
  - Professional Pie
- Area of Specialization
  - 0.2%-0.5% make it pro
- Promote Lifelong Physical Activity
- Unfulfilled Childhood Dreams

American Dream

Student Athletes	Men's Basketball	Women's Basketball	Football	Baseball	Men's Ice Hockey	Men's Soccer
High School Student Athletes	538,676	433,120	1,086,627	474,791	35,198	410,982
High School Senior Student Athletes	153,907	123,749	310,465	135,655	10,057	117,423
NCAA Student Athletes	17,984	16,186	70,147	32,450	3,964	23,365
NCAA Freshman Roster Positions	5,138	4,625	20,042	9,271	1,133	6,676
NCAA Senior Student Athletes	3,996	3,597	15,588	7,211	881	5,192
NCAA Student Athletes Drafted	46	32	254	678	7	101
Percent High School to NCAA	**3.3%**	**3.7%**	**6.5%**	**6.8%**	**11.3%**	**5.7%**
Percent NCAA to Professional	**1.2%**	**0.9%**	**1.6%**	**9.4%**	**0.8%**	**1.9%**
Percent High School to Professional	**0.03%**	**0.03%**	**0.08%**	**0.50%**	**0.07%**	**0.09%**

Social Risks- "I Just Want To Have Fun"

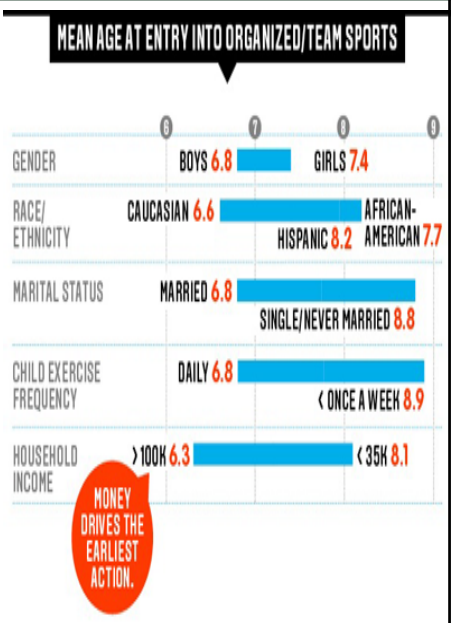
- Overdependence
- Social Isolation
- Problem Solving Skills
- Maladaptive Behaviors

Money Is The Root Of All Evil

- Youth Sports Movement
  - $7 Billion Industry
- Youth Sports Tourism
  - Fastest Growing Segment in Travel
- Columbus Dispatch
  - Non-profit Groups-$5 Billion/Year in 2010

Odds of Going Pro	Odds
Odds of a high school football player making it to the NFL	1 in 6,000
Odds of a hgh school baseball player making it to MLB	1 in 4,000
Odds of a high school basketball player making it to the NBA	1 in 10,000
Odds of a high school soccer player receiving a full ride to a Div I or II School	1 in 90

The above is taken from a study on youth sports by Michigan State University. It surveyed 10,000 children ages 5-14 nationwide.



A Parent's Influence

- YOUTH FOOTBALL PARENT OUT OF CONTROL - YouTube

What To Tell Parents?

1) Well-Rounded Individual Leads To Success
   - Late Specialization Works
2) Enjoyment/Intrinsic Motivation
3) Supportive Not Authoritative
4) No Penalty For Starting Late

VS.

Summary

1) Specialization in a single sport before adolescence is discouraged
2) Clinicians should work with parents and coaches to strive for early recognition of overuse injuries
3) Be alert for signs and symptoms of overtraining including decline in performance, weight loss, apathy and fatigue
4) High risk injuries can lead to nonunion, result in chronic pain, and/or lead to the development of degenerative joint disease

19 y/o lacrosse player p/w with 3 days of persistent axillary pain and swelling especially with weight-lifting. Pain remains despite reduction in overhead training but still practices lacrosse. PE- localized swelling with tenderness and firmness over left axilla. Supine there is prominent venous structures with left UE > right. Which of the following is the presumed diagnosis?

a) Superficial phlebitis
b) Pectoralis major tear
c) Labral tear
d) Effort induced thrombosis
e) Lymphangitis

Questions

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Return to Work Issues for the Primary Care Providers

L. Bruce Hensley, D.O.

Learning Objective:

Discuss when the patient resume may resume previous job.

Discuss the physical requirements.

Discuss medications that could create an issue.

NOTES

Medical Clearance of the Psychiatric Patient

Michael C. Carlisle, D.O.

Learning Objective:

Describe the concept of medical clearance.

Present medical problems that present similar to psychiatric problems.

Discuss life-threatening psychiatric disorders.

NOTES

Physician Employment:
How to Fly Solo/
Start or Restart a Private Practice

Mark J. Nadaud, CPA/ABV
&
John J. King, CPA

Learning Objectives:

Provide information and advice regarding the Medical Practice consolidation movement in order to make informed business decisions.

Flying Solo

Physician Employment

"How to Start/Re-Start a Practice"

John J. King, CPA
Managing Partner

Mark J. Nadaud, CPA/ABV
Director

Todays Objective

To provide information and advice to practicing physicians regarding the Medical Practice consolidation movement in order to make informed business decisions

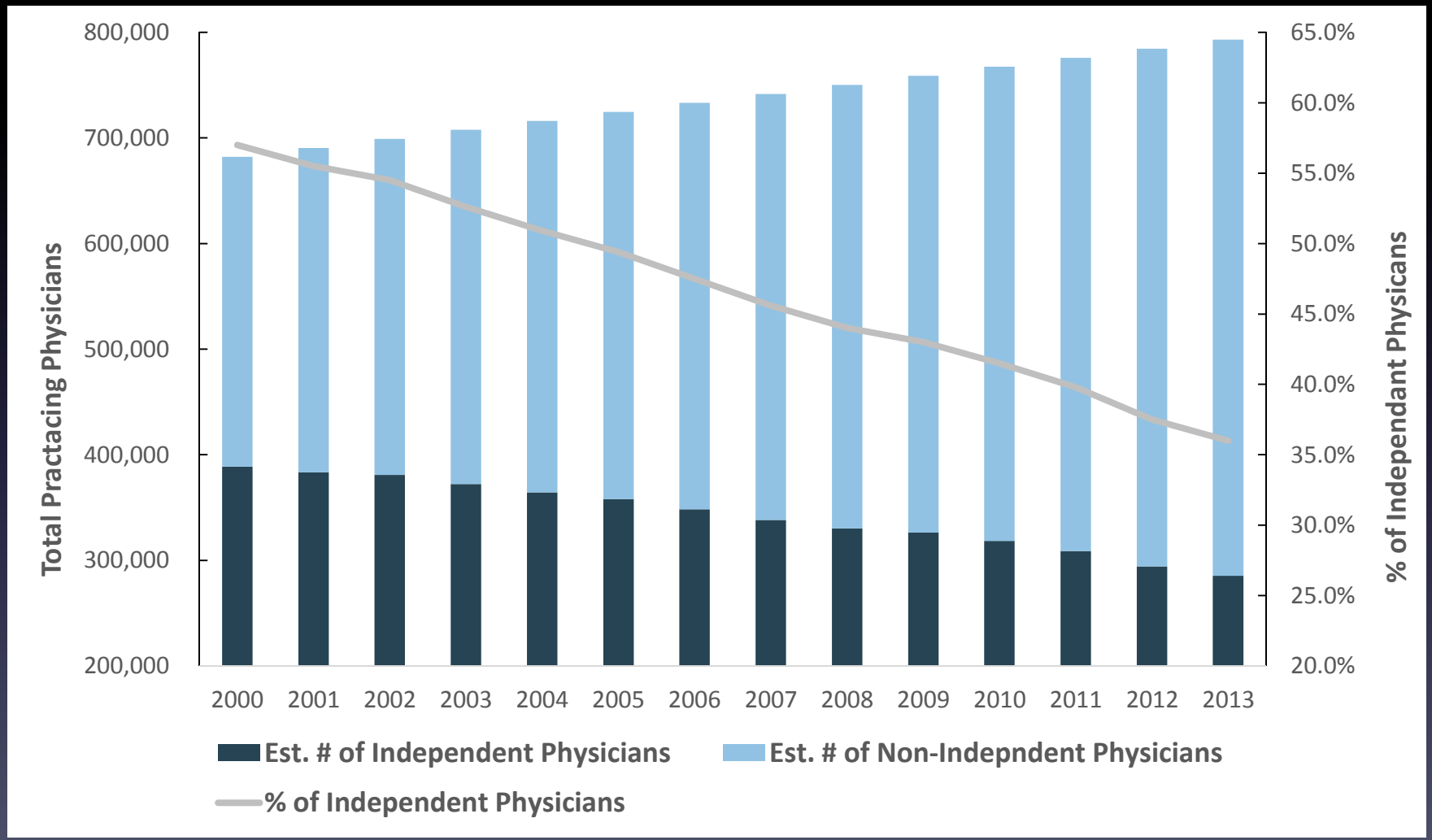

KEEP
SELL

Discussion Topics

- History of the Consolidation
- Pros / Cons of Selling
- Making the Right Decision
- Flying Solo
- Medical Group Formation
- Practice Sale Considerations

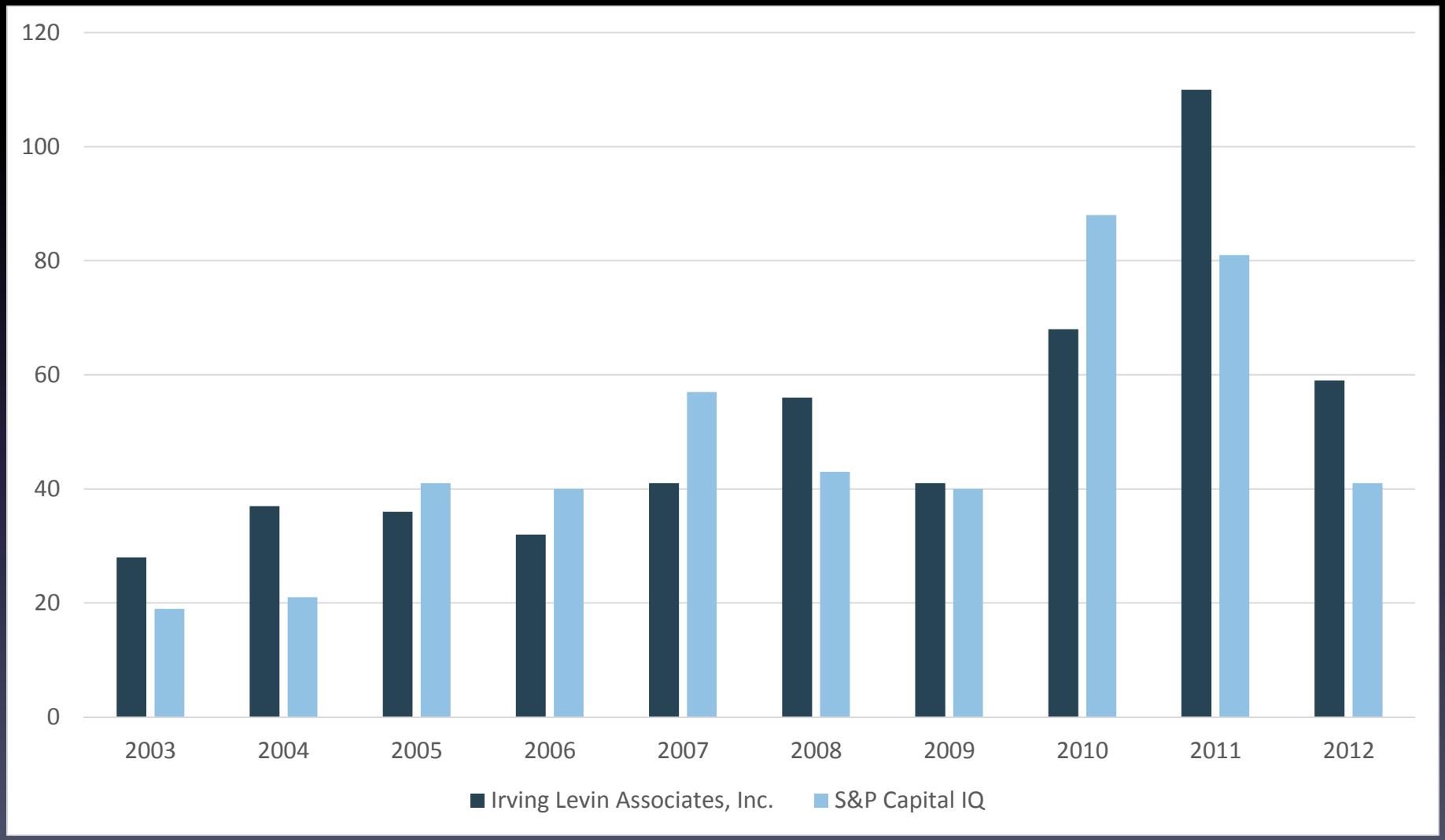
History of Medical Consolidation

Independent vs. Non-Independent



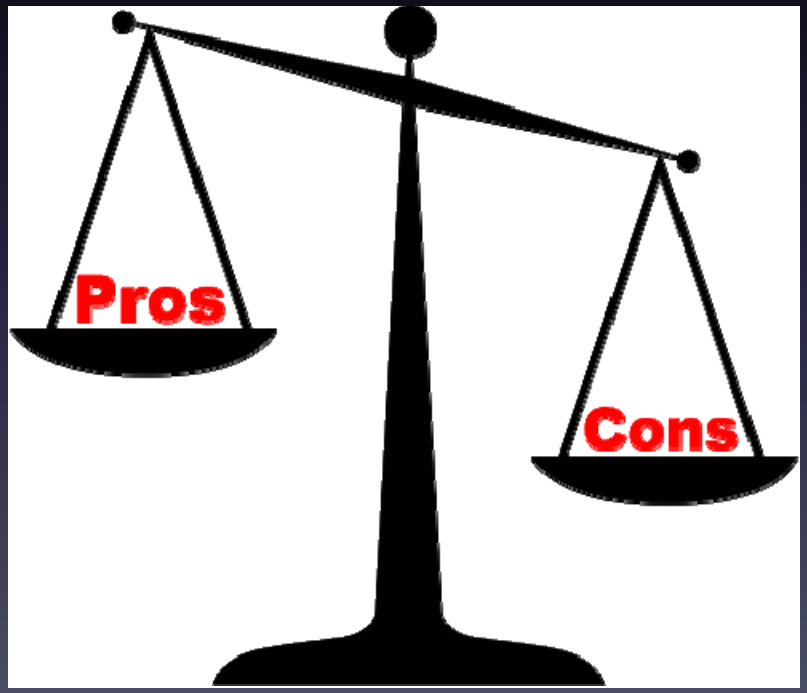
Source: Healthcare Appraisers, Inc.

Mergers & Acquisition Activity



Source: Healthcare Appraisers, Inc.

Pros and Cons of Selling



Pros

- The check will clear
- Administrative duties
- Incomes are often higher
- Work-life balance
- Job security
- Access to additional resources and state of the art equipment
- Higher reimbursement rates

Cons

- You aren't in charge
- Compensation can be changed
- You may be judged by new metrics (monthly quotas)
- Administrative duties
- Introduction to new technology

How to Make the Right Decision?!?!

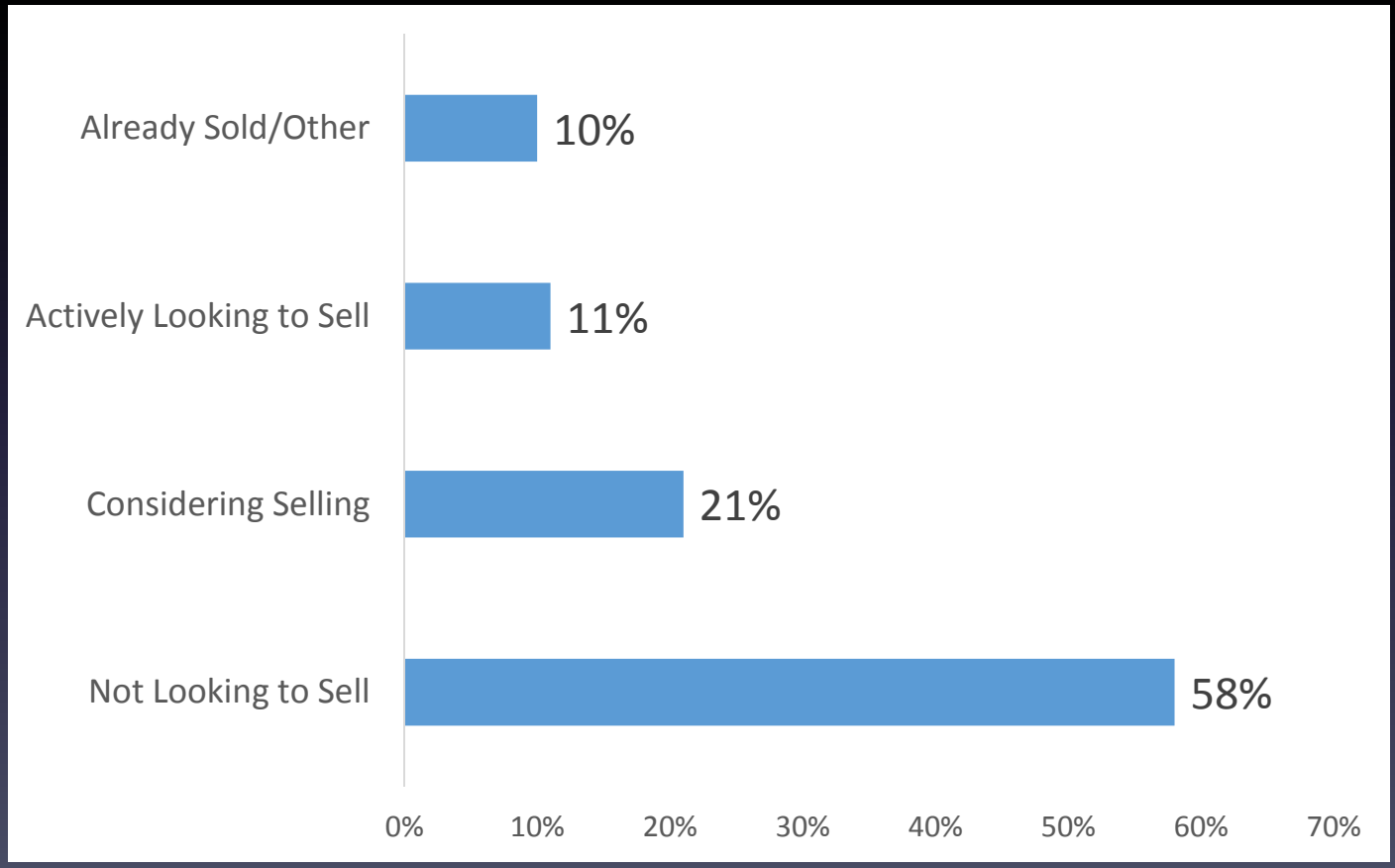
- Talk to colleagues
- Does your view of the future agree with the hospital?
- Weigh pros and cons
- Compensation
- Discuss options with your CPA/Business Advisor

Market Forces to Consider

Reimbursement	Rising Technology Costs ("EHR")	Pressure to Consolidate
Growing Regulatory Pressures	Privacy Rules	Burdens of Billing and Collections
Data Collection Requirements	Student Debt	Health of the Population

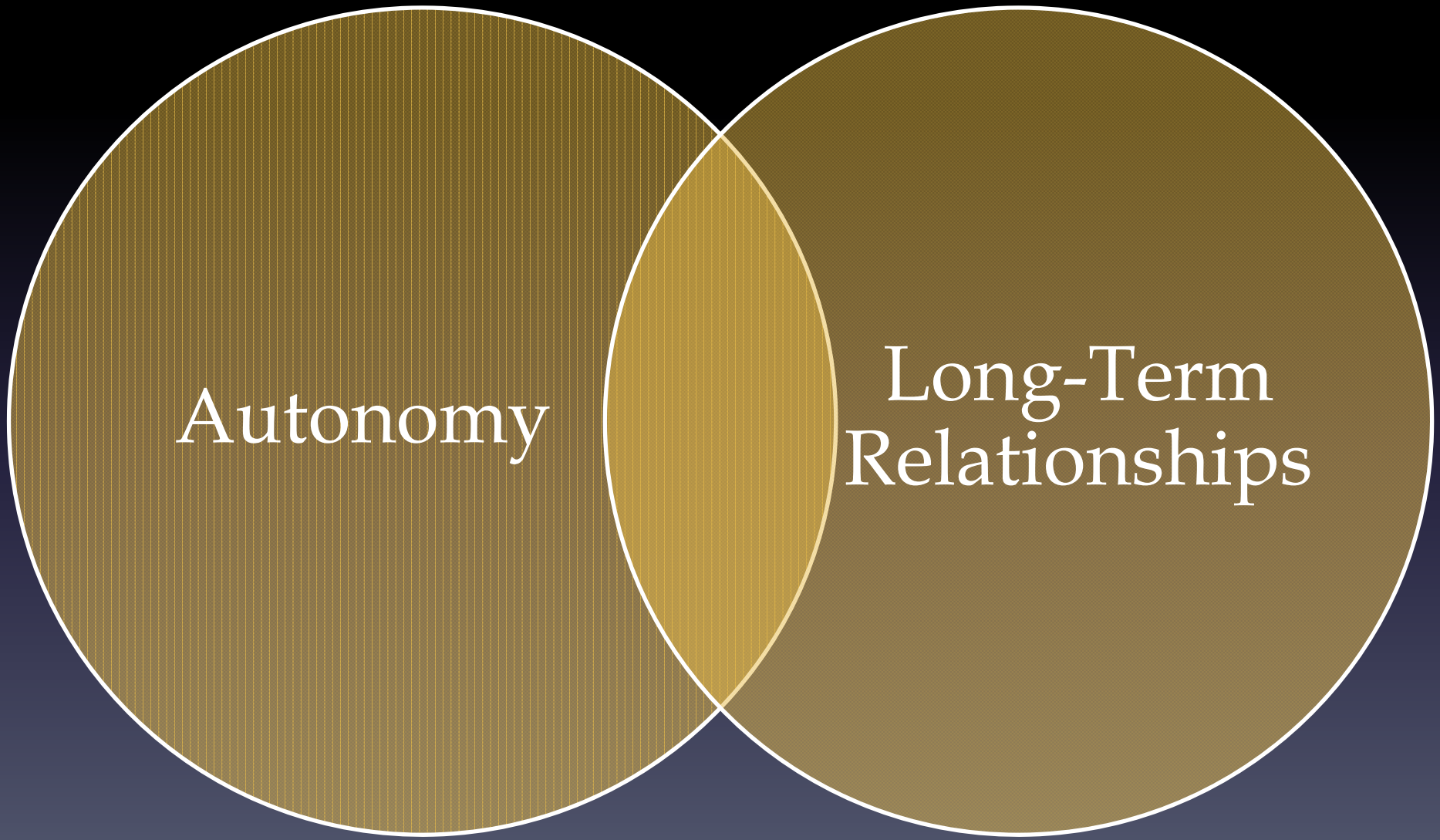
FLYING SOLO

58% of Physicians do not Want to Sell

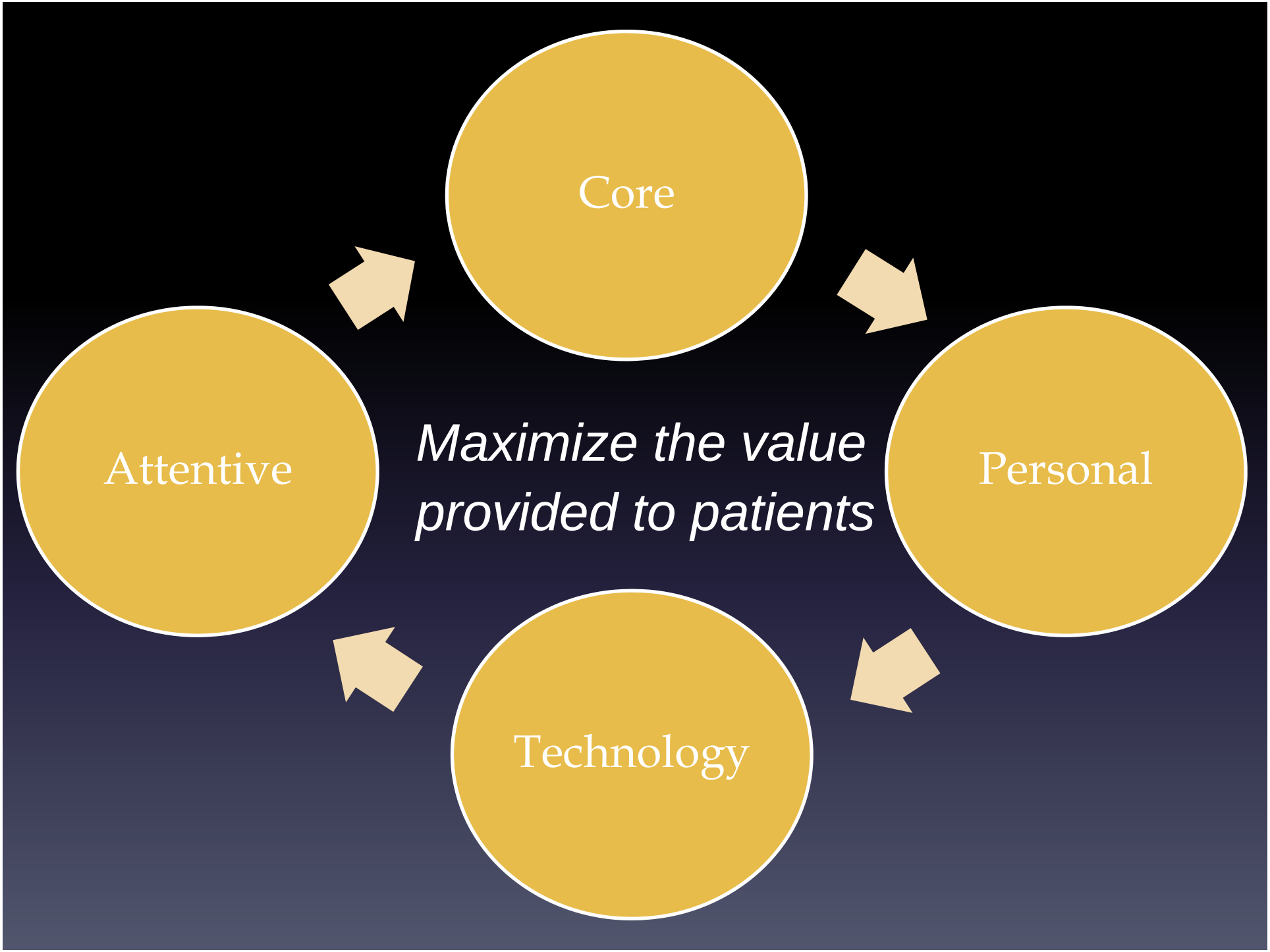


Source: CareCloud and QuantiaMD

Why Stay Independent?

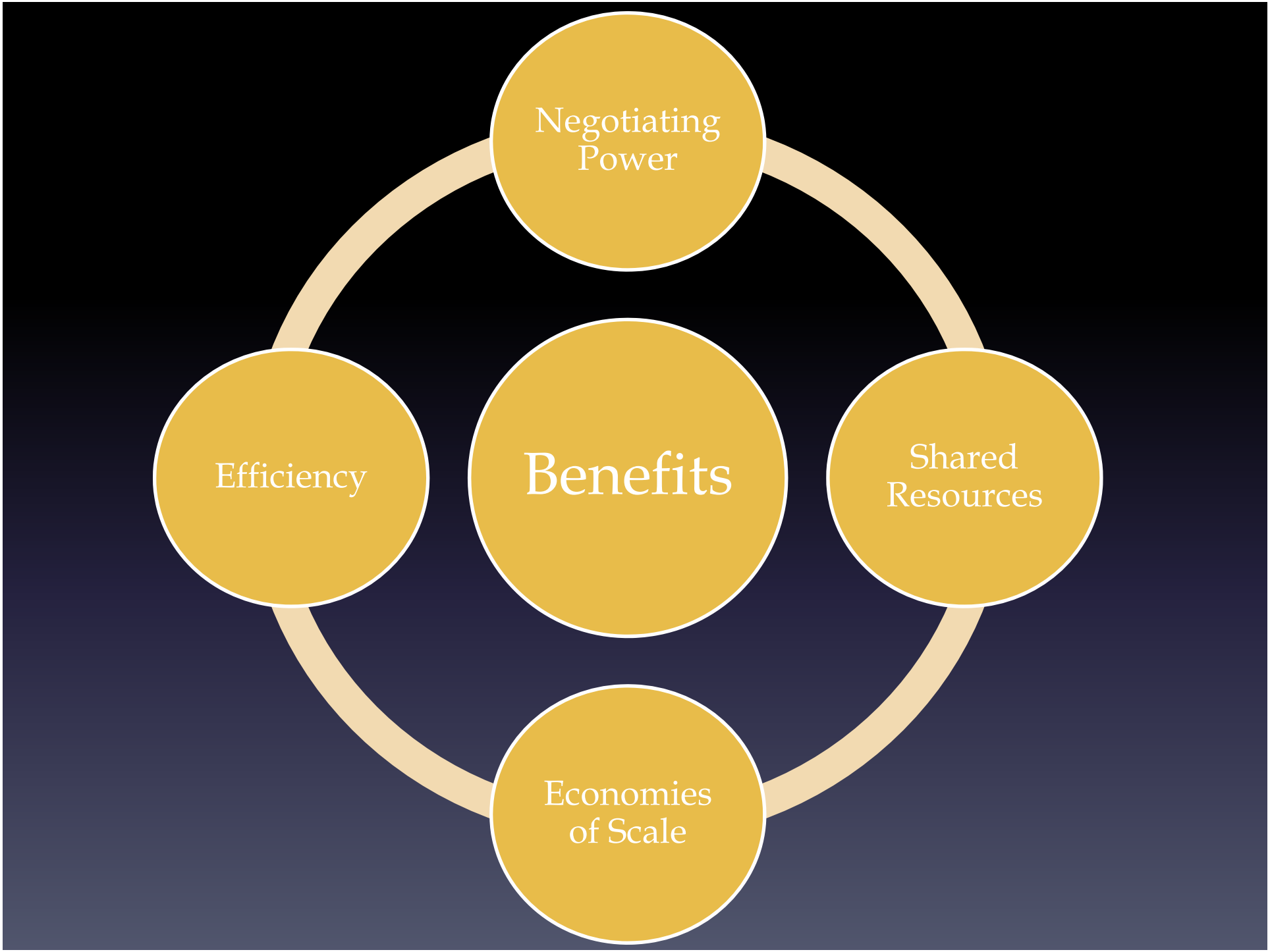


Independence is NOT Impossible


Core
Personal
Technology
Attentive
Maximize the value provided to patients

Medical Group Formation

"Strength in Numbers"


Negotiating Power
Efficiency
Benefits
Shared Resources
Economies of Scale

Why Form a Medical Group

- Greater patient convenience and competitive advantages
- Enhanced access to managed care contracts
- Greater access to contracts with hospitals
  - Exclusive, hospital based contracts for specialty services
  - Medical-director agreements
  - Joint ventures
- Ability to keep referrals within the group
  - Increase revenue and profitability

Why Form a Medical Group (Cont.)

- Greater ability to afford expensive new medical equipment
- Improved quality of care and physician resources
- Positive impact on operating efficiency through:
  - Ability to spread costs
  - Hire professional managers
  - Diversify revenue sources
- Reduced "on-call" time for each physician
- Perceived "safety in numbers" in an increasingly difficult health care environment

Goals of a Merger

- Aligning providers to better coordinate and manage patient care
- Providing quality care at better cost
- Creating an organization that will enforce compliance with established goals and metrics
- Coordinating development of approved clinical processes
- Developing enhanced recruitment opportunities
- Assisting with physician manpower planning
- Assisting with strategic and succession planning
- Developing new service lines

What you need to do

1

Objective of the Group

- Purpose of the Group (Vision Statement)
- Identify Goals and Objectives
- Achievability of the goals

2

Assemble the Planning Team

- Some or All Physicians
- Practice Management Consultant (CEO)
- Office Manager
- CPA
- Attorney

3

Operational Issues

- Choice of Entity
- Capitalization
- Ownership Interest
- Management and Control
- Compensation
- Withdrawal from the group
- Agreement to form group

4

Group Formation

- Corporate Organizational documents
- Apply for a new group provider number
- Establish books and records
- Office space and equipment expense
- Obtaining new materials and phone numbers
- Securing insurance coverage
- Establishing new bank accounts

Tips of Integration

Make Connections	•Market Research •Investment •Independence •Culture
Build out Management Team	•Hire non-physician CEO •Create a Board of Directors
Determine Level of Integration	•Physician Leadership •Performance Monitoring •Payor Communications •Compensation
Investigate Integrated Business Models	•Managed Service Organizations (“MSO”) •Independent Physician Associations (“IPA’) •Accountable Care Organizations (“ACO”)

Practice Sale Considerations

No Easy Task

Since the sale of a practice is for all intents and purposes irrevocable, physicians are encouraged to think long and hard before signing on the dotted line.

What you should know

What Physicians should know

- Motivational Factor
  - Quality of life, Job Security, Resources, technology
- Form of Purchase
  - Asset vs. Stock
- Structure
  - Various tax implications
- Saleable Assets
  - Tangible assets, Accounts Receivable, Intangible Assets
- Valuation Methodologies
  - Asset, Income, & Market Approach

What Physicians should know (Cont.)

- Employment and Compensation
  - Guaranteed income (1-5 years), production based
- Regulatory Compliance
  - Anti-kickback laws, self-referral legislation, state medical laws, etc.
- STARK
  - Prohibits the making of referrals for certain health services covered by Medicare or Medicaid if there is a financial relationship between the referring physician and the entity receiving payments
- Fair Market Value vs. Commercial Reasonableness
  - Fair market value requires a willing buyer and willing seller
  - Commercial reasonableness under STARK

Begin Transition Planning 3-5 Years Prior to Sale

- Understanding Market Trends
- Increase Production/Collection
- Management by Statistics
- Track and Monitor Practice Performance
- Key Performance Indictors (“KPIs”)

Understanding Value

… "fair market value" is the price at which a property would change hands between a willing buyer and a willing seller when the former is not under any compulsion to buy and the latter is not under any compulsion to sell"...

Value Determined by 3 Categories of Assets

1. Tangible Assets
2. Accounts Receivable
3. Intangible Assets

   ("Goodwill")

Factors Impacting Value

- Overhead
- Patients
- Treatment Mix
- Market Conditions
- Market Trends
- Demographics
- Owner Transition
- Competition
- Technology
- Staff
- Management Systems
- Revenue Trend
- Collections Ratio
- Type of Practice
- Fees
- Facility

Beware of Asset Allocation!

Choose Carefully

- Evaluate the Purchaser
- Look for Experience

Avoiding These Common Mistakes

- Selling to an Unknown Buyer
- Focusing more on Term than Termination
- Forgetting to Specify What You Aren't Selling
- Tax Implications
- Being Too Trusting
- Failing to Secure Future Payments
- Restrictive Covenant
- Failing to Guard Against Future Owners

Consult Your Trusted Advisors

Questions?

Thank You

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- For more than 25 years, King Barrett LLP has been serving individuals and business clients in a diverse range of industries including:
  - Medical
  - Dental
  - Veterinary
  - Professional Services

- We are dedicated to providing individuals and business owners in Ohio and the Midwest with innovative tax, accounting, financial planning, and business management solutions combined with expert advice that can help them succeed financially.

Client Services List

ACCOUNTING SERVICES

[✓] CFO/Controller Services

[✓] Bookkeeping assistance

[✓] Accounting systems setup and training

[✓] Tax planning and preparation

[✓] Cash Flow analysis

[✓] Financial Statement preparation and analysis

[✓] Analyzing Key Performance Indicators ("KPI's")

TRANSACTION SERVICES

[✓] Mergers and Acquisitions

[✓] Practice Brokerage

[✓] Valuations and Fairness Opinions

[✓] Succession planning

[✓] Tax planning for business acquisitions and dispositions

[✓] Financial and accounting due diligence

TAX AND BUSINESS PLANNING AND PREPARATION

[✓] Federal, state, and local income tax strategies

[✓] Estate, gift, and trust tax return preparation

[✓] Individual tax planning and preparation

[✓] Ensuring Multi-state and local tax compliance

RETIREMENT PLANNING SERVICES

[✓] Estate planning and administration

[✓] Defined Benefit, Profit Sharing and 401(k) plans

[✓] Trusted third-party administrator (TPA)

ADVISORY SERVICES

[✓] Profitability Consulting

[✓] Internal Control implementation

[✓] Practice Management

[✓] Bank and private financing assistance

International Volunteer Work:
The Perils and Pearls

Karen L. Asher, D.O.
&
Thomas E. Asher, D.O.

Learning Objectives:

Prepare for international medical work.

Discuss probable problems of international travel and culture.

Educate potential physician volunteers on resources, diseases and treatments.

Humanitarian Aid Workers

If you are traveling overseas to provide aid—such as disaster relief or missionary work—you may face more health risks than regular tourists. You may be more exposed to the local population and have less-secure lodgings. If you are traveling in the aftermath of a natural disaster, you may have to contend with floodwater, debris, or other hazards. However, since you are an aid worker, it is especially critical to protect your health. If you become sick or injured, not only will you be unable to provide aid, you will also add to the burden of the local health care system. With careful preparation, however, you can minimize the risks to your health.

Pre-Travel Care

As soon as possible, schedule a visit with a travel medicine specialist, who can provide vaccines, medicines, and advice on how to stay safe and healthy while you are traveling. You should also plan a visit with your regular doctor to make sure you're physically fit for the demands of the work. If you'll be gone for a long time, a dental check-up before you leave is a good idea as well.

Aid work can be demanding, and medical facilities in disaster areas are often strained or nonexistent. Therefore, if you have a serious chronic illness, such as heart disease or diabetes, or are pregnant, consider whether there are other ways for you to support the cause.

Avoiding Injury in a Disaster Area

Injuries and motor vehicle accidents are common risks anywhere in the world, so select safe transportation and always wear a seatbelt. Be sensitive to possible physical dangers, such as debris, unstable buildings, and downed power lines. In a conflict area, be aware of landmines or other explosive hazards.

What to Pack

Humanitarian aid workers often need to pack more than other travelers, especially if they are going to be in an area where supplies are limited and the water supply is compromised. In addition to your travel health kit, consider whether you might need any of the following:

- First-aid supplies
- Water filter or purification tablets
- Nonperishable food
- Gloves (rubber or leather)
- Bed net (in areas with malaria)
- Extra pair of prescription glasses
- Toilet paper
- Sewing kit
- Laundry detergent
- Flashlight and spare batteries
- Candles and matches or lighter
- Zip-top bags
- Safety goggles

Humanitarian aid work is stressful, and taking along a personal item, such as a family photo, can be comforting. You should also bring photocopies of important documents, such as your passport and medical license.

When You Return

Seek medical care if you were injured during your trip or become ill after returning. Make sure your doctor knows that you recently returned from doing humanitarian aid work overseas. More than 30% of aid workers report depression after returning home, so take time to rest and readjust. If you continue to feel depressed, you may wish to seek counseling.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Checklist for Patients Being Evaluated for Ebola Virus Disease (EVD) in the United States

Upon arrival to clinical setting/triage

- ❑ Assess the patient for a fever (subjective or ≥ 100.4°F / 38.0°C)
- ❑ Determine if the patient has symptoms compatible EVD such as headache, weakness, muscle pain, vomiting, diarrhea, abdominal pain or hemorrhage
- ❑ Assess if the patient has a potential exposure from traveling to a country with widespread Ebola transmission* or having contact with an Ebola patient in the 21 days before illness onset
  Suspect Ebola if fever or compatible Ebola symptoms and an exposure are present
  See next steps in this checklist and the Algorithm for Evaluation of the Returned Traveler for Ebola at http://www.cdc.gov/vhf/ebola/pdf/ebola-algorithm.pdf

Upon initial assessment

- ❑ Isolate patient in single room with a private bathroom and with the door to hallway closed
- ❑ Implement standard, contact, & droplet precautions
- ❑ Notify the hospital Infection Control Program at _____
- ❑ Report to the health department at _____

Conduct a risk assessment for: High-risk exposures

- ❑ Percutaneous (e.g., needle stick) or mucous membrane exposure to blood or body fluids from an EVD patient
- ❑ Direct skin contact with skin, blood or body fluids from an EVD patient
- ❑ Processing blood or body fluids from an EVD patient without appropriate PPE
- ❑ Direct contact with a dead body in an Ebola-affected area without appropriate PPE

Low-risk exposures

- ❑ Household members of an EVD patient or others who had brief direct contact (e.g., shaking hands) with an EVD patient without appropriate PPE
- ❑ Healthcare personnel in facilities with EVD patients who have been in care areas of EVD patients without recommended PPE

Refer to *Guidance on Personal Protective Equipment To Be Used by Healthcare Workers During Management of Patients with Ebola Virus Disease in U.S. Hospitals, Including Procedures for Putting On (Donning) and Removing (Doffing)* (hyperlink: http://www.cdc.gov/vhf/ebola/hcp/procedures-for-ppe.html)

During aerosol-generating procedures

- ❑ Limit number of personnel present
- ❑ Conduct in an airborne infection isolation room
- ❑ Don PPE as described in the *Guidance on Personal Protective Equipment To Be Used by Healthcare Workers During Management of Patients with Ebola Virus Disease in U.S. Hospitals, Including Procedures for Putting On (Donning) and Removing (Doffing)* (hyperlink: http://www.cdc.gov/vhf/ebola/hcp/procedures-for-ppe.html)

Patient placement and care considerations

- ❑ Maintain log of all persons entering patient's room
- ❑ Use dedicated disposable medical equipment (if possible)
- ❑ Limit the use of needles and other sharps
- ❑ Limit phlebotomy and laboratory testing to those procedures essential for diagnostics and medical care
- ❑ Carefully dispose of all needles and sharps in puncture-proof sealed containers
- ❑ Avoid aerosol-generating procedures if possible
- ❑ Wear PPE (detailed in center box) during environmental cleaning and use an EPA-registered hospital disinfectant with a label claim for non-enveloped viruses**

Initial patient management

- ❑ Consult with health department about diagnostic EVD RT-PCR testing***
- ❑ Consider, test for, and treat (when appropriate) other possible infectious causes of symptoms (e.g., malaria, bacterial infections)
- ❑ Provide aggressive supportive care including aggressive IV fluid resuscitation if warranted
- ❑ Assess for electrolyte abnormalities and replete
- ❑ Evaluate for evidence of bleeding and assess hematologic and coagulation parameters
- ❑ Symptomatic management of fever, nausea, vomiting, diarrhea, and abdominal pain
- ❑ Consult health department regarding other treatment options

This checklist is not intended to be comprehensive. Additions and modifications to fit local practice are encouraged.

* See 2014 Ebola Outbreak in West Africa—Case Counts or http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/case-counts.html to determine if a country has widespread Ebola transmission

** See Interim Guidance for Environmental Infection Control in Hospitals for Ebola Virus or http://www.cdc.gov/vhf/ebola/hcp/environmental-infection-control-in-hospitals.html

*** See Interim Guidance for Specimen Collection, Transport, Testing, and Submission for Persons Under Investigation for Ebola Virus Disease in the United States or http://www.cdc.gov/vhf/ebola/hcp/interim-guidance-specimen-collection-submission-patients-suspected-infection-ebola.html

DOFFING BIOLOGICAL PPE - EBOLA PATIENTS

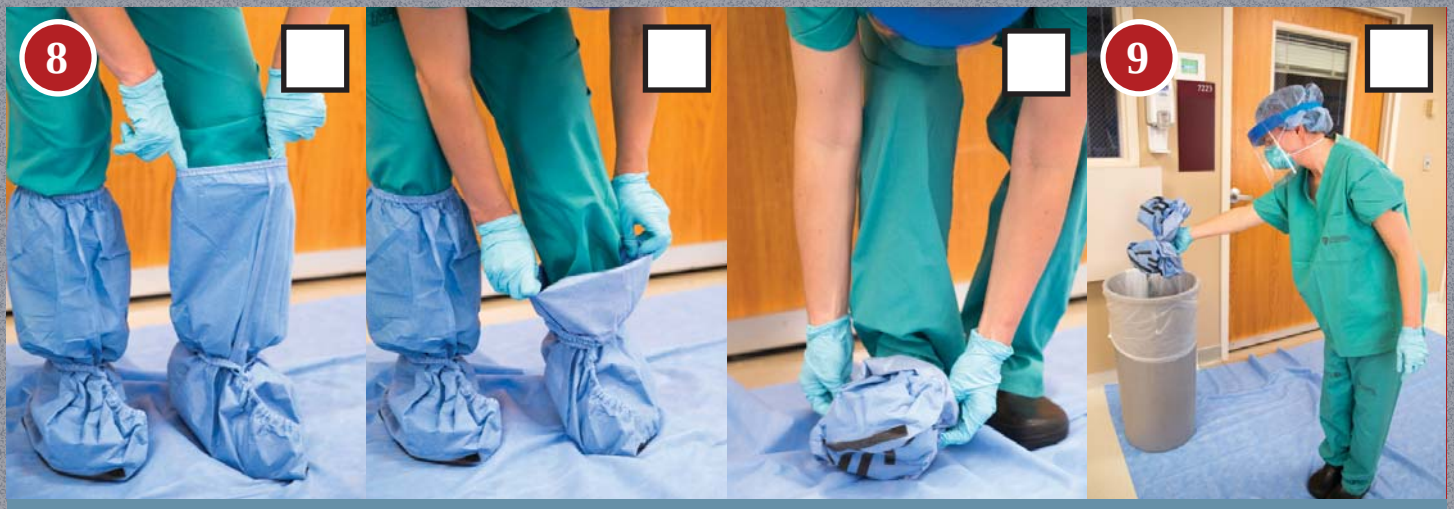
1 Bleach wipe the long cuff KC500 Purple Nitrile Gloves before opening the door to the patient room.
2 Step out of room onto the doffing pad with trash receptacle nearby.

3 Once on the doffing pad, if you taped the gloves to the gown, remove the tape gently and discard it before removing the gloves. 4 Remove the long cuff KC500 Purple Nitrile Gloves using glove-in-glove technique and discard them in the trash.

If the inner standard patient care gloves are accidentally removed during the doffing of the nitrile gloves, additional clean gloves are available on the doffing pad.

DOFFING BIOLOGICAL PPE - EBOLA PATIENTS

5 Begin gently removing the gown. Ties should be untied if possible to reduce aerosolization. 6 Keep clean gown sleeves over your gloved hands as much as possible to prevent contamination of the gloved fingers as you gather the gown, keeping the dirty surfaces to the inside, rolling it up gently. 7 Discard in trash.



8 Remove the leg/boot covers one at a time. Roll the dirty side in as you remove them if possible, being very mindful of where the dirty side may come in contact with things around you. 9 Step into a clean area of the doffing pad and discard covers in trash. Refrain from returning to the soiled area from this point forward.

DOFFING BIOLOGICAL PPE - EBOLA PATIENTS

10 Remove the inner standard patient care gloves using glove-in-glove technique and place them in the trash. 11 Perform hand hygiene, but do not leave the doffing pad (use available hand sanitizer). 12 Apply new clean gloves from the doffing pad.

13 Remove the face shield. Grab the rear strap and pull it over the head forward, gently allowing the face shield to fall forward. 14 Dispose of the face shield in the trash.

DOFFING BIOLOGICAL PPE - EBOLA PATIENTS

15 Holding the lower corner of the N95 Respirator firmly, but exposing as little of your gloved hand as possible to its dirty surface, remove each strap of the N95 respirator over the head. 16 Gently place the N95 respirator in the trash. The surgical cap may move with the respirator straps as they are removed. 17 Remove the surgical cap with gentle motions, touching as little of its contaminated surfaces as possible. 18 Place surgical cap in trash.

19 Step off the doffing pad, gather it up carefully rolling the dirty surface inward. 20 Place rolled doffing pad in trash receptacle.

DOFFING BIOLOGICAL PPE - EBOLA PATIENTS

21 Remove the standard patient care gloves using glove-in-glove technique. 22 Place gloves in trash. 23 Perform hand hygiene. 24 Proceed to Shower.

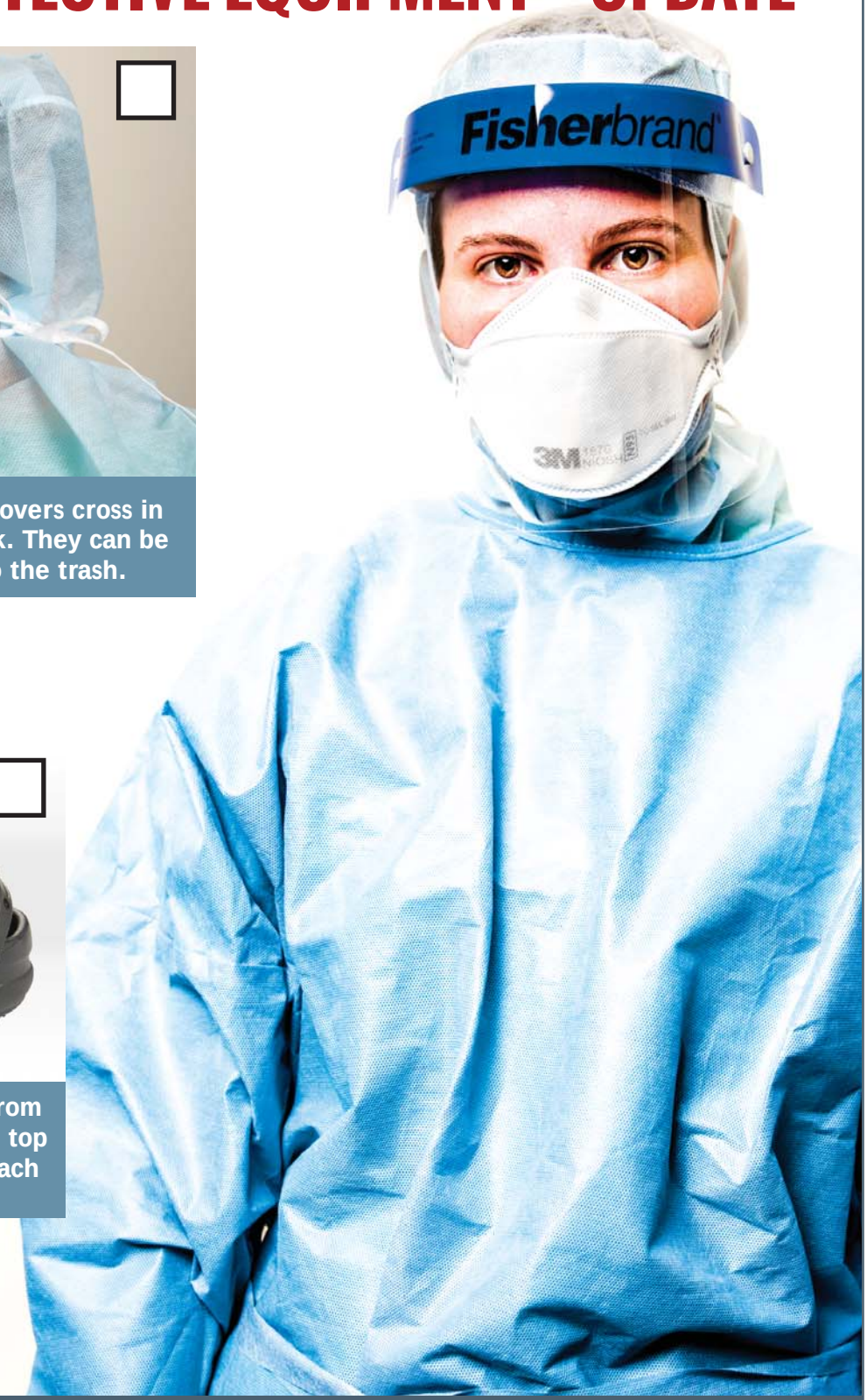
25 Perform post Vital Signs and 26 rehydrate.

DOFFING BIOLOGICAL PPE - EBOLA PATIENTS

PERSONAL PROTECTIVE EQUIPMENT - UPDATE

A The ties for the head and neck covers cross in front and then tie a bow in the back. They can be untied and gently pulled off into the trash.

B Before staff members step from the doffing pad to the floor, the top and bottom of each shoe is bleach wiped.

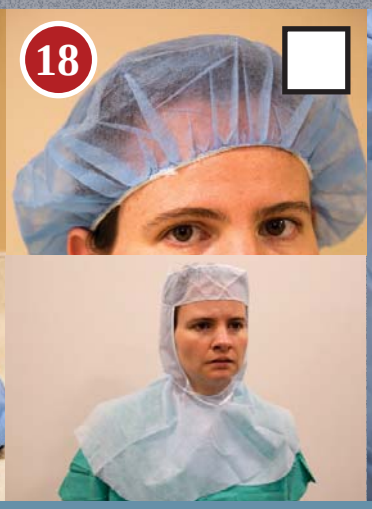


DONNING BIOLOGICAL PPE - EBOLA PATIENTS

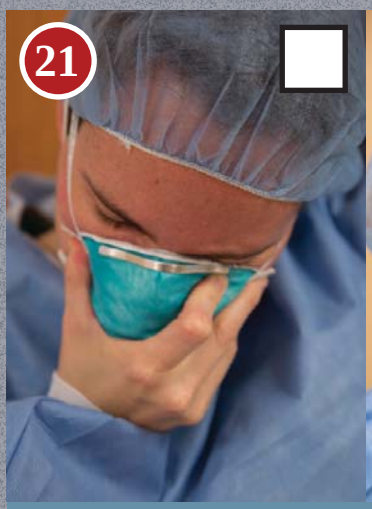
EQUIPMENT: (1) SURGICAL GOWN, (2) SURGICAL CAP/HAIR COVER, (3) FACE SHIELD, (4) STANDARD PATIENT GLOVES, (5) DOFFING PAD (LARGE FLUID REPELLENT FABRIC OR PLASTIC DRAPE), (6) SURGICAL BOOT COVERS, (7) N95 RESPIRATOR, (8) LONG CUFF KC500 PURPLE NITRILE GLOVES, (9) TRASH RECEPTACLE, (10) DUCT TAPE, (11) APRON.

(12) Perform hand hygiene. (13) Apply scrubs and plastic washable footwear (such as Crocs). (14) Remove all jewelry. (15) Take and record vital signs. (16) Hydrate.

DONNING BIOLOGICAL PPE - EBOLA PATIENTS



17 Apply boot covers, 18 surgical cap, and 19 surgical gown. NOTE: ALL TIES should be properly secured with a SIMPLE BOW. Ensure all fit well and cover the intended areas.
20 Perform hand hygiene.



21 Apply N95 respirator. 22 Seal mask to the face ensuring straps are not crossed and properly located at the crown of the head and base of the neck. 23 Perform a fit check of the respirator, breathing deeply in and out, feeling with your hands for any air leakage.

DONNING BIOLOGICAL PPE - EBOLA PATIENTS

24 Apply face shield (over surgical cap and N95 straps). 25 Perform hand hygiene. 26 Apply standard patient care gloves. Bring cuffs of gown over the patient care glove cuff.

27 Apply long cuff KC500 Purple Nitrile gloves over the standard patient care gloves. Make sure that the glove cuff covers the gown sleeve adequately to prevent exposure when providing patient care. 28 If activities performed in the room are likely to dislodge the cuff, it is acceptable to tape the gown sleeve and glove cuff to one another.

! If the patient's condition warrants, additional personal protective equipment may be added to these guidelines. This may include items such as Tyvek suits, powered air purifying respirators, and aprons.

IN ROOM ACTIVITIES

A third pair of standard patient care gloves should be worn when caring for the patient may contaminate the hands. Aprons will also be available in the room for high splash activities. Bleach wipes may be used to decontaminate the long cuff KC500 Purple Nitrile Gloves if necessary.

DONNING BIOLOGICAL PPE - EBOLA PATIENTS

PERSONAL PROTECTIVE EQUIPMENT - UPDATE

Ⓐ The headcovers were pulled over the ears during patient care for additional protection.

Ⓑ The blue N95 masks were causing skin breakdown on noses. The white tri-fold N95 mask was found to be more comfortable for long term use.

Ⓒ Headcovers which covered more of the neck and tie at the lower rear neck were identified. Ⓓ The ties for the head and neck covers cross in front and then tie a bow in the back. It is worn under the gown. Ⓔ The mask and face shield are worn over it. Ⓕ Ensure the faceshield and headcover overlap to protect the forehead.

Ocular Complications of Diabetes: New Trends in Management

Carol R. Kollarits, M.D.

Learning Objectives:

Recognize the importance of yearly ophthalmic exams for all diabetics.

Advise patients on new treatments for diabetic eye problems.

Express patients' adherence to treatment regimens for management of their blood glucose and HbA1c levels.

OCULAR COMPLICATIONS OF DIABETES

NEW TRENDS IN MANAGEMENT
Have we made any progress in the last 43 years?

- We no longer do hypophysectomy for proliferative diabetic retinopathy (PDR).
- We no longer do therapeutic abortion for PDR in pregnant diabetic mothers.

Diabetic retinopathy, particularly diabetic macular edema, is still the leading cause of blindness in working age adults.

What's new: The anti-VEGF drugs and intraocular steroids may work better at resolving diabetic macular edema than laser treatment alone. If your patient complains about the cost, ask if his ophthalmologist can use Avastin instead of Lucentis.

Diabetics require cataract surgery earlier than non-diabetics of the same age.

What's new: Cataract surgery is vastly improved with new intraocular lens designs and smaller incisions than ever before. The Femtosecond laser is now being used to make incisions to correct astigmatism and perform a perfectly circular opening in the anterior capsule, and then to cube the nucleus. The jury is not yet back on whether the greater precision that the laser brings to the procedure is worth the increase in cost ($3,000 per eye, not covered by insurance).

Diabetics have an increased risk for developing glaucoma.

What's new: Selective laser trabeculopexy is low risk, usually effective in lowering intraocular pressure, and saves the patient money by reducing or eliminating glaucoma medications. This is not the same laser used for retinal laser treatments.

What's really new:

- Alcon has licensed Google's smart lens technology for ocular and systemic disease management.
- An adeno-associated virus (AAV)-based platform for gene therapy for retinitis pigmentosa will start human trials at U of M in 2015. Work is underway for gene therapy for age-related macular degeneration, and hopefully, diabetes and diabetic retinopathy.

Bonus information: Diabetic gastroparesis may be reversed in some patients with one tablet of sildenafil daily.

Carol R. Kollarits, M.D.

Eye Institute of Northwestern Ohio

3509 Briarfield Blvd.

Maumee, Ohio 43537

419-865-3866

New DSM V Criteria for Autism

Shanna K. Kralavic, D.O.

Learning Objectives:

Define the DSM 5 criteria for autism spectrum disorders.

Explain the rationale for merging the autism diagnoses into one category.

Identify evaluation tools and resources for autism spectrum disorders.

NOTES

SATURDAY, NOVEMBER 15, 2014 8.5 hours

7:00 a.m.	Registration
7:00 a.m.-9:00 a.m.	Breakfast Buffet Served ***- West Pathway***
7:50 a.m.-8:00 a.m.	Opening Remarks - ***Orange/Nile Rooms*** *Nicholas G. Espinoza, D.O.*
8:00 a.m.-9:00 a.m.	Advancements in Medical Weight Loss: Diet and Drugs *Mohammed S. Alo, D.O.*
9:00 a.m.-10:00 a.m.	Wound Care Update *Munier M. Nazzal, M.D., FRCS, FACS, RVT, RPVI*
10:00 a.m.-10:30 a.m.	Break/View Exhibits - ***West Pathway***
10:30 a.m.-11:30 a.m.	The Dizzy Patient: An Approach to the Work UP and Management of Vertigo *Ellen L. Baxter, D.O.*
11:30 a.m.-12:30 p.m.	New Anti-Coagulant Guidelines *Daniel J. Evans, D.O., FACC, FACOI*
12:30 p.m.-12:45 p.m.	Lunch Buffet Line
12:45 p.m.-1:45 p.m.	Authentic Leadership: Why Leadership That Matters Begins With You. *Wesley B. Gipe*
1:45 p.m.-3:15 p.m.	Alzheimer's Disease Mechanisms and Early Diagnosis at Mild Cognitive Impairment *Robert G. Nagele, PhD*
3:15 p.m.-3:30 p.m.	***Break/View Exhibits – West Pathway***
3:30 p.m.-5:30 p.m.	Osteopathic Ground Game *Sean R. Kerger, D.O., FAOASM &* *Richard G. Schuster, D.O.*
Or	
	Aloeswood Room
3:30 p.m.-4:30 p.m.	E-Cigarettes: The Good, The Bad and The Ugly *Tracey O'Neal Hooker, D.O., MHA*
4:30 p.m.-5:30 p.m.	Benign Prostatic Hyperplasia Update *Salvador E. Peron, M.D.*

Advancements in Medical Weight Loss: Diet and Drugs

Mohamed S. Alo, D.O.

Learning Objectives:

Examine the scope of obesity problems.

Discuss diets that work.

Examine and discuss drugs for medical weight loss.

NOTES

Wound Care Update

Munier M. Nazzal, M.D., FRCS, FACS, RVT, RPVI

Learning Objective:

Perform evaluation of patients with wounds.

Define types of wounds.

Review comprehensive wound management.

NOTES

The Dizzy Patient:
An Approach to the Work Up and Management of Vertigo

Ellen L. Baxter, D.O.

Learning Objective:

Identify the differential diagnosis for the dizzy patient.

Form a systematic approach to narrowing the differential.

Create a diagnostic and treatment approach for your patient.

NOTES

New Anti-Coagulant Guidelines

Daniel J. Evans, D.O., FACC, FACOI

Learning Objective:

Recognize unique treatments for anti-coagulation.

NOTES

Authentic Leadership:
Why Leadership that Matters Begins with You

Wesley B. Gipe

Learning Objectives:

Discuss and clearly differentiate between leadership and management skills and determine when to apply each.

Examine their own leadership styles and identify opportunities for improvement.

NOTES

Alzheimer's' Disease: New Mechanisms and Early Diagnosis Using Blood-Based Biomarkers

Robert G. Nagele, PhD

Learning Objectives:

Update and comprehend the pathogenesis of Alzheimer's Disease.

Delineate the role of aging-associated changes in the brain vasculature and chronic breakdown of the blood-brain barrier in post-surgical delirium and as a trigger for Alzheimer's Disease.

Discuss progress towards the goal of early detection of Alzheimer's Disease at the mild cognitive impairment and even pre-symptomatic phases.

Alzheimer's Disease Mechanisms and Early Diagnosis at Mild Cognitive Impairment

Robert Nagele, Ph.D.
NJ Institute for Successful Aging
and
Department of Medicine
RowanSOM

DISCLOSURES

Durin Technologies, Inc.
Founder, Chief Scientific Officer, Stockholder

Beren Technologies, Inc.
Founder , Chief Scientific Officer
Stockholder

Funding
Michael J Fox Foundation
Alzheimer's Association
Osteopathic Heritage Foundation
Foundation Venture Capital Group
Boye Foundation
GlaxoSmithKline

AD Statistics

AD is the most common cause of dementia among people age 65 and older.

- Estimate that around 4.5 million people now have AD.
- For every 5-year age group beyond 65, the percentage of people with AD doubles.

- By 2050, 13.2 million older Americans are expected to have AD - **if** the current numbers hold and **if** no preventive treatments become available.

Alzheimer's Disease Hits Home

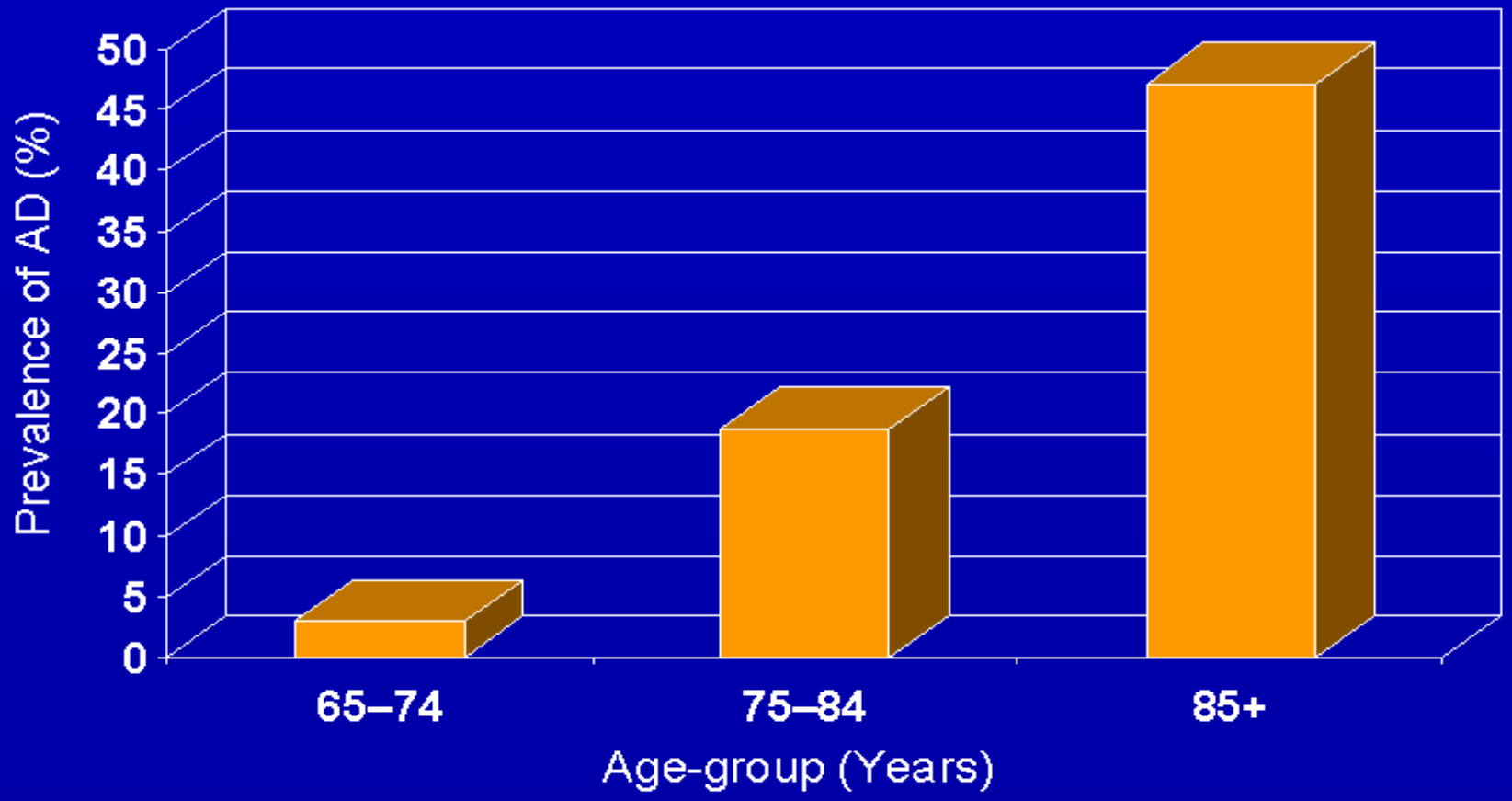
Nagele Family

My Grandparents

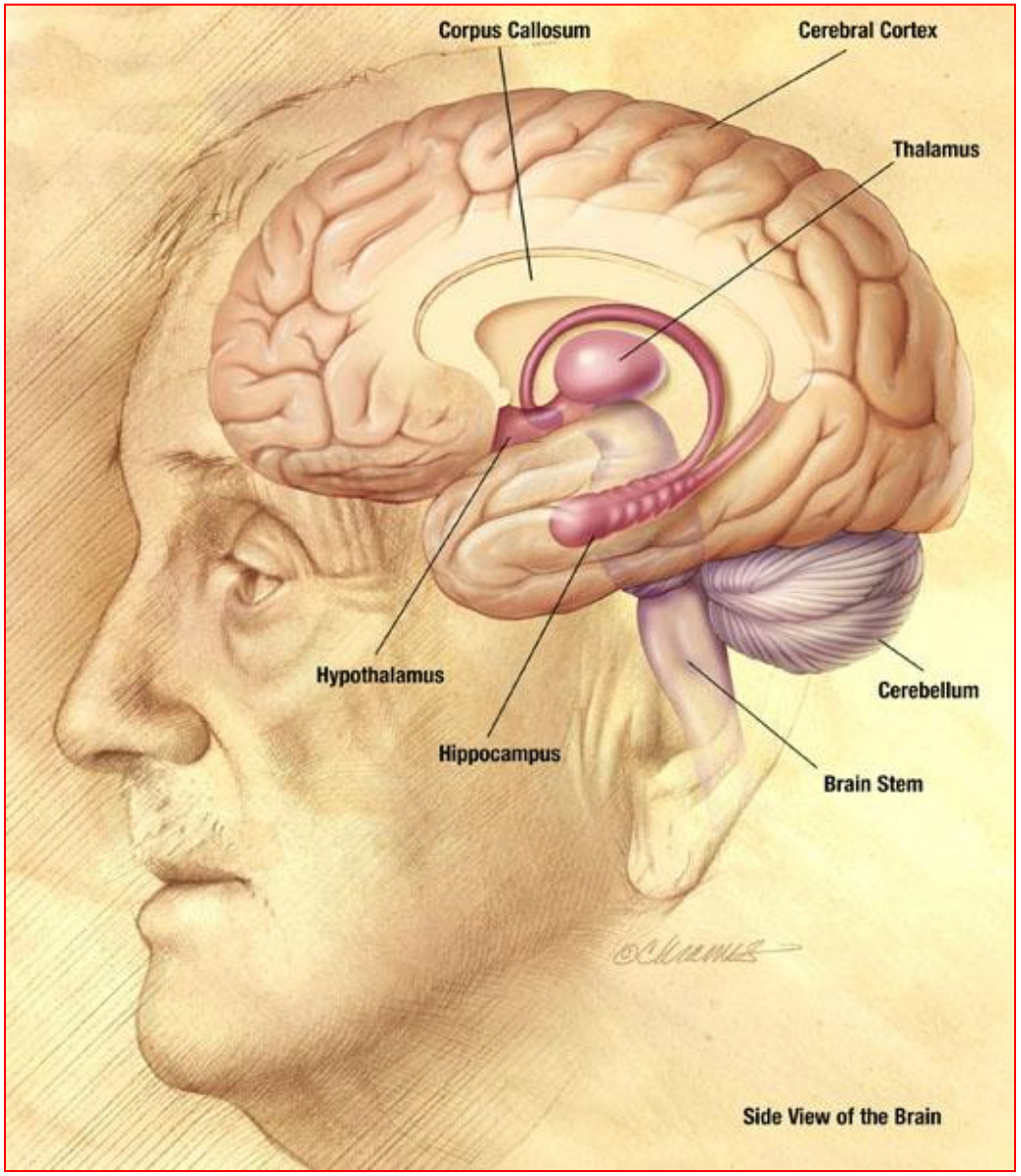
My Mother's Siblings

And now my father and mother-in-law

Prevalence of AD by Age



How Does AD Happen?



Inside the Human Brain

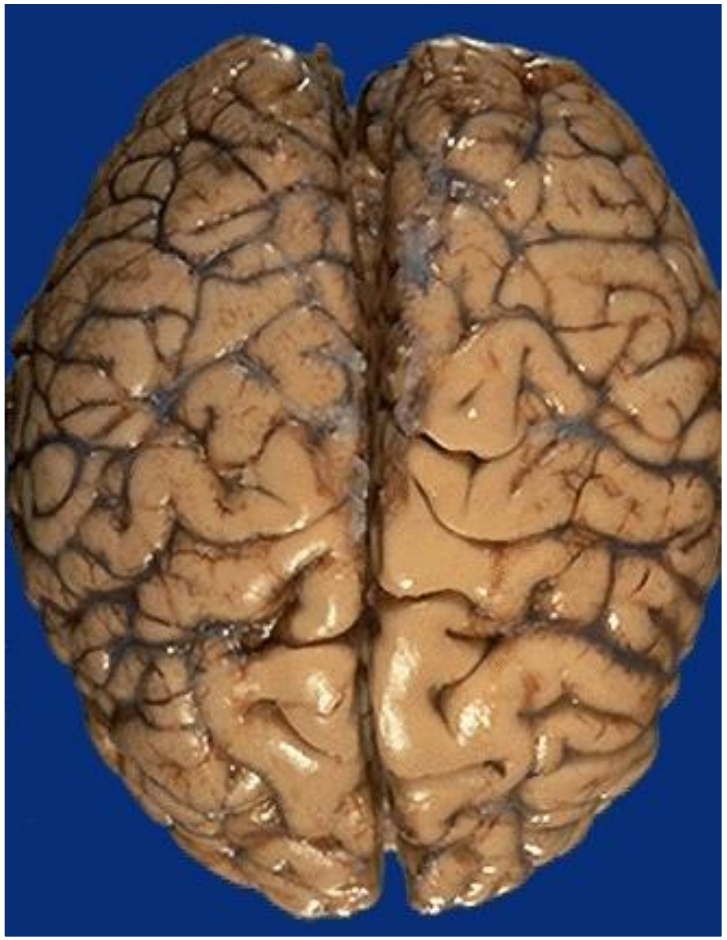
To understand AD, it's important to know a bit about the brain…

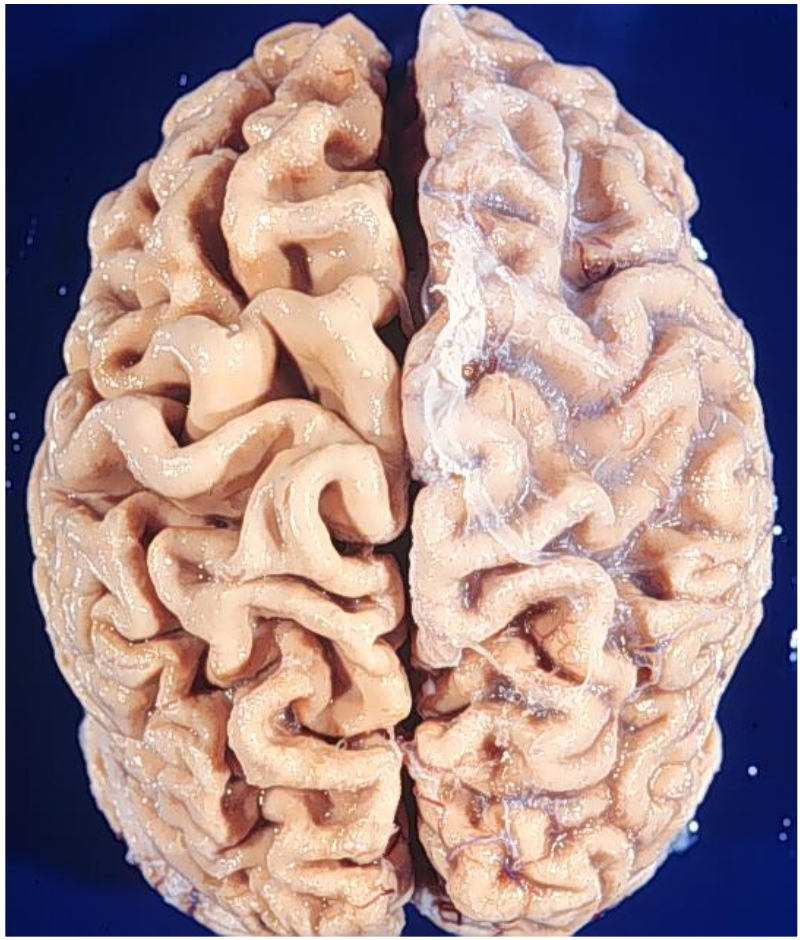
The Brain's Vital Statistics

- Adult weight: about 3 pounds
- Adult size: a medium cauliflower
- Number of neurons: 100,000,000,000 (100 billion)
- Number of synapses (the gap between neurons): 100,000,000,000,000 (100 trillion)

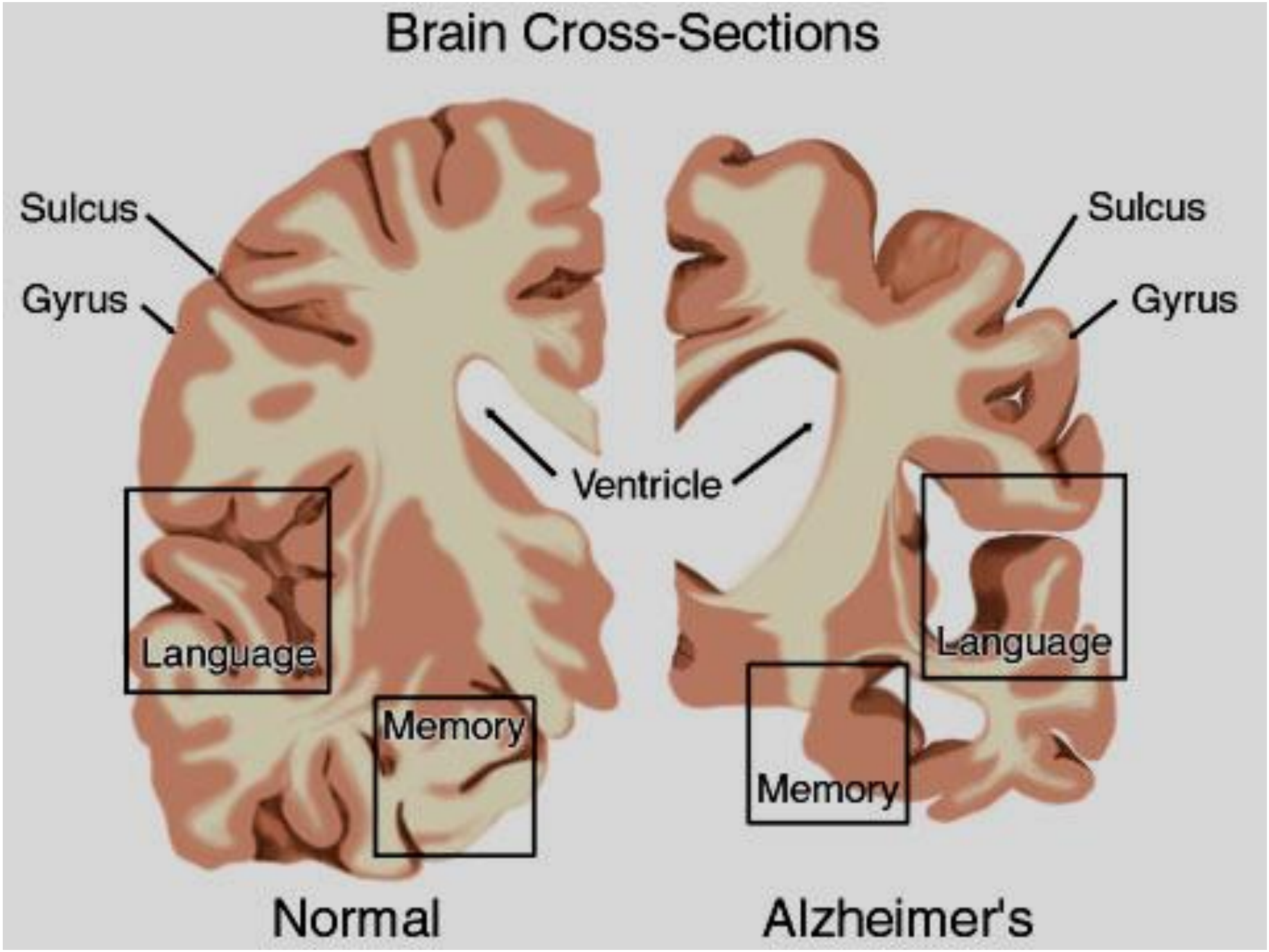
Normal vs Alzheimer Brain

Gross Pathology

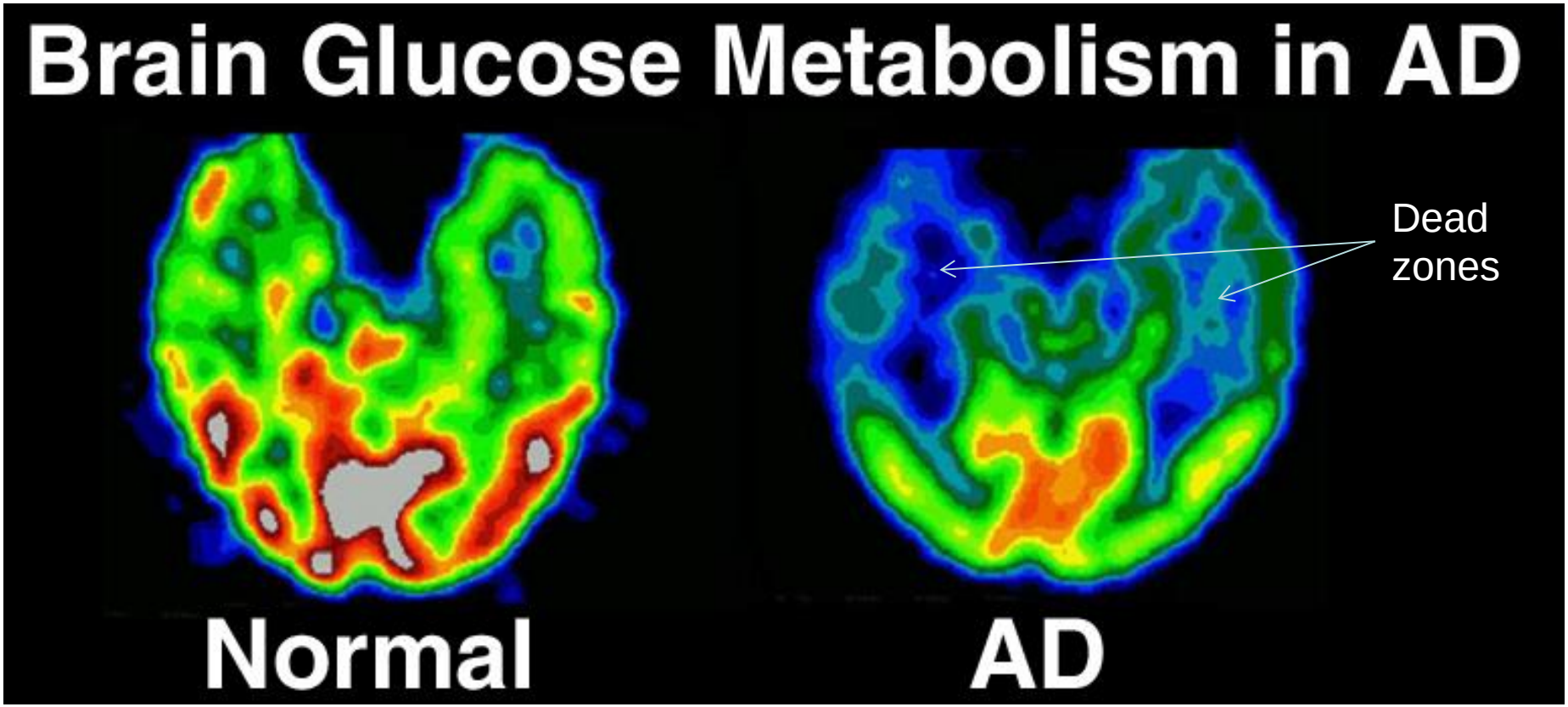




Brain shrinkage – thinning of gyral folds – broadening of fissures


Brain Cross-Sections
Sulcus
Gyrus
Ventricle
Language
Memory
Sulcus
Gyrus
Language
Memory
Normal
Alzheimer's

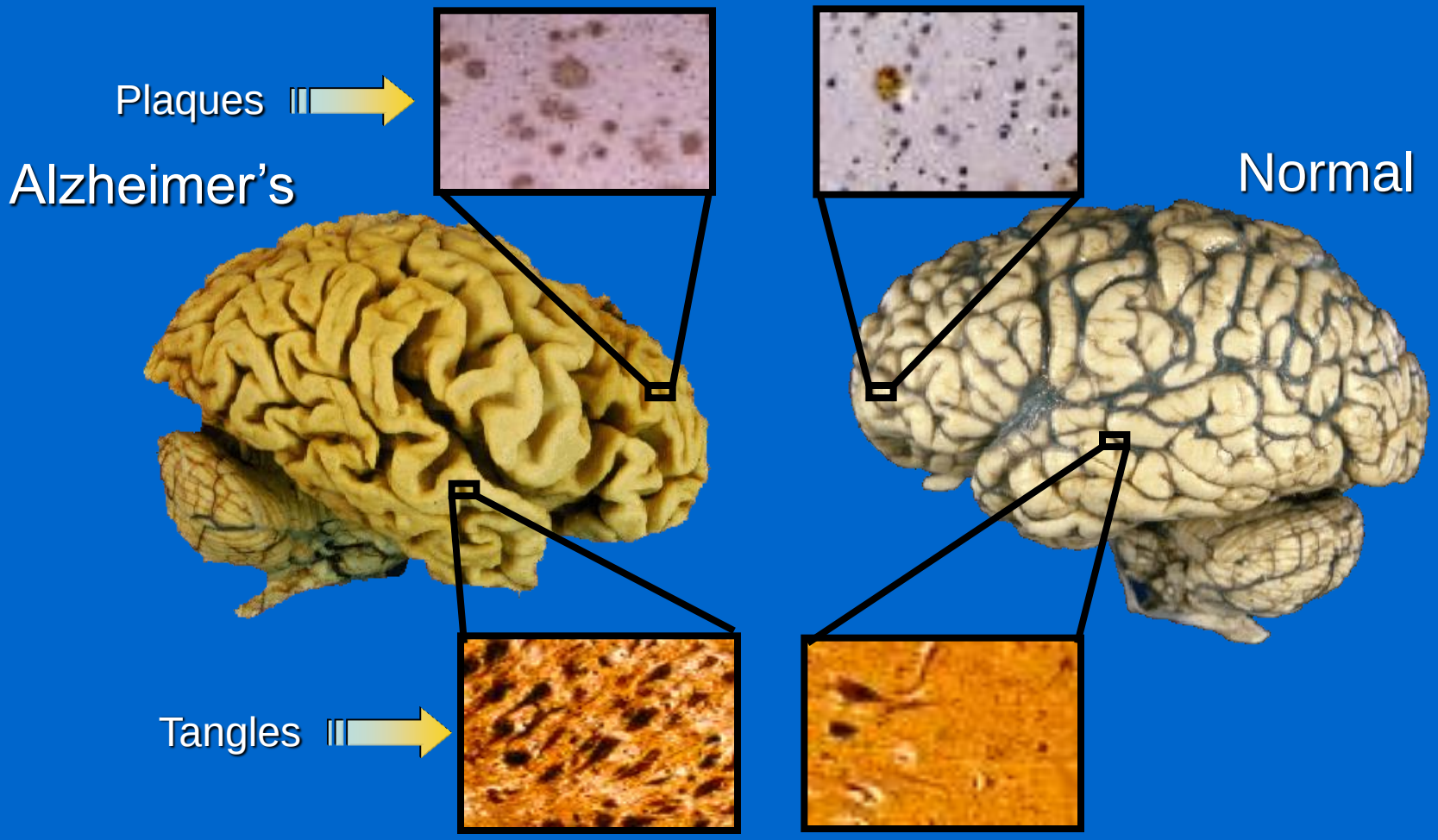
PET scans show much reduced glucose utilization in the AD brain compared to controls



Reason: Rampant cell death means less cells capable of metabolizing glucose

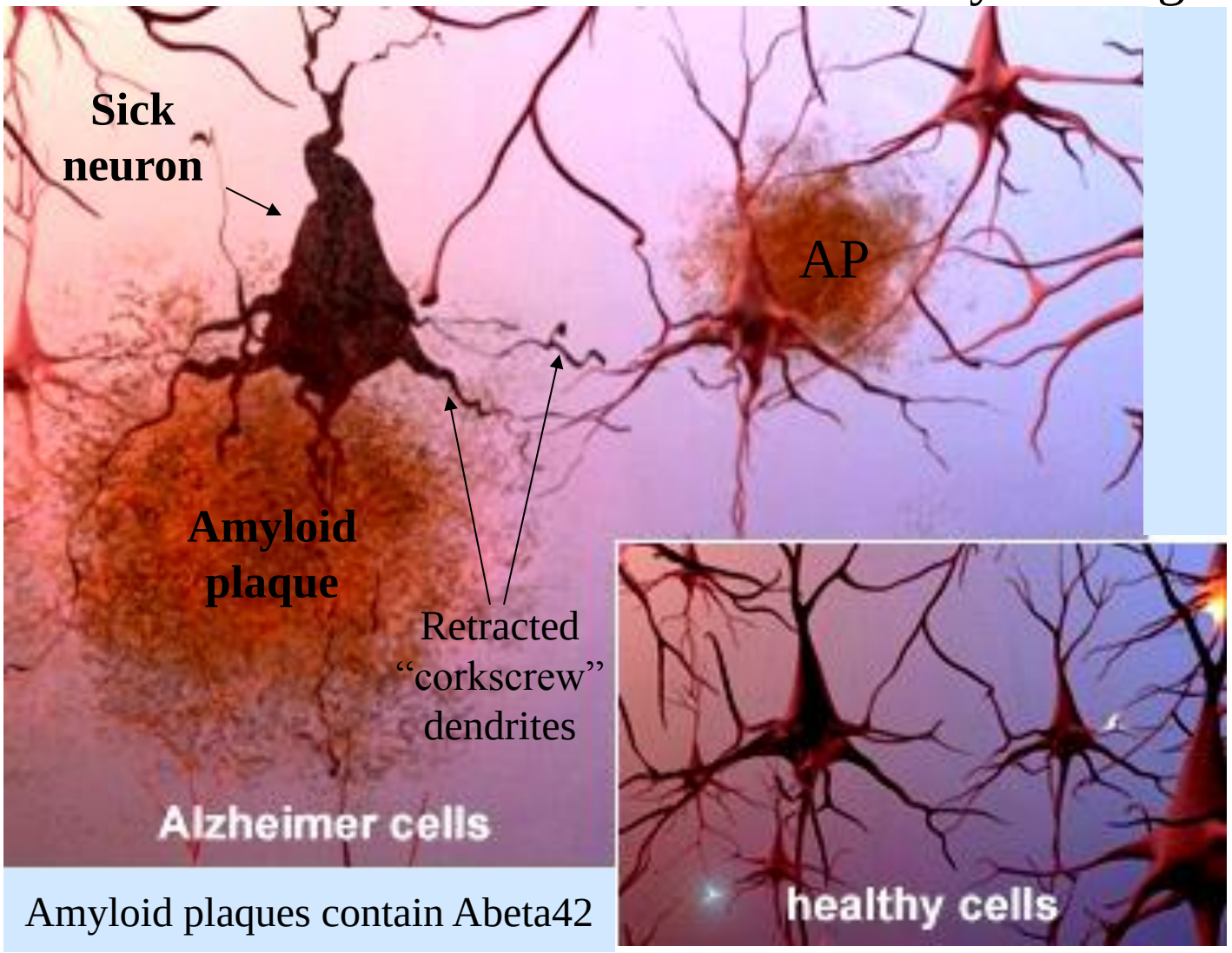
Amyloid Plaques and Neurofibrillary Tangles

Pathological Hallmarks of Alzheimer's Disease



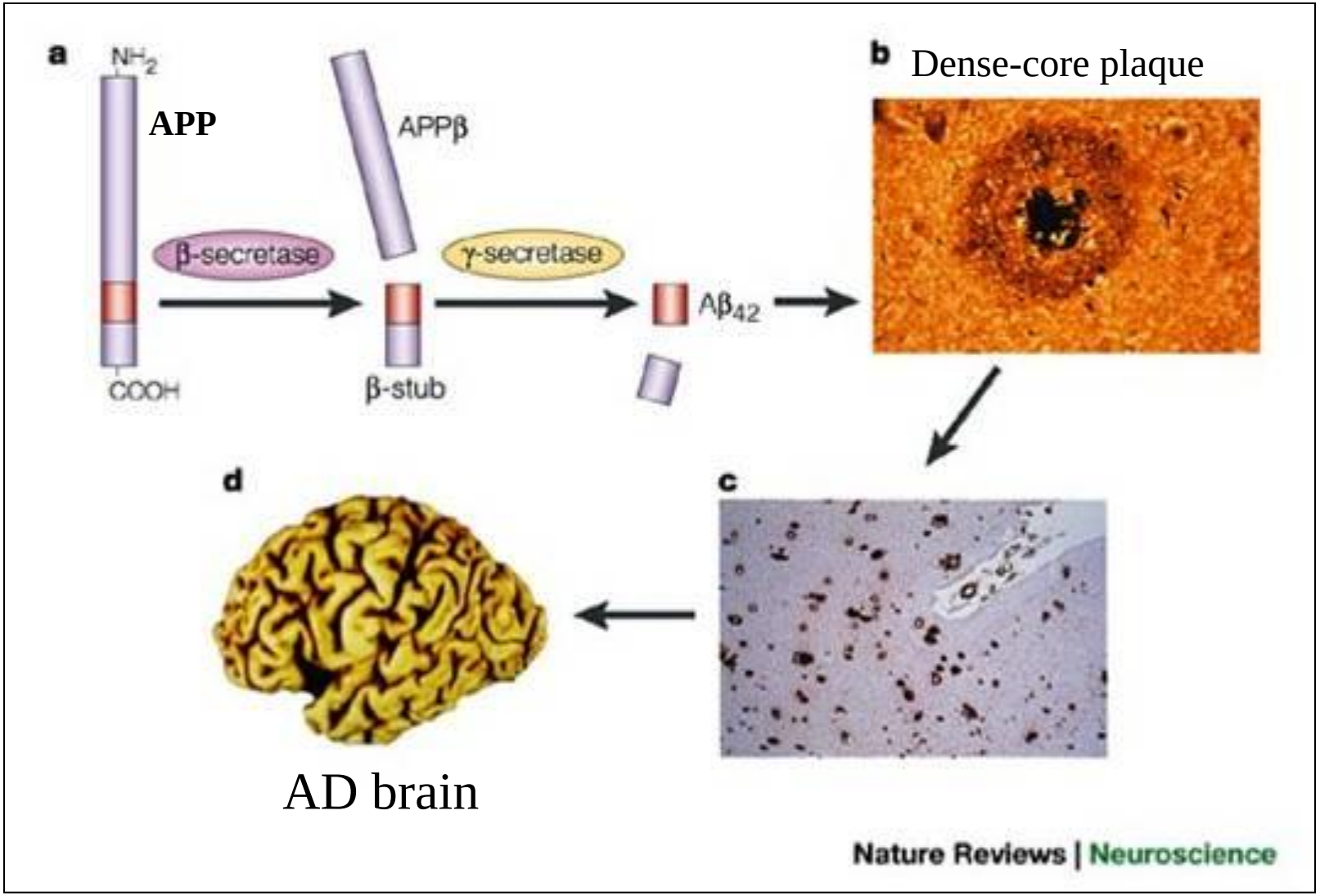
Courtesy of Harry Vinters, MD.

Amyloid (Abeta42) deposition makes neurons sick.
Sick neurons retract their axons and dendrites and lose synaptic connections with each other → Loss of memory and cognition



Amyloid plaques contain Abeta42

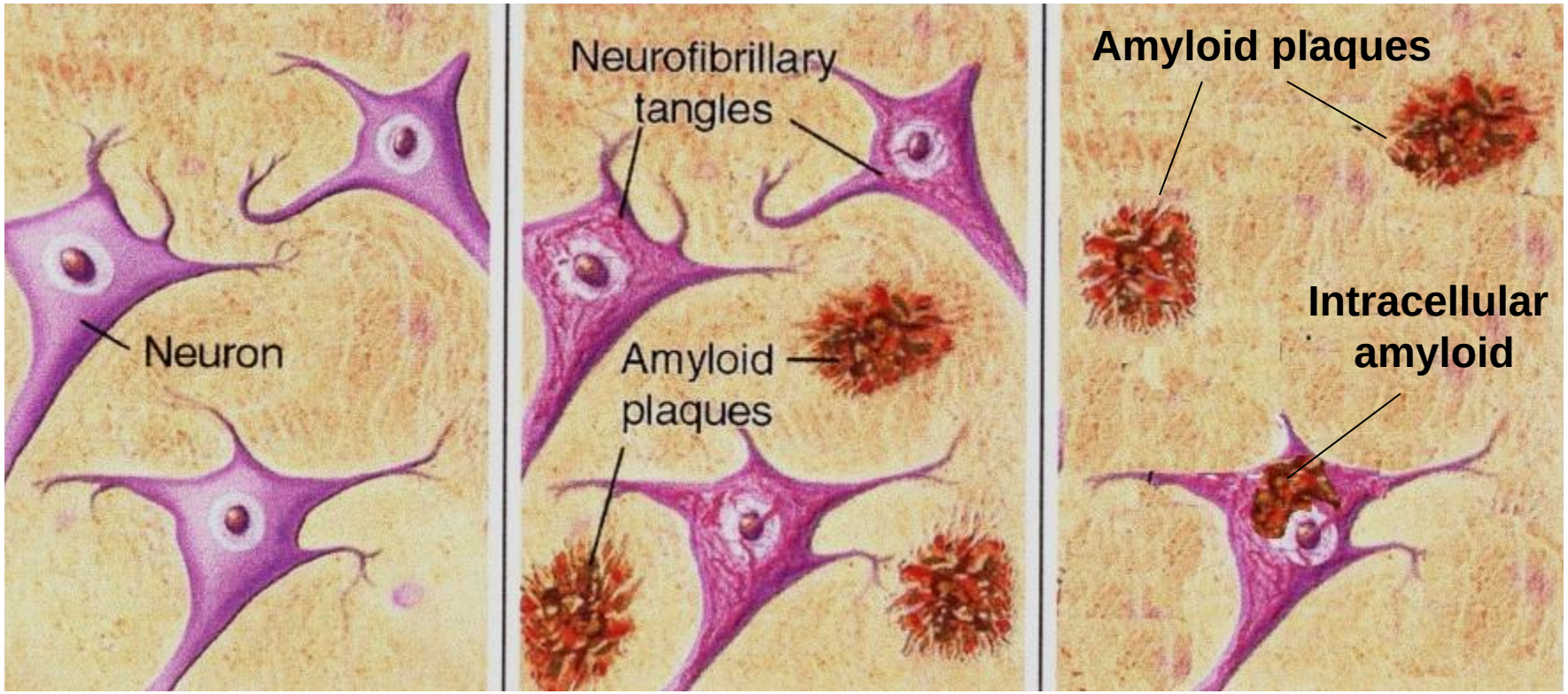
Amyloid beta (Abeta42) deposits in the brain and arises from sequential cleavage of the amyloid precursor protein



Alzheimer's Disease

How Amyloid (Abeta42) Deposits in the Brain

Old Model | **Our New Model**



Normal healthy brain

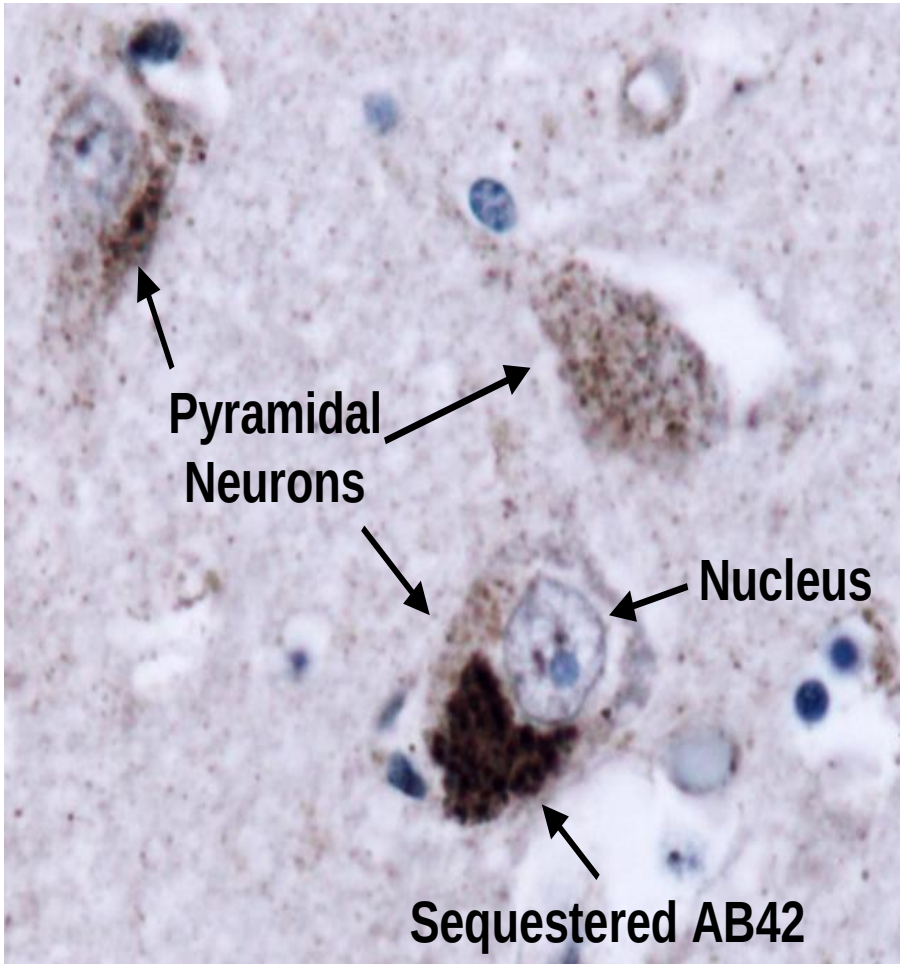
AD brain
Extracellular amyloid

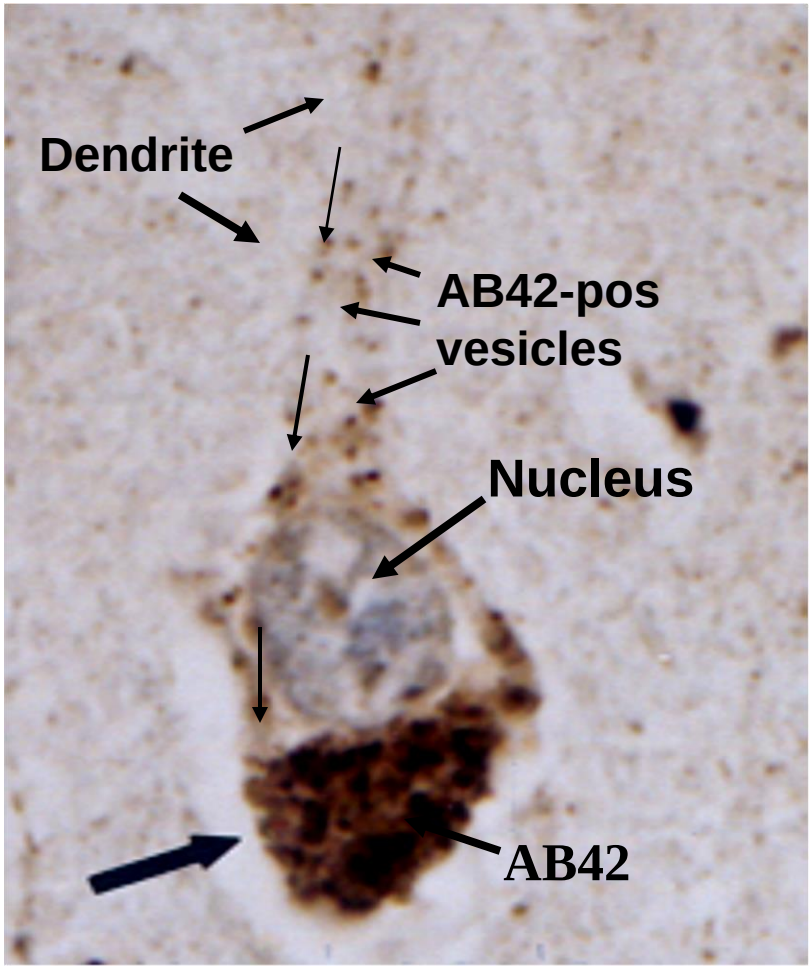
AD brain
Intracellular amyloid

New Model Means New Potential Drug Targets

In AD, neurons accumulate excessive Abeta42 (amyloid) prior to cell lysis and amyloid plaque formation

AD brain sections immunostained for Abeta42 (AB42)

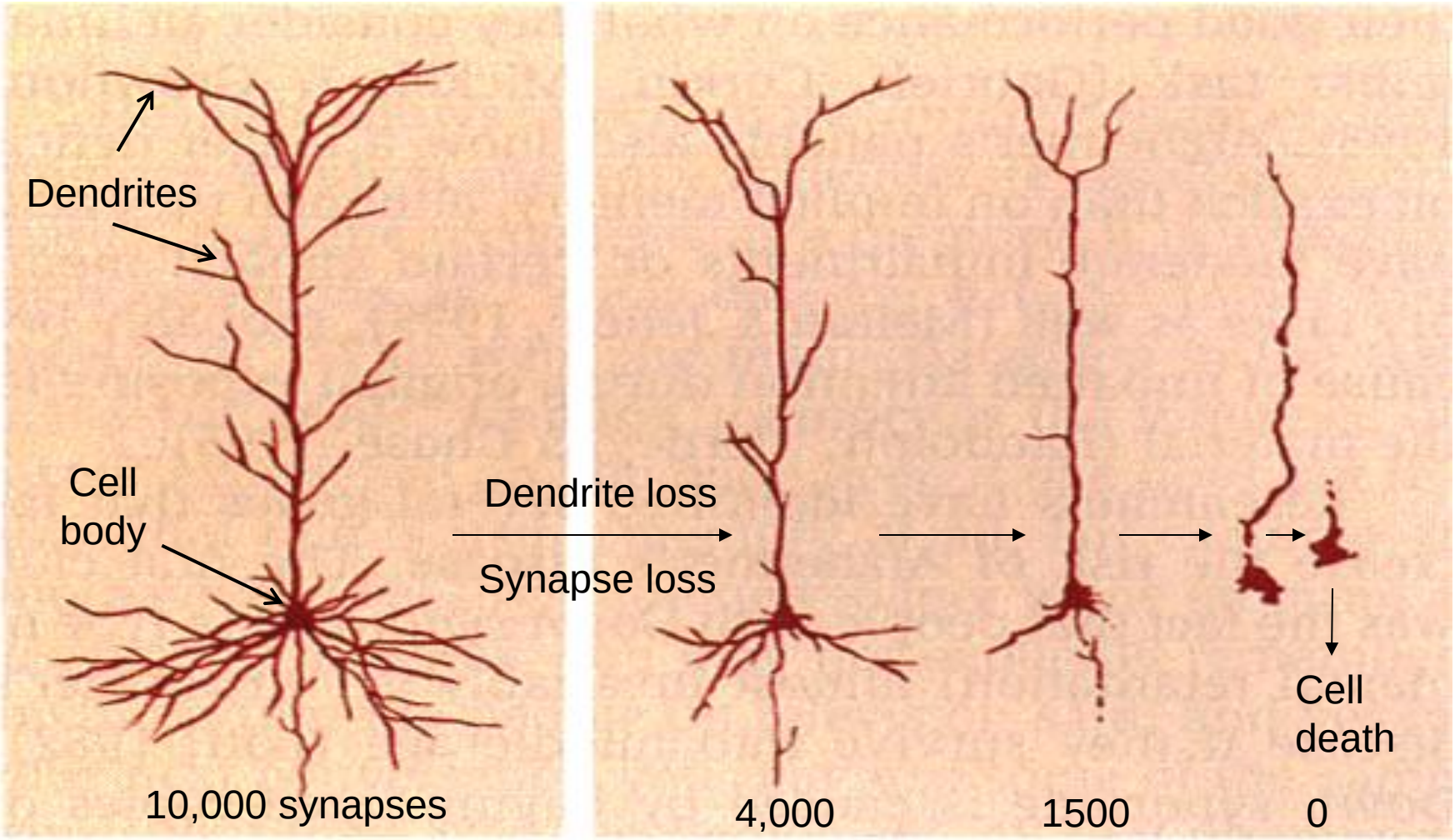




Note abundant Abeta42-positive (presumably) endocytic vesicles

Alzheimer's is a synaptic loss disease

Normal versus progressively degenerating pyramidal neuron



Months to years – Synaptic loss is tied to onset of symptoms

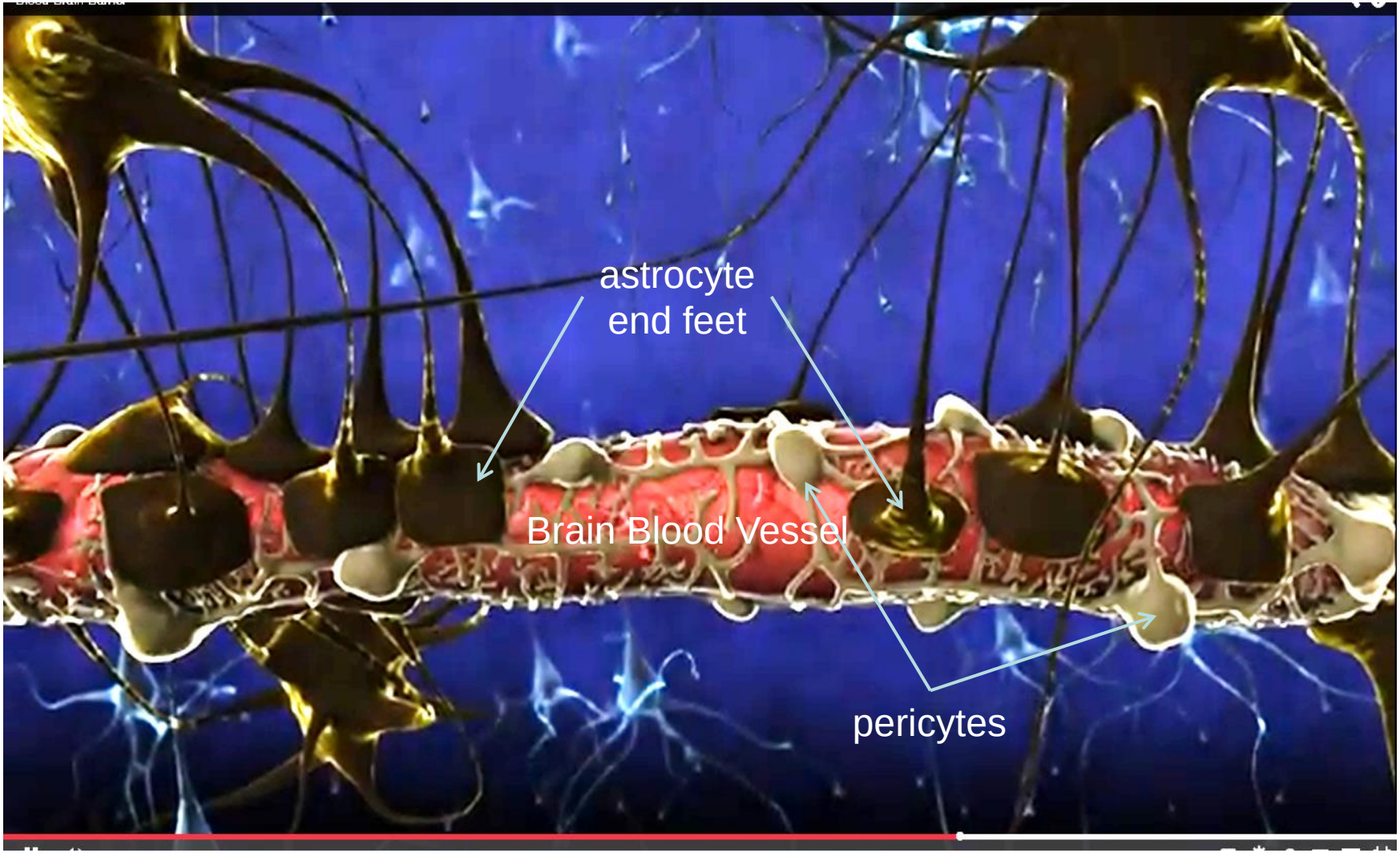
How can we stop amyloid deposition in the brain?

Answer: Find the source

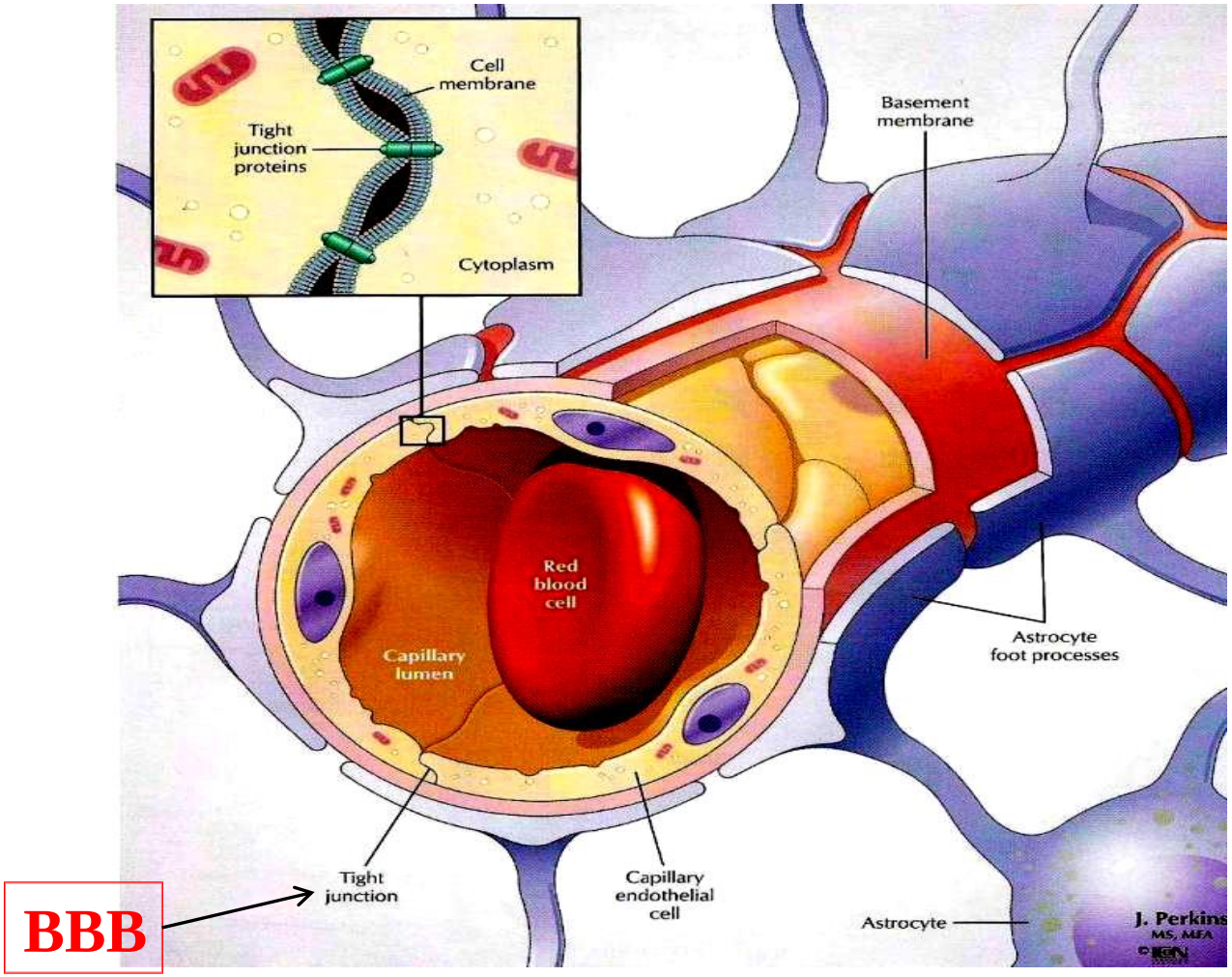
The blood is a major source.

In healthy brains, the blood-brain barrier (BBB) keeps the soluble amyloid in the vessel.

Blood-brain barrier



Tight junctions:
the primary structural correlate of the BBB



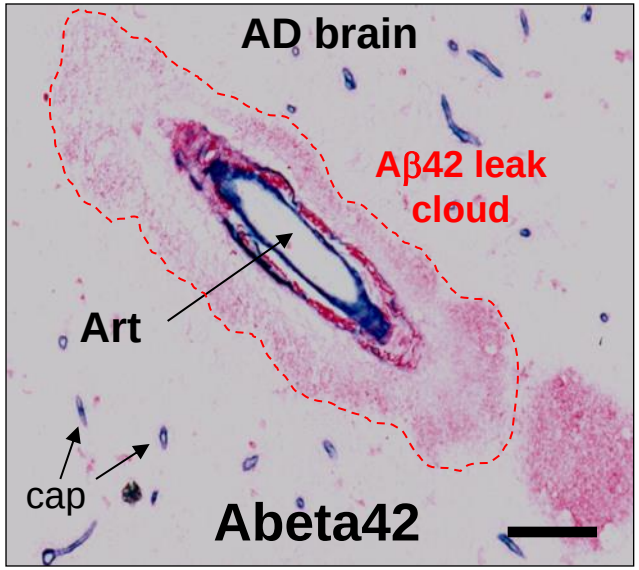
BBB

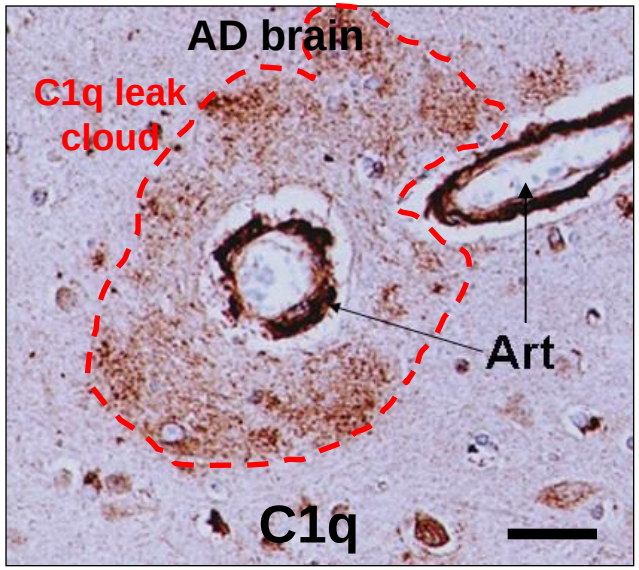
The BBB prevents the entry of most plasma components into the brain

In all AD brains, the BBB is defective

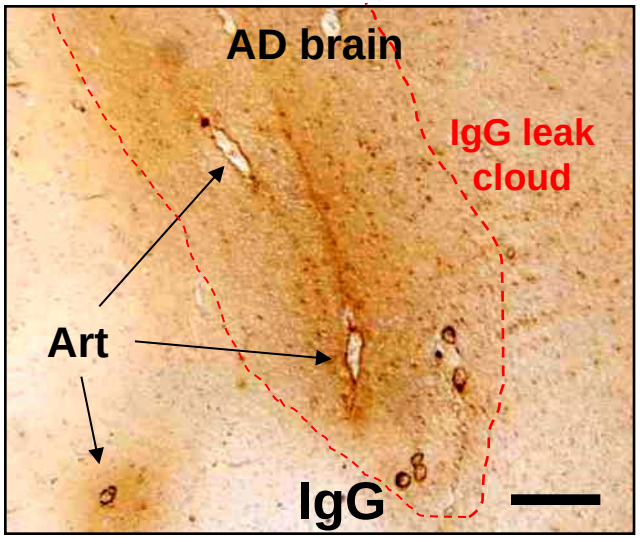
Plasma components (including Abeta42) can now leak into the brain and form vascular leak clouds

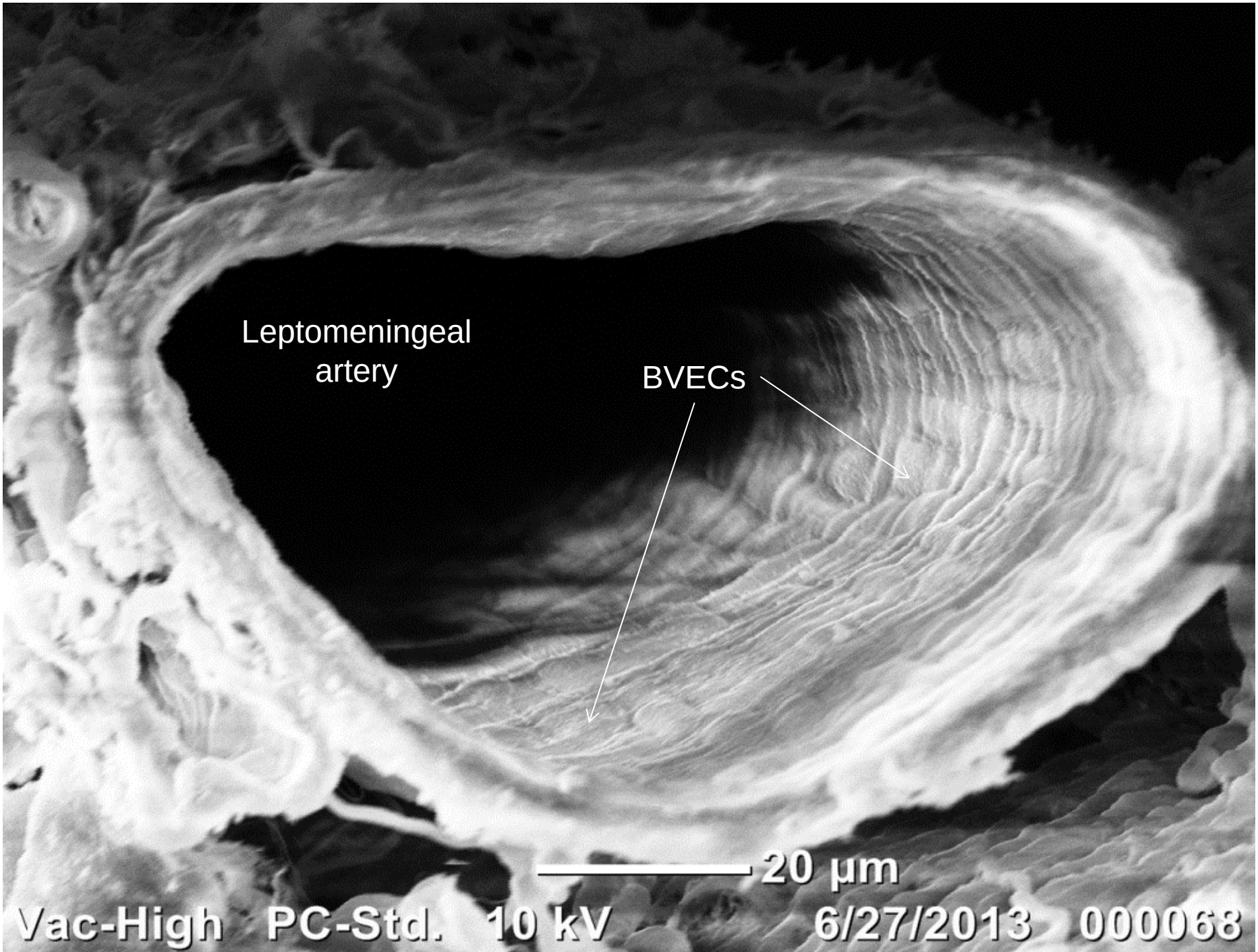
Abeta42



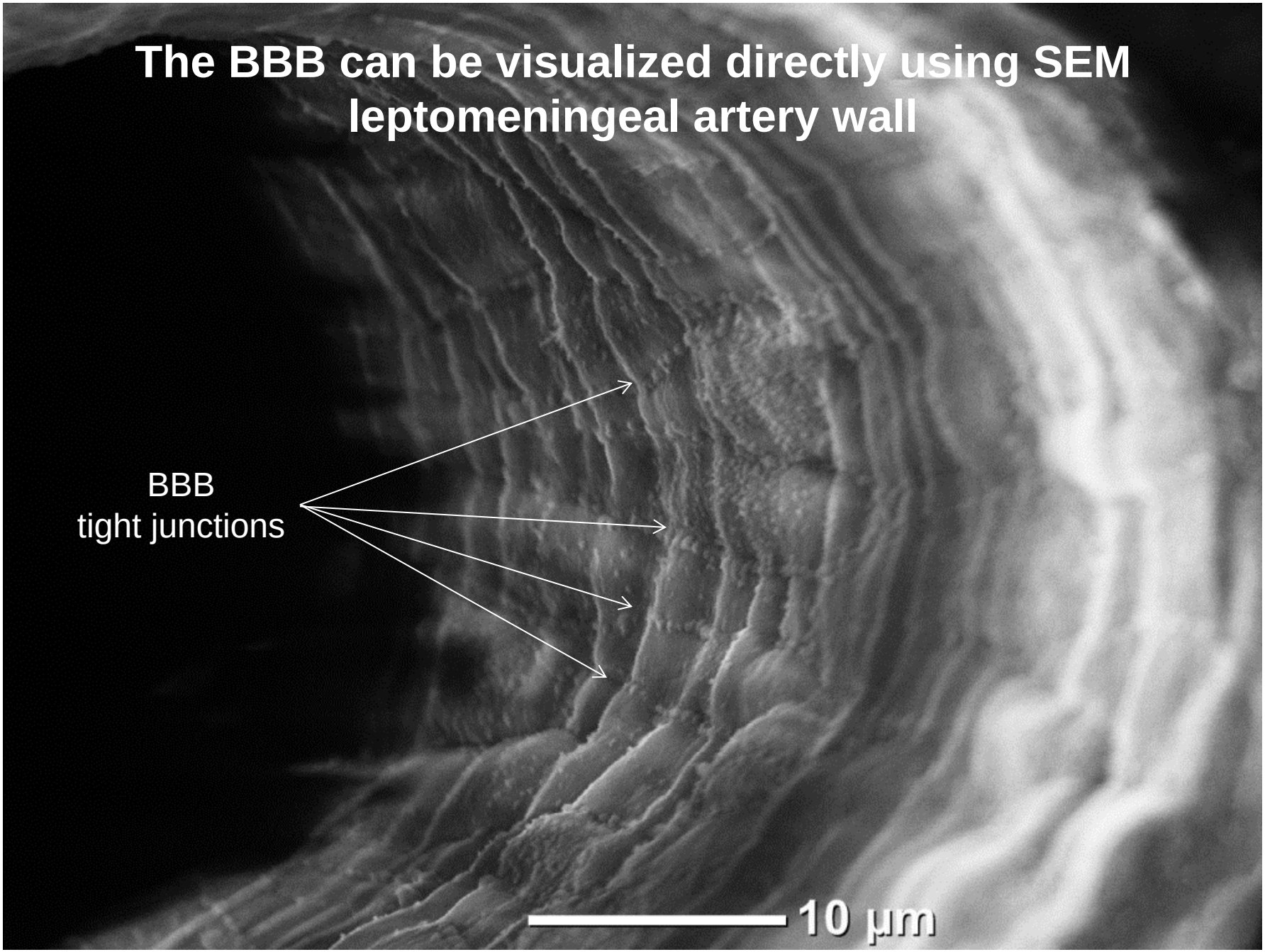


Abeta42 leak suggests that the main source of soluble amyloid beta (Abeta) in the brain is the blood

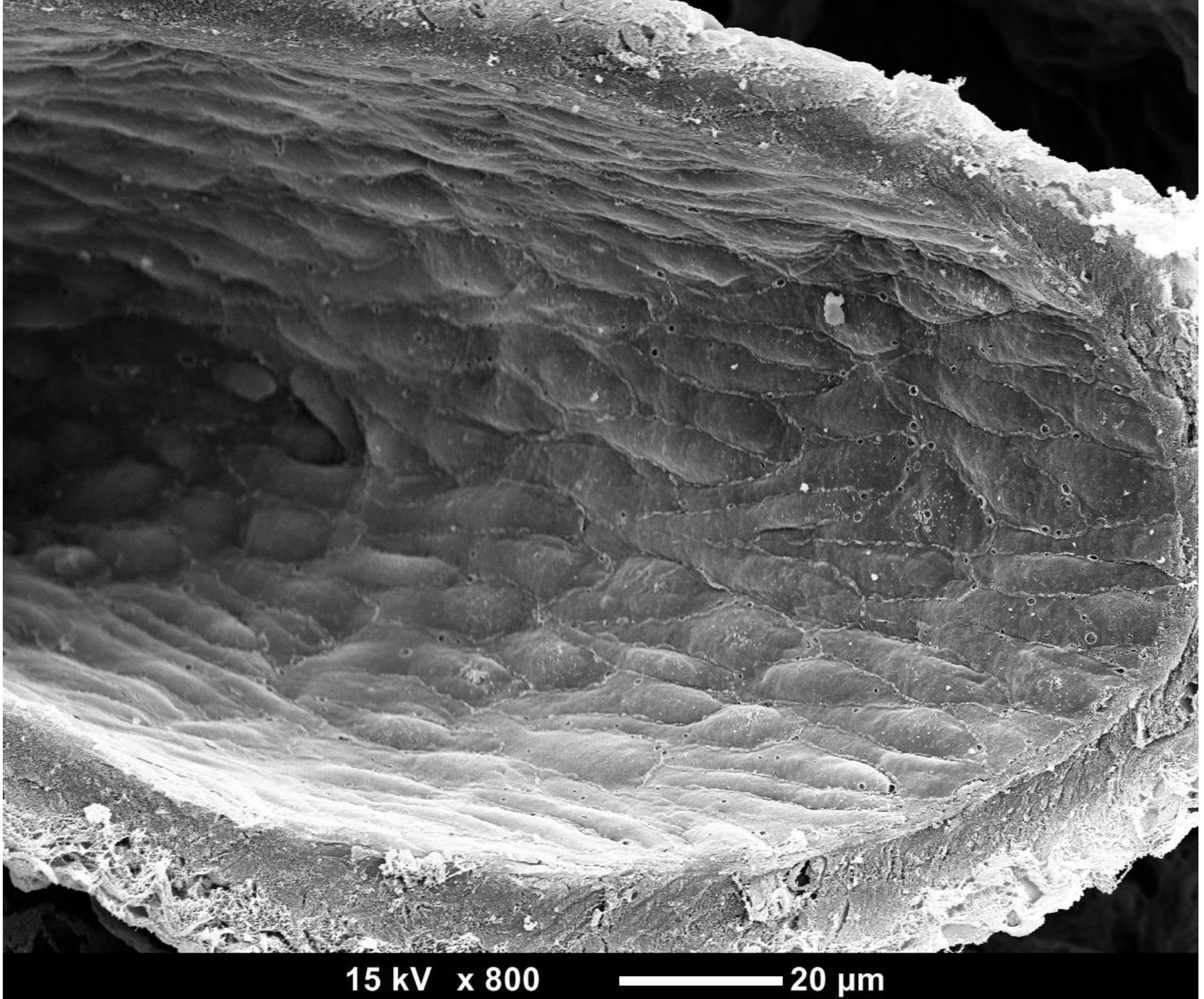



Leptomeningeal
artery
BVECs
20 µm
Vac-High PC-Std. 10 kV 6/27/2013 000068

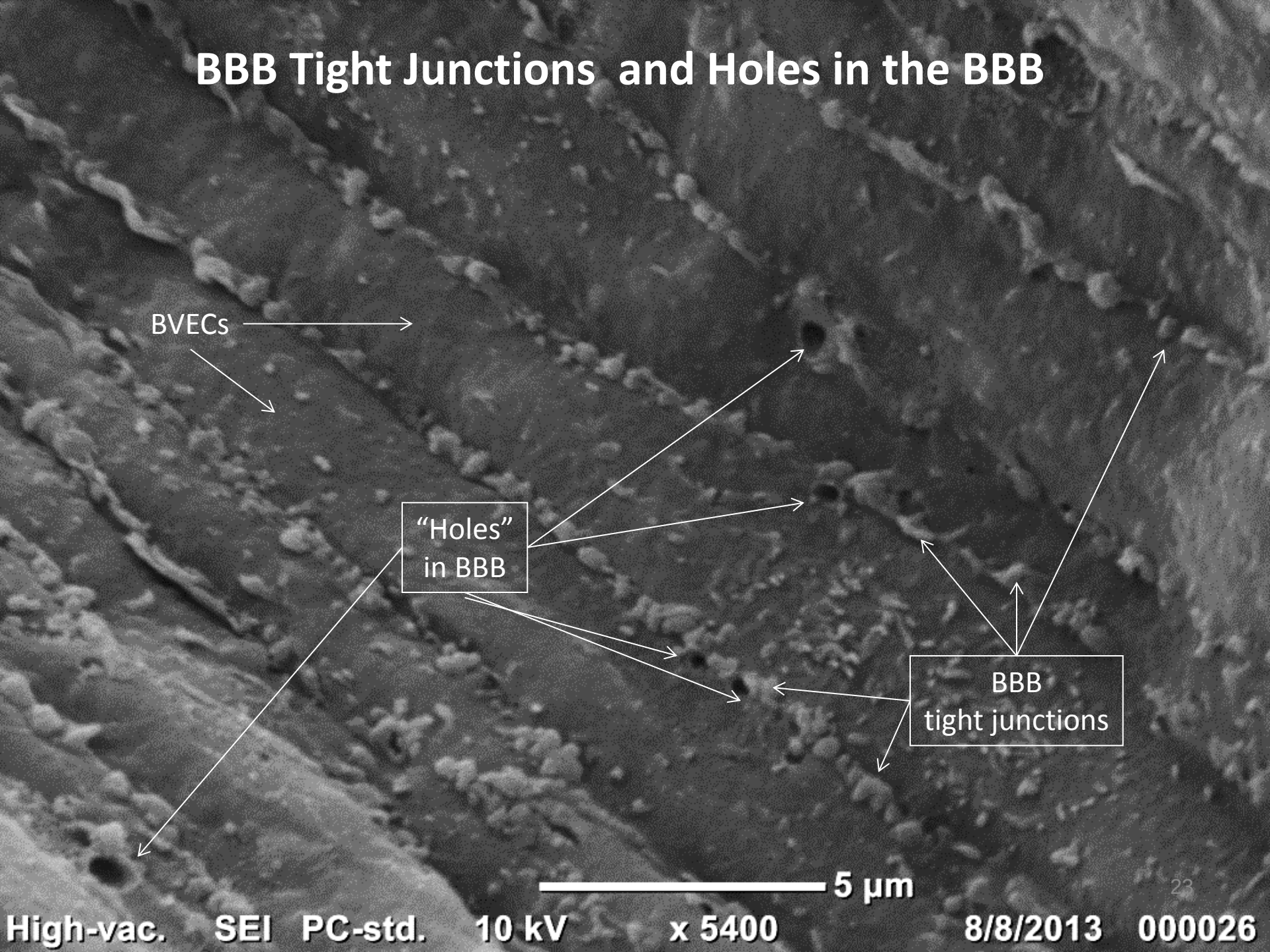
The BBB can be visualized directly using SEM
leptomeningeal artery wall



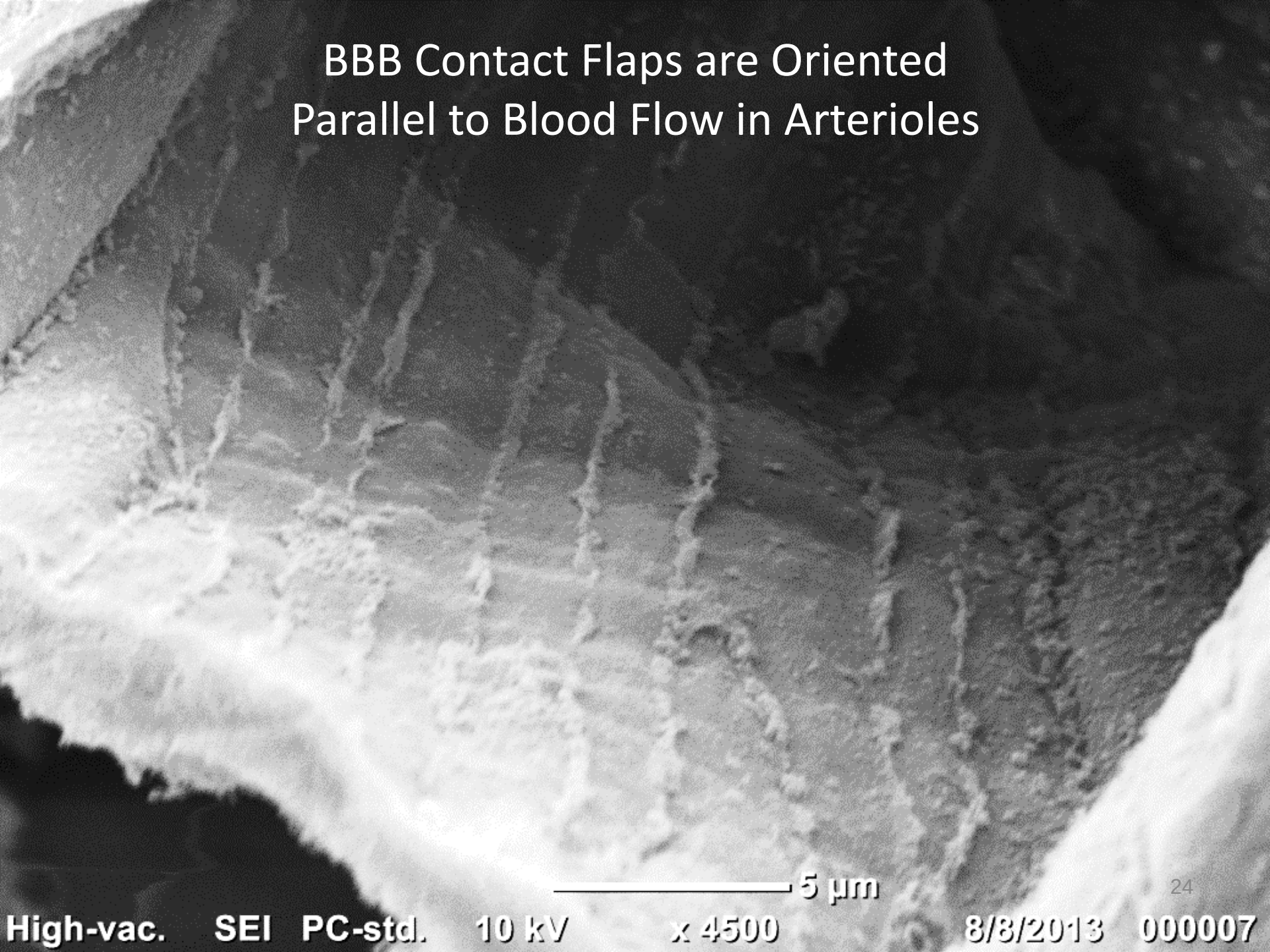
Arrows point to BBB – looks like rows of dots


15 kV x 800
20 µm

BBB Tight Junctions and Holes in the BBB

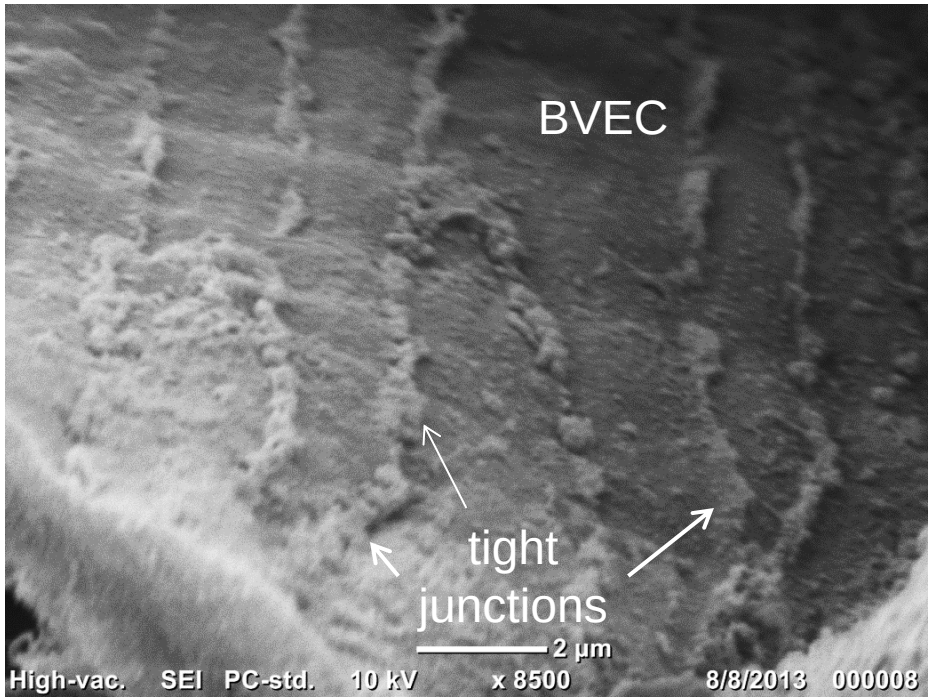


BBB Contact Flaps are Oriented Parallel to Blood Flow in Arterioles

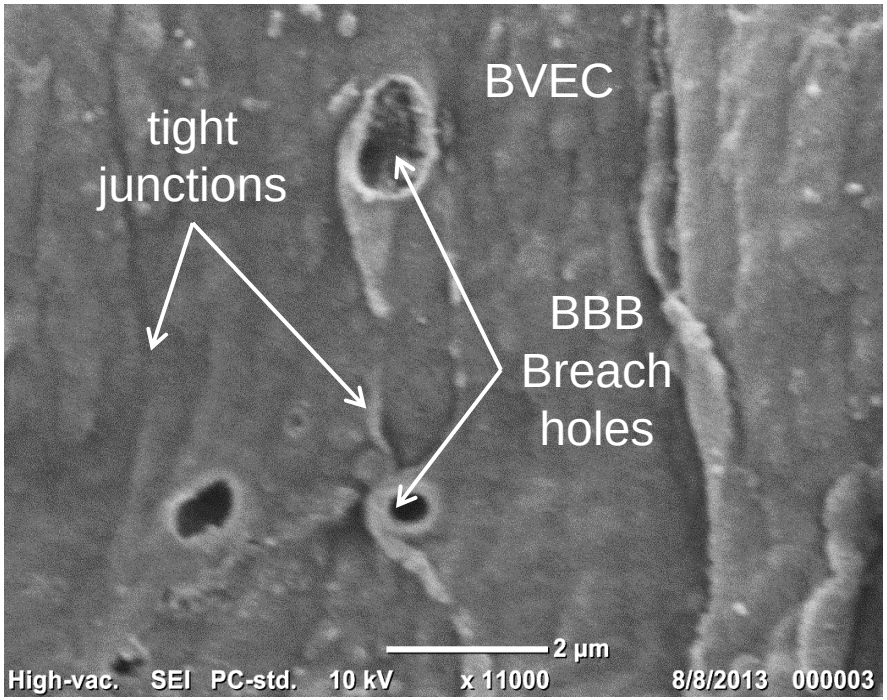


Anesthesia causes short-term BBB breakdown

- Probable mechanism of post-surgical delirium and trigger of dementia-



Control



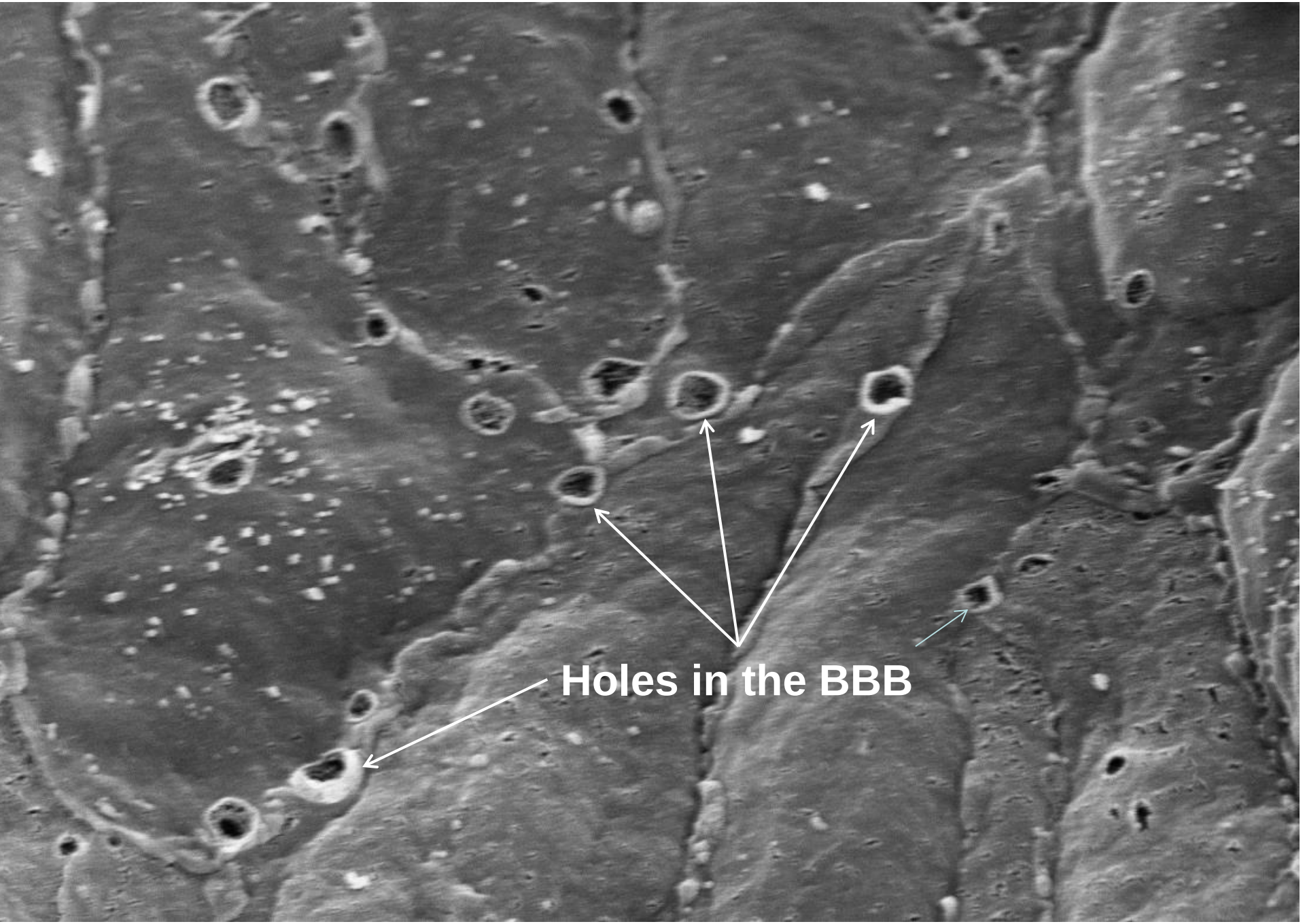
3 hr surgical plane anesthesia
sevoflurane

Results

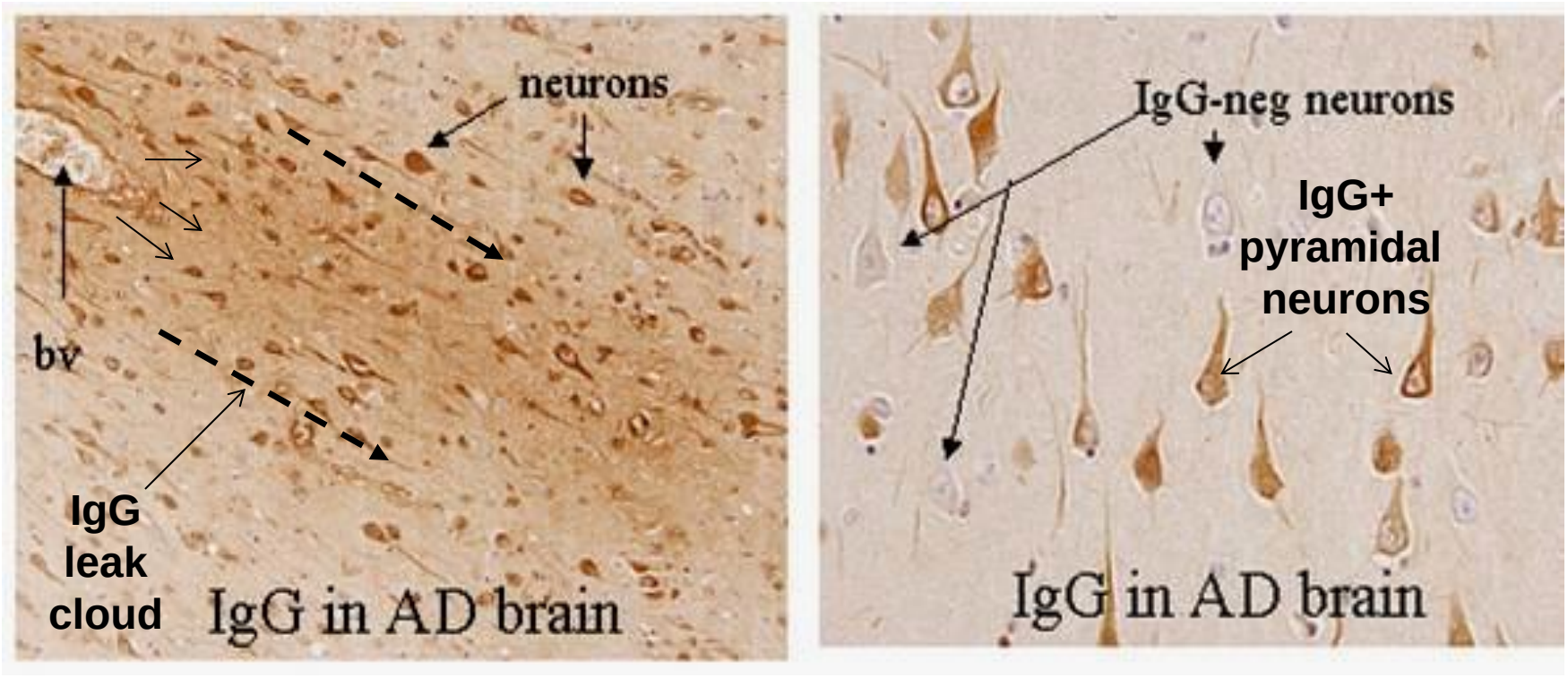
1. Anesthesia (**sevoflurane** and **isoflurane**) induces immediate changes in the surfaces of brain vascular endothelial cells (BVECs), including a profound **smoothing of surface membranes** and visible **holes in the BBB.**

2. **Old rats showed much more** anesthetic-induced BBB breakdown

*Collaboration with Dept. of Anesthesiology at Johns Hopkins via **Eli Levin DO-PhD***
Manuscript in preparation


Holes in the BBB

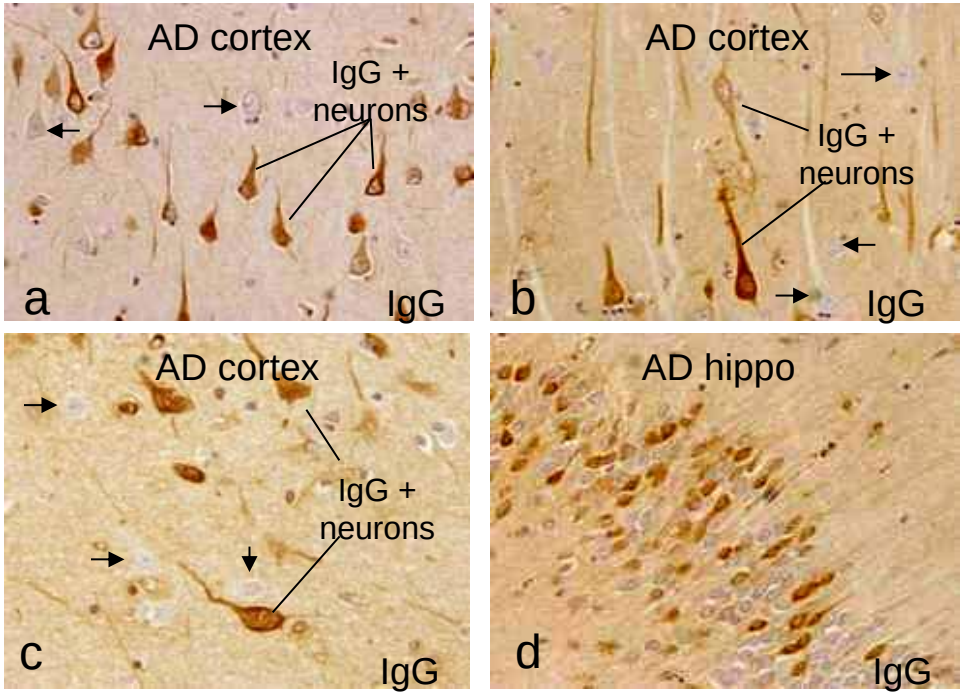
Brain-reactive antibodies leak from blood vessels and bind to pyramidal neurons in AD brains



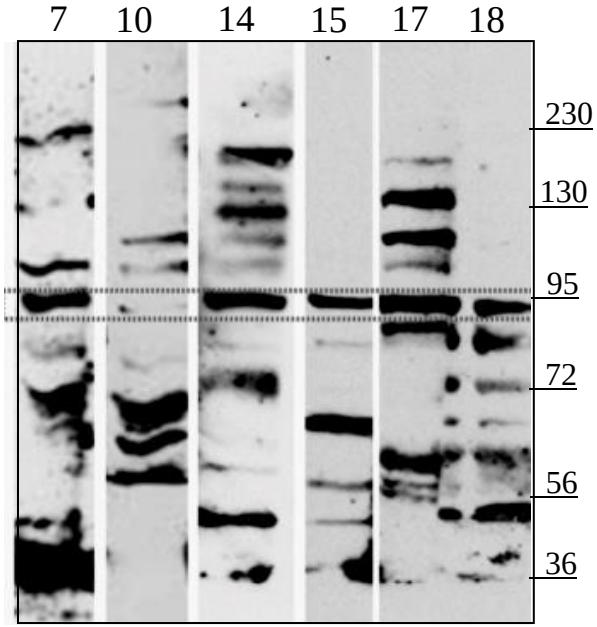
AD brain cerebral cortex

BBB breakdown, autoantibody influx and Alzheimer's disease

Neurons with antibodies (brown color) bound to their surfaces are abundant in all AD brains



Western blot analysis reveals numerous brain-reactive autoantibodies in the blood



Human brain protein probed with human sera

Brain-reactive autoantibodies are nearly ubiquitous in human sera and may be linked to pathology in the context of blood–brain barrier breakdown

Eli C. Levin[a,b], Nimish K. Acharya[b], Min Han[b], Semah B. Zavareh[b], Jonathan C. Sedeyn[b], Venkateswar Venkataraman[c], Robert G. Nagele[a,]*

[a]New Jersey Institute for Successful Aging, University of Medicine and Dentistry of New Jersey, 2 Medical Center Drive, Stratford, New Jersey 08084, USA
[b]Graduate School of Biomedical Sciences, University of Medicine and Dentistry of New Jersey, 2 Medical Center Drive, Stratford, New Jersey 08084, USA
[c]Department of Cell Biology, University of Medicine and Dentistry of New Jersey, 2 Medical Center Drive, Stratford, New Jersey 08084, USA

Levin et al., 2010 Brain Research, 1345(23):221-232.

How do neurons respond to autoantibody binding?

Answer

They clean their surfaces by internalizing surface-bound autoantibodies via endocytosis and degrade them in lysosomes

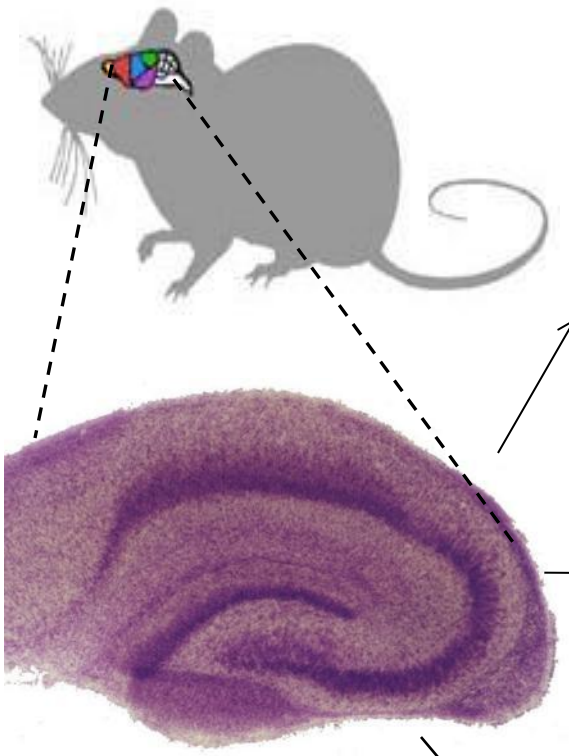
The pathological significance

Abeta42 (amyloid) bound to neuronal cell surfaces is also internalized. Within the lysosomal compartment, Abeta42 self-assembles into fibrils that cannot be degraded.

↓

This drives chronic amyloid accumulation within neurons.

Brain-reactive autoautoantibodies in human serum can drive amyloid deposition in mouse neurons *in vitro*



Mouse Brain Slice Cultures

No Treatment – 24 h

a IHC – human IgG

HS1 only – 24 h

ML

PCL

b IHC - human IgG

HS1 only – 24 h

IgG+ neurons

c IHC - human IgG

AB42 only - 24 h

d IHC – human IgG

AB42 only - 24 h

AB42+ neurons

e IHC – AB42

HS1 + AB42 - 24 h

AB42+ neurons

f IHC – AB42

HS1 + AB42 – 24 h

IgG+ neurons

g IHC – human IgG

HS1 + AB42 – 24 h

AB42+ neurons

h IHC – AB42

HS8 + AB42 – 24 h

AB42+ neurons

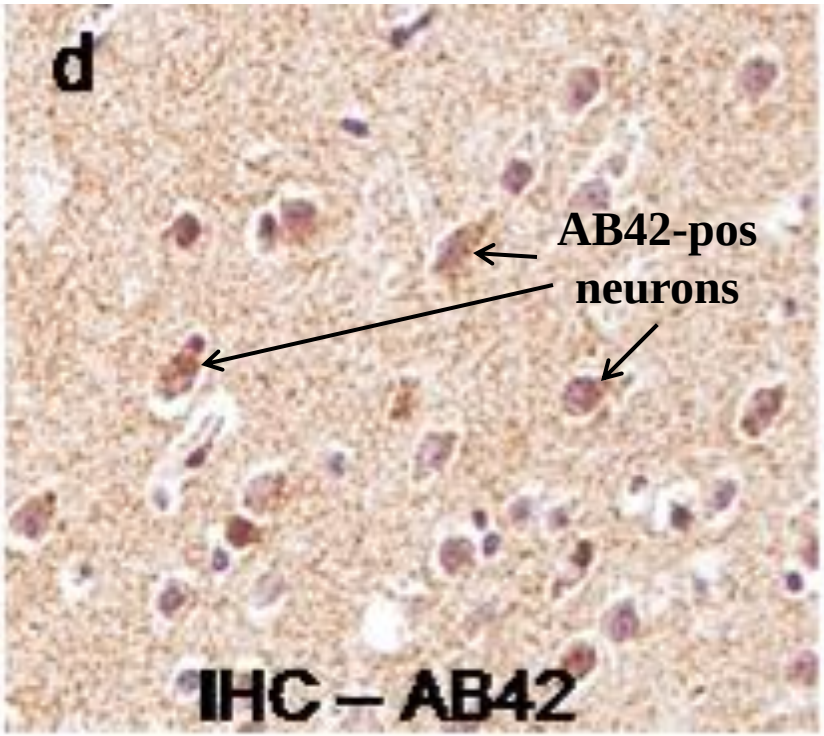
i IHC – AB42

Nagele et al. 2011
J. Alzheimer's Disease

Result: Human autoantibodies dramatically accelerate amyloid deposition in pyramidal neurons in mouse brain

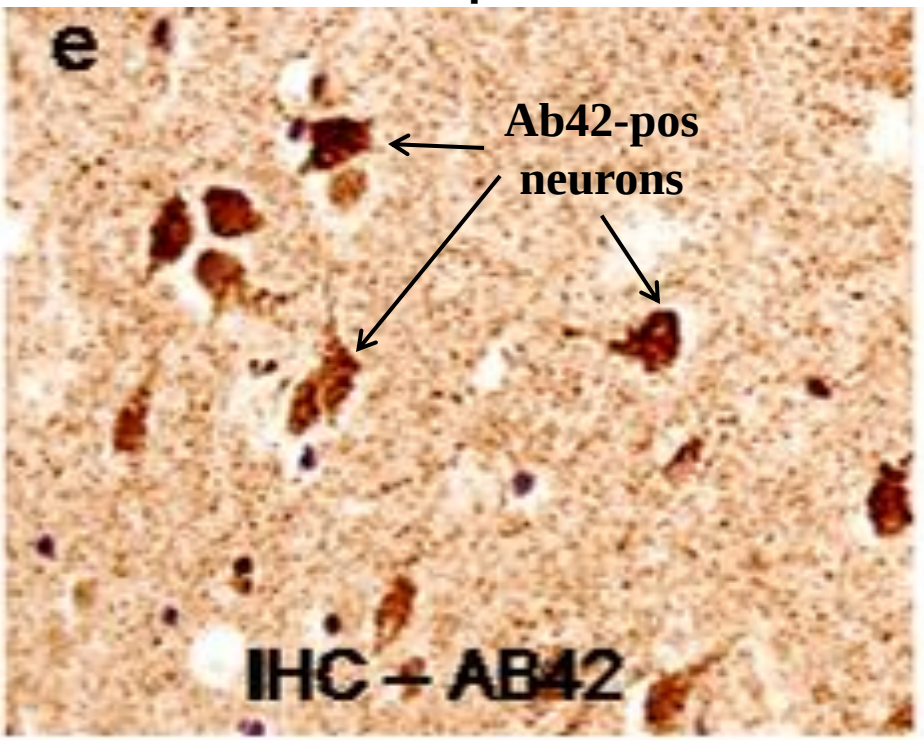
Adult mouse brain slice cultures treated with human serum Ig and Abeta42

Abeta42 alone



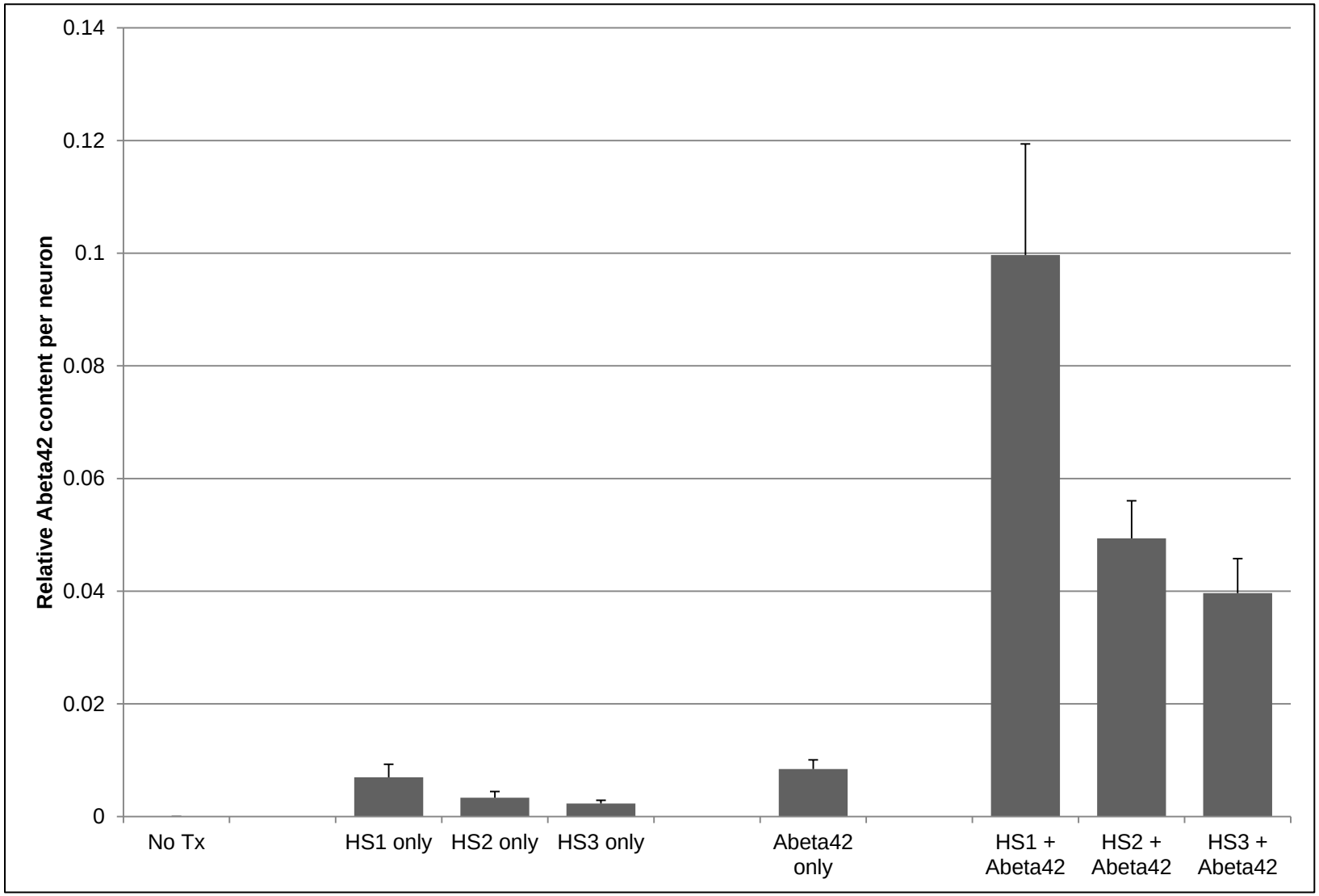
Very little AB42 internalization

Human serum plus Abeta42



Heavy AB42 internalization

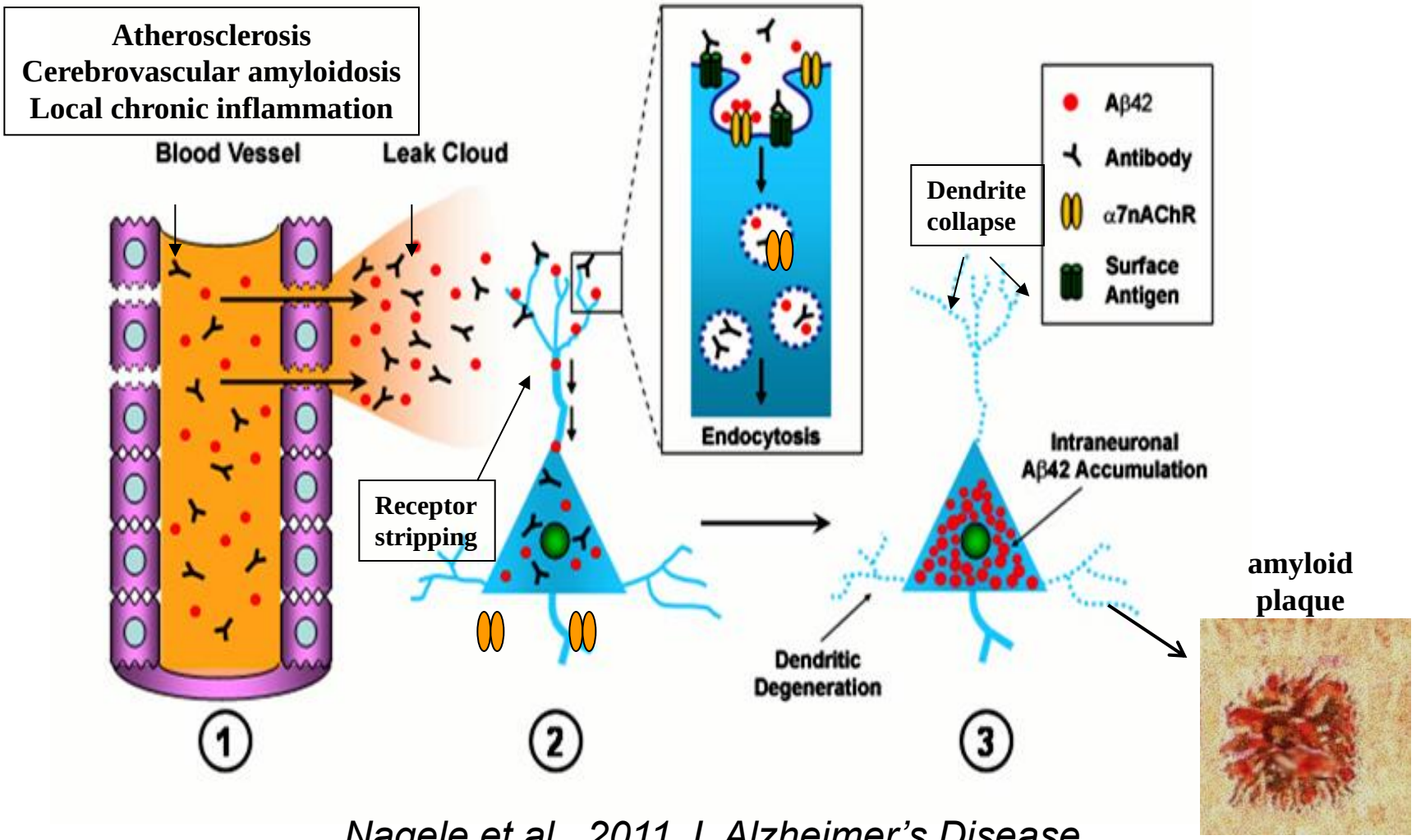
Human autoantibodies enhance intraneuronal Aβ42 deposition in mouse brain slice cultures with different potencies



BBB breakdown triggers Alzheimer's disease

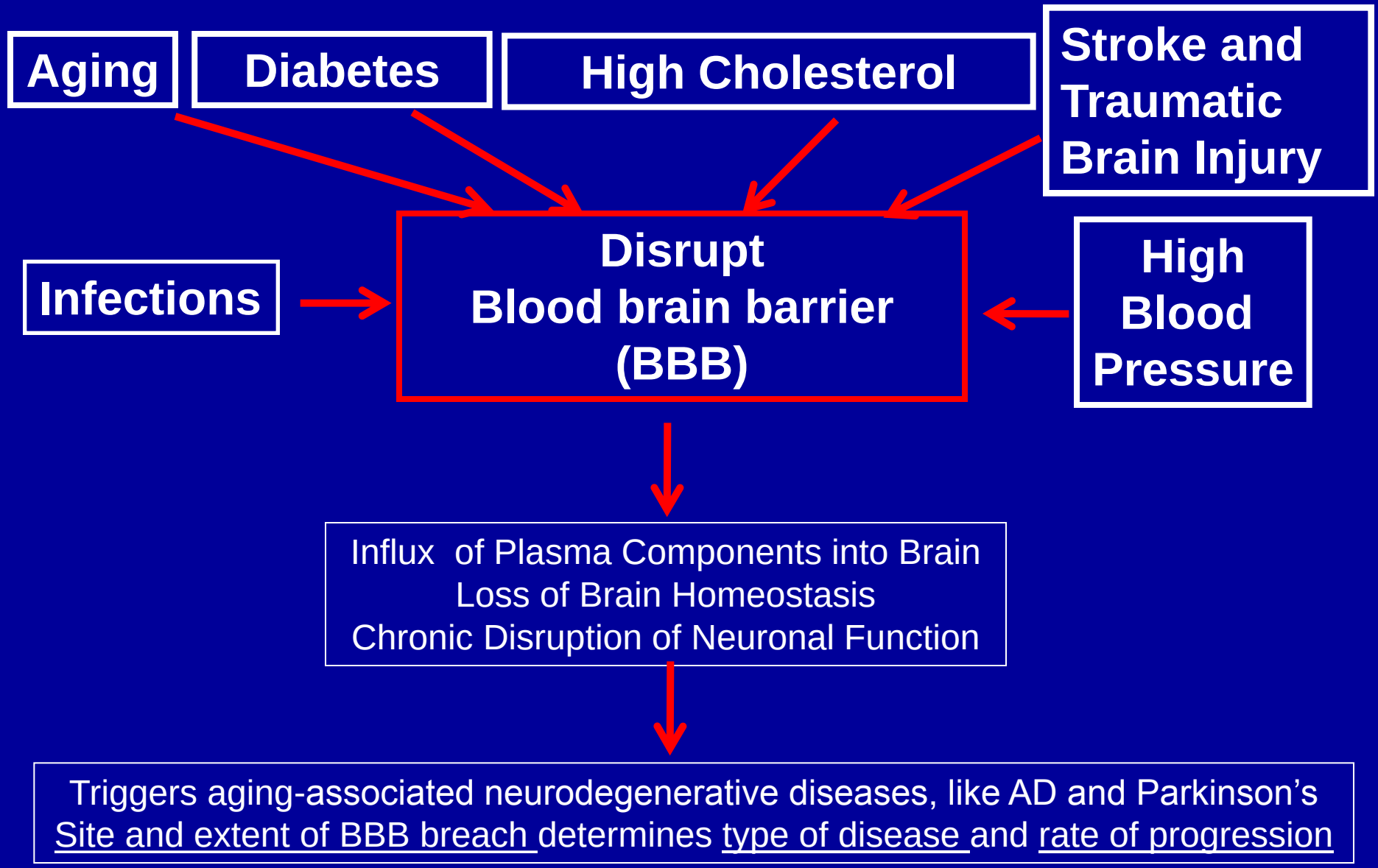
Causes intraneuronal amyloid (Abeta) deposition

Binding of autoantibodies to targets on neuronal surfaces induces endocytosis
Chronic endocytosis drives surface-bound Abeta42 into neurons



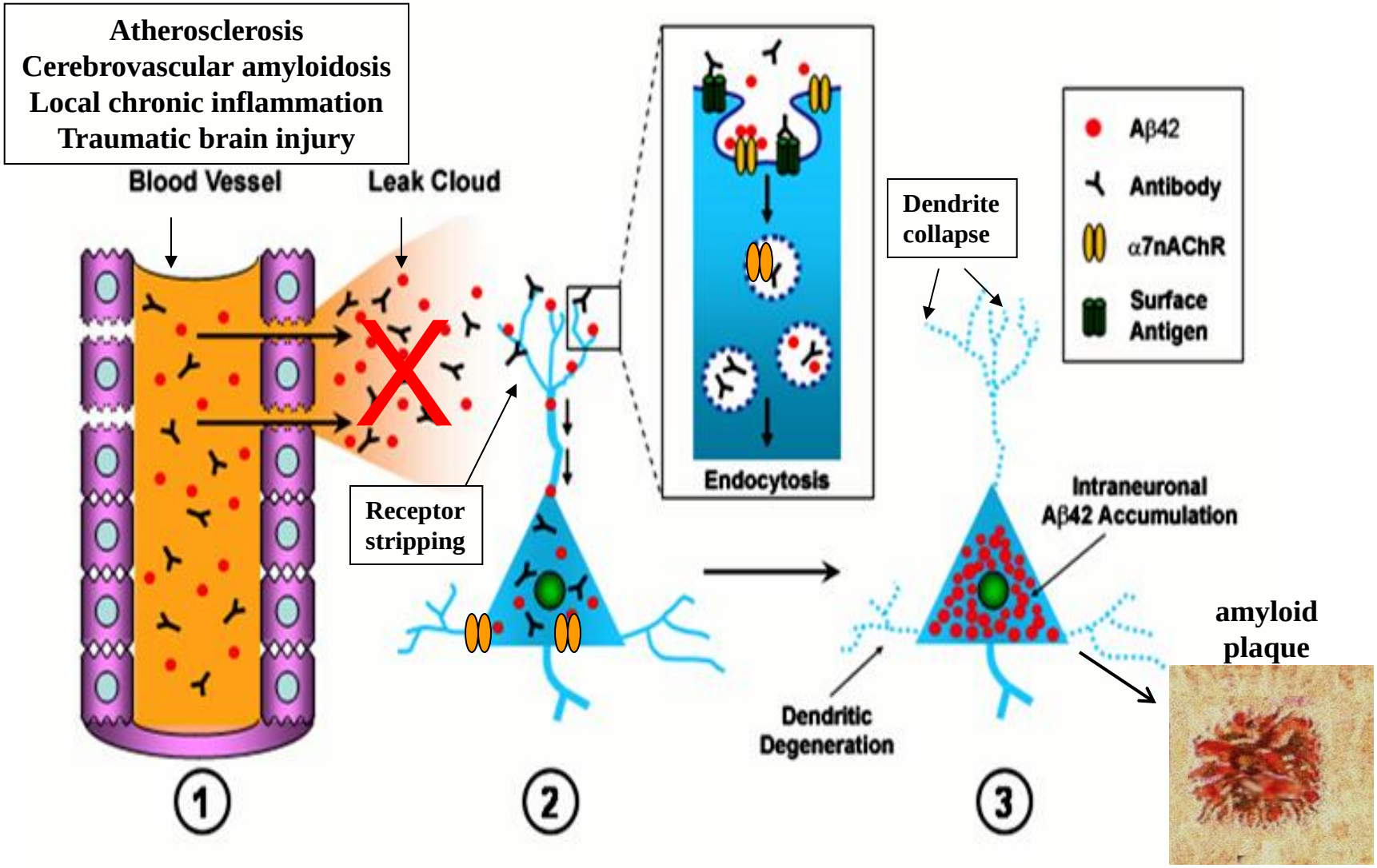
Nagele et al., 2011 J. Alzheimer's Disease

Hypothesis – BBB breakdown can trigger neurodegenerative diseases



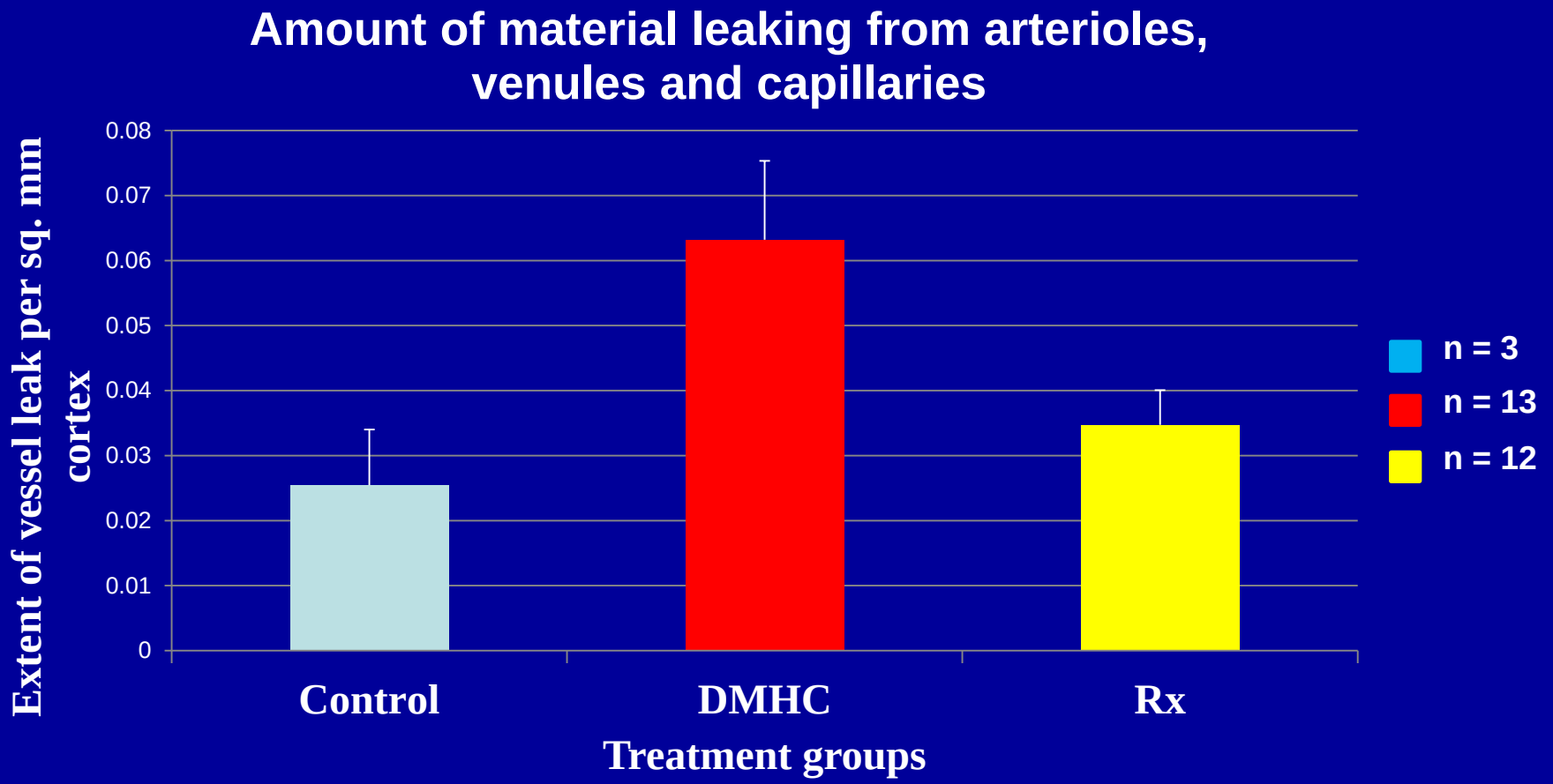
Develop drugs/therapies that maintains/repairs BBB integrity

(e.g., Darapladib blocks BBB breakdown in diabetic/hypercholesterolemic (DMHC) pigs



Acharya et al., 2013 J. Alzheimer's Disease

Diabetic/hypercholesterolemic (DMHC) pigs showed the greatest extent of BBB leak and Darapladib reduces vascular leak to control levels



Treatment groups	P-value
DMHC/C	0.033088
DMHC/Rx	0.097645
Rx/C	0.298917

Darapladib Blocks Blood-Brain Barrier Breakdown
A Global Treatment for All Neurodegenerative Diseases?

Journal of Alzheimer's Disease 35 (2013) 179–198
DOI 10.3233/JAD-122254
IOS Press

Diabetes and Hypercholesterolemia Increase Blood-Brain Barrier Permeability and Brain Amyloid Deposition: Beneficial Effects of the LpPLA2 Inhibitor Darapladib

Nimish K. Acharya[a,e], Eli C. Levin[a,e], Peter M. Clifford[a,e], Min Han[a,e], Ryan Tourtellotte[f], Dean Chamberlain[f], Michael Pollaro[f], Nicholas J. Coretti[a,e], Mary C. Kosciuk[a], Eric P. Nagele[a], Cassandra DeMarshall[a], Theresa Freeman[b], Yi Shi[b], Chenbing Guan[c], Colin H. Macphee[d], Robert L. Wilensky[g] and Robert G. Nagele[a,*]

[a]*New Jersey Institute for Successful Aging at University of Medicine and Dentistry of New Jersey (UMDNJ) - School of Osteopathic Medicine, Stratford, NJ, USA*
[b]*Thomas Jefferson University, Philadelphia, PA, USA*
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[e]*Graduate School of Biomedical Sciences, University of Medicine and Dentistry of New Jersey, Stratford, NJ, USA*
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[g]*Hospital of the University of Pennsylvania, Philadelphia, PA, USA*

Handling Associate Editor: Thomas Shea

Funded by GlaxoSmithKline

I think we all agree

Early treatment of Alzheimer's disease (in fact any disease),
has the potential benefit of slowing or stopping disease progression
before too much brain devastation and loss of function has occurred.

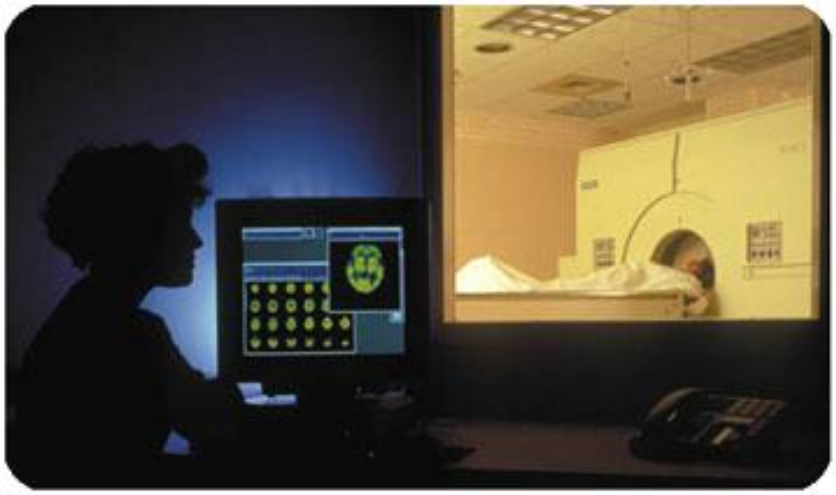
But

Early treatment requires early diagnosis

Current AD Diagnostic Methods

Tools used to diagnose AD:

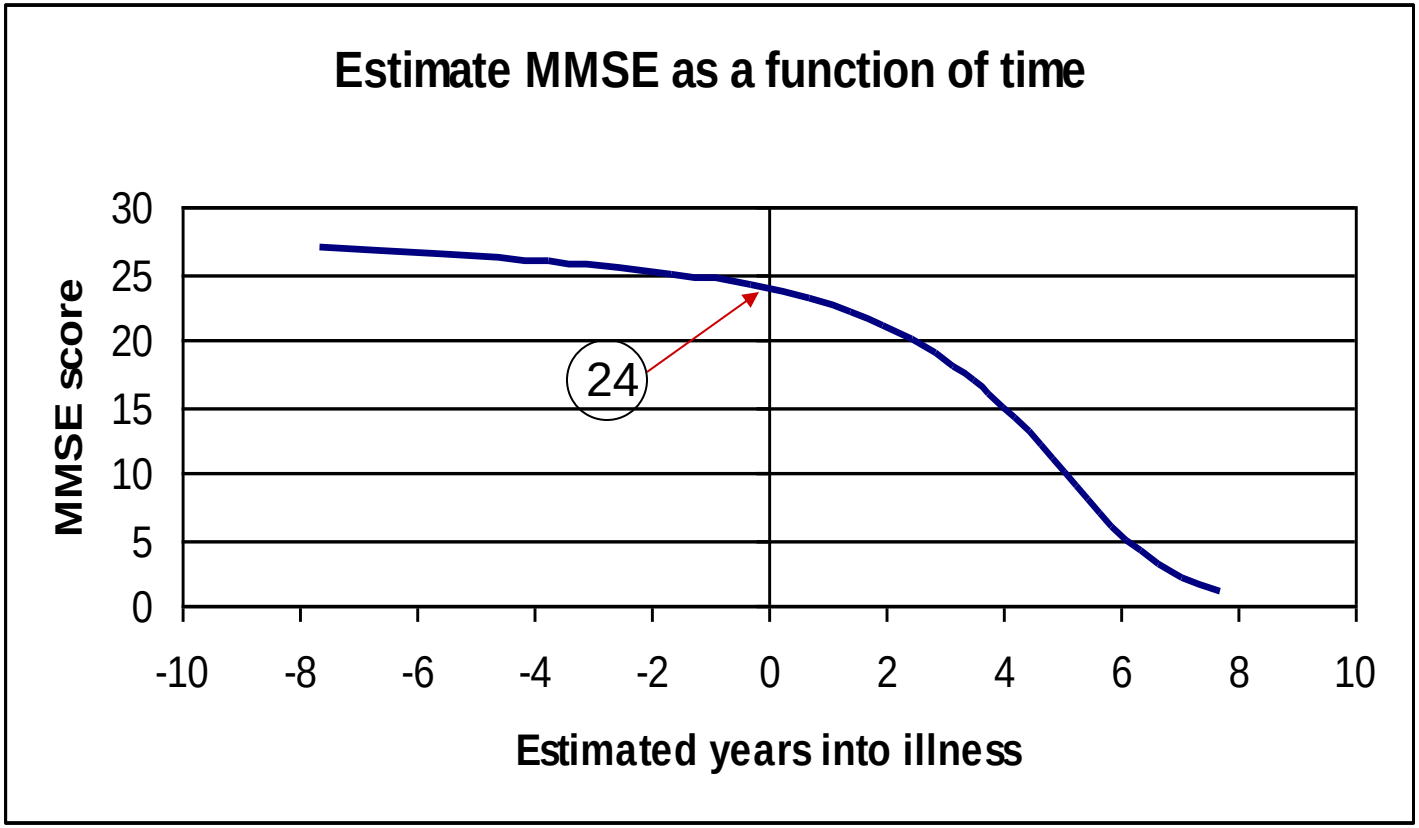
- A detailed patient history
- Information from family and friends
- Physical and neurological exams and lab tests
- Neuropsychological/cognitive tests
- Imaging tools such as CT scan, or magnetic resonance imaging (MRI).



Problem: These assess symptoms. AD pathology is already pretty far advanced by the time symptoms appear and a definitive diagnosis can be made using these methods.

In other words, it may be too late for treatments to be effective

ALZHEIMER'S DISEASE ASSESSMENT
Mini Mental State Exam (MMSE)



Limitations:
False-positives (usually depression with pseudodementia)
False negatives (early dementia in high functioning patients)
Lack of comprehensiveness

Important Note: *AD begins 8-10 years before symptoms are detectable!!*

Criteria and Market for an Early Alzheimer's Diagnostic

Diagnosis of AD is expensive and based on detection of telltale symptoms, results from neurological and neuropsychiatric tests and brain imaging. The pathology has already been underway for years.

Accurate early diagnosis of AD at the mild cognitive impairment (MCI) stage is not yet possible.

No blood or laboratory tests for AD exist – the annual world market for a diagnostic test that can detect AD at the early MCI stage is $3.5 billion.

An intensive worldwide search is underway for useful AD biomarkers and a diagnostic blood test for AD.

Ideal criteria for any diagnostic test include that it must be:

- -specific
- -reliable and reproducible
- -non-invasive or minimally invasive
- -simple to perform
- -affordable

Early detection of AD at the MCI stage is the goal – because it allows early treatment

Autoantibodies as Blood-Based Disease-Specific Biomarkers: We have discovered that thousands of autoantibodies are present in all human serum

Protein Microarray

Nearly 2,000 autoantibodies are detected using 9,486 human protein targets - this reflects only 1/3 of the total human proteome

Effects of Age and Gender on Number of Autoantibodies in the Blood

Age	N	% Female	Antibody Count	P value
< 45	10	33.3	1498.2 ± 545.7	<45 vs. 45-65: 0.0021
45 - 65	32	18.2	2335.6 ± 1009.5	45-65 vs. >65: 0.37
> 65	15	60	2647.8 ± 1139.2	<45 vs. >65: 0.0028

Sex	N	Age	Antibody Count	P value
Female	18	57.6 ± 18.7	2772.5 ± 714.8	0.004
Male	39	53.1 ± 15.1	2039.3 ± 1092.7	
Total	166	62.4 ± 16.3	1996.9 ± 1051.9	

Nagele et al., 2013 PLoS ONE

This discovery has pointed the way to our new disease diagnostics

OPEN ACCESS Freely available online

PLOS ONE

Natural IgG Autoantibodies Are Abundant and Ubiquitous in Human Sera, and Their Number Is Influenced By Age, Gender, and Disease

Eric P. Nagele[1,3], Min Han[1,2], Nimish K. Acharya[1,2], Cassandra DeMarshall[1,2], Mary C. Kosciuk[1], Robert G. Nagele[1]*

1 Biomarker Discovery Center, New Jersey Institute for Successful Aging, University of Medicine and Dentistry of New Jersey, Stratford, New Jersey, United States of America, **2** University of Medicine and Dentistry of New Jersey-Graduate School of Biomedical Sciences at the School of Osteopathic Medicine, Stratford, New Jersey, United States of America, **3** Durin Technologies, Inc., New Brunswick, New Jersey, United States of America

Abstract

The presence of self-reactive IgG autoantibodies in human sera is largely thought to represent a breakdown in central tolerance and is typically regarded as a harbinger of autoimmune pathology. In the present study, immune-response profiling of human serum from 166 individuals via human protein microarrays demonstrates that IgG autoantibodies are abundant in all human serum, usually numbering in the thousands. These IgG autoantibodies bind to human antigens from organs and tissues all over the body and their serum diversity is strongly influenced by age, gender, and the presence of specific diseases. We also found that serum IgG autoantibody profiles are unique to an individual and remarkably stable over time. Similar profiles exist in rat and swine, suggesting conservation of this immunological feature among mammals. The number, diversity, and apparent evolutionary conservation of autoantibody profiles suggest that IgG autoantibodies have some important, as yet unrecognized, physiological function. We propose that IgG autoantibodies have evolved as an adaptive mechanism for debris-clearance, a function consistent with their apparent utility as diagnostic indicators of disease as already established for Alzheimer's and Parkinson's diseases.

Citation: Nagele EP, Han M, Acharya NK, DeMarshall C, Kosciuk MC, et al. (2013) Natural IgG Autoantibodies Are Abundant and Ubiquitous in Human Sera, and Their Number Is Influenced By Age, Gender, and Disease. PLoS ONE 8(4): e60726. doi:10.1371/journal.pone.0060726

This Study Shows That…..

1. All human serum typically contains thousands of autoantibodies targeting a wide variety of proteins.

2. Individual autoantibody profiles are stable over long time periods (spanning many years in healthy individuals).

3. Similar autoantibody profiles are also found in the rat, mouse and swine, suggesting evolutionary conservation among all mammals.

4. The total number of different autoantibodies is strongly influenced by age, gender and the presence of disease.

What is the function of all of these autoantibodies?

Hypothesis

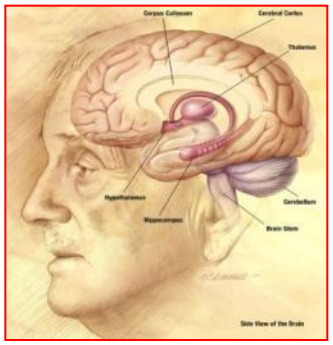
Autoantibodies are involved in the clearance of debris generated by the body on a day-to-day basis.

If so, then……..

The presence of disease leads to production of excessive debris from the organ affected

….and this leads to an increased abundance of autoantibodies responsible for the clearance of disease-associated debris

Detecting Disease-Specific Autoantibody Profiles Using Human Protein Microarrays



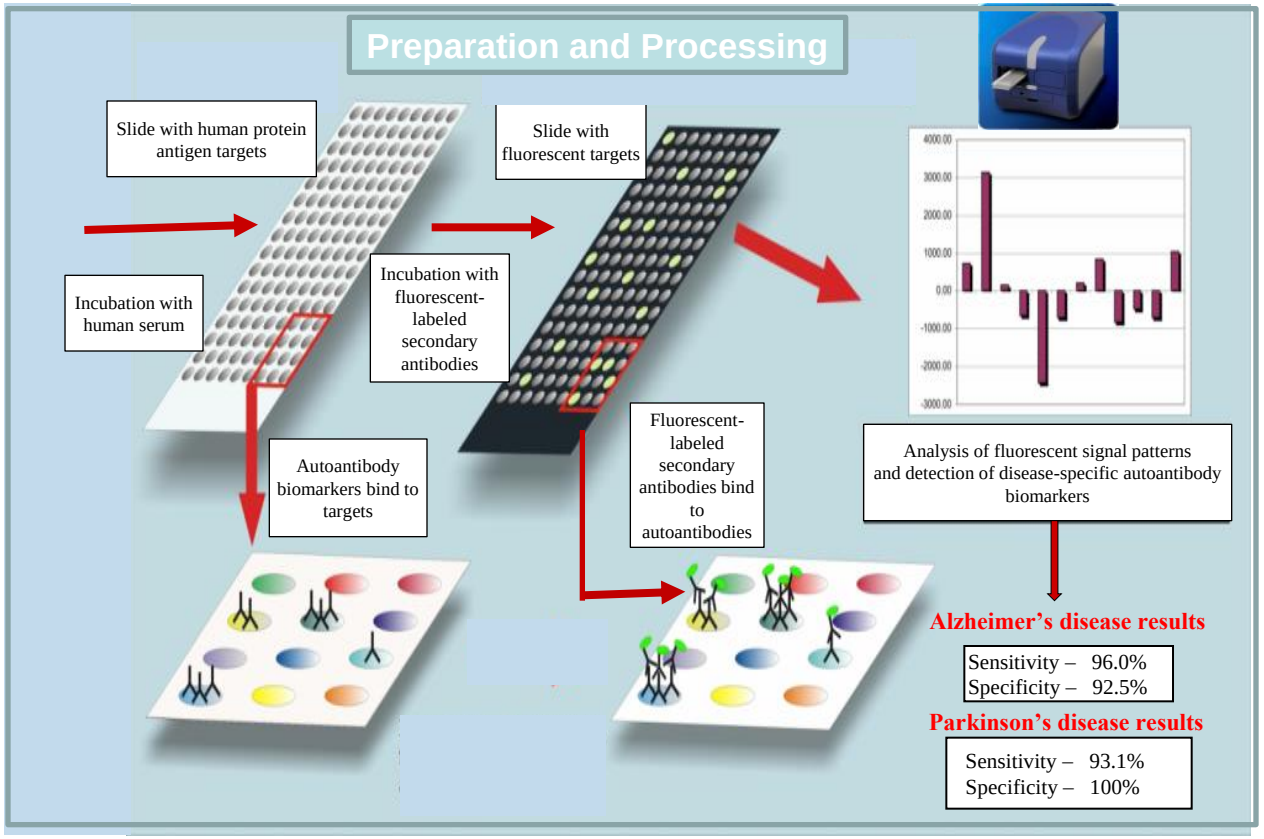
Alzheimer's disease

Autoantibody production

1. Neurons die – which type of neurons depends on brain region affected
2. Dead neurons release their debris into the surrounding cerebrospinal fluid (CSF)
3. Debris enters bloodstream and activates the immune system
4. Immune system generates many autoantibodies to clear debris
5. Durin detects disease-specific autoantibodies as biomarkers

1 drop of blood

Technology based upon the identification of disease specific autoantibody profiles in blood samples employing proprietary patterns of protein targets.



Alzheimer's Disease – completed!
Parkinson's Disease – completed!
Multiple Sclerosis – nearly complete
Autism – in progress

Funded by The Osteopathic Heritage Foundation

Autoantibody Biomarker Selection Strategy
Training and Testing Sets

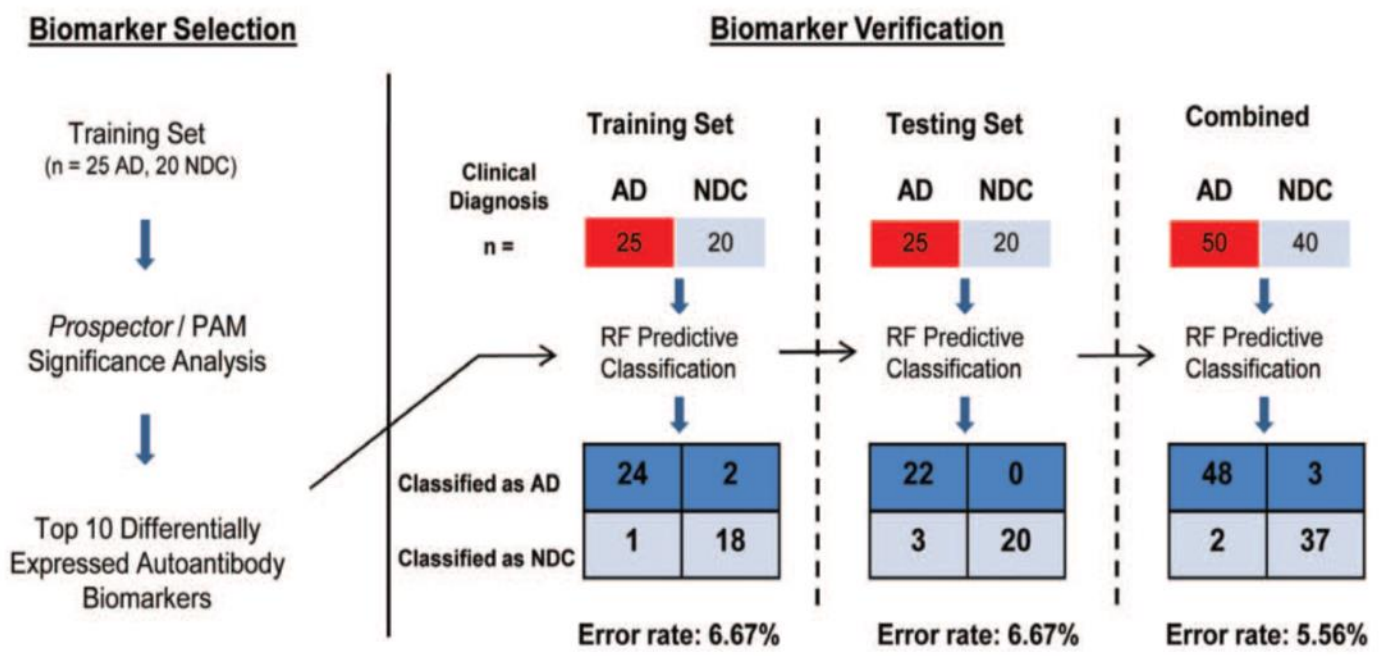


Figure 1. Biomarker selection and Training / Testing Analysis. Before biomarker selection, our total sample pool was split into two randomized groups: the Training Set and Testing Set. *Prospector* and *PAM* statistical analyses were performed on the Training Set to identify the top 10 most significant autoantibody classifiers of AD and NDC. We then verified the diagnostic accuracy of these selected biomarkers by using *Random Forest* to predict sample classification in the Training Set, Testing Set, and then both sets combined.
doi:10.1371/journal.pone.0023112.g001

Alzheimer's Disease Results

Mild-moderate disease

1. *D*etected 451 autoantibodies showing significantly higher prevalence in AD compared to controls ($p < 0.01$) – these are potentially useful as AD biomarkers.

2. Selected the top 10 autoantibodies showing the largest difference in group prevalence as our diagnostic indicators.

3. Using only the top 10 indicators, AD sera were distinguished from control sera with a **sensitivity of 96.0% and specificity of 92.5%**

Diagnostic accuracies of the 10 selected AD biomarkers in different sample demographics

Table 2. Diagnostic accuracies of selected biomarkers.

	AD (n = 50) vs.					Earlier-stage AD (n = 35) vs.		Later-stage AD (n = 15) vs.	
	All NDC	Older Control	Younger Control	PD*	Breast Cancer	All NDC	Older Control	All NDC	Older Control
	n = 40	n = 20	n = 20	n = 29	n = 30	n = 40	n = 20	n = 40	n = 20
Sensitivity %	96.0	98.0	98.0	90.0	98.0	97.1	97.1	86.7	93.3
Specificity %	92.5	85.0	90.0	79.3	83.0	92.5	90.0	97.5	90
PPV%	94.1	94.2	96.1	88.2	90.7	91.9	94.4	92.9	87.5
NPV %	94.9	94.4	94.7	82.1	96.2	97.4	94.7	95.1	94.7

**The biomarkers used for this classification are those of Table 5; all others are the biomarkers identified in Table 3.*

doi:10.1371/journal.pone.0023112.t004

Biomarker Performance Details

1. The 10 autoantibody biomarkers diagnosed AD blood samples with 96.0% sensitivity and 92.5% specificity (n=90; 50 AD, 40 Non-Demented Controls).

2. The top 10 selected biomarkers diagnosed AD with over 90% accuracy in the following subgroups tested
   1. earlier-stage AD – makes early AD diagnosis possible
   2. later-stage AD,
   3. all stages of AD (early plus late)

3. AD patients could be distinguished from Parkinson's disease and breast cancer patients, the latter confirming that our test shows no general bias for disease.

Alzheimer's Diagnostic Proof of Concept Study
Published August 3, 2011

OPEN ACCESS Freely available online

PLoS one

Diagnosis of Alzheimer's Disease Based on Disease-Specific Autoantibody Profiles in Human Sera

Eric Nagele[1☯], Min Han[2,3☯], Cassandra DeMarshall[2], Benjamin Belinka[1], Robert Nagele[3*]

1 Durin Technologies, Inc., New Brunswick, New Jersey, United States of America, **2** Graduate School of Biomedical Sciences, School of Osteopathic Medicine, University of Medicine and Dentistry of New Jersey, Stratford, New Jersey, United States of America, **3** New Jersey Institute for Successful Aging, School of Osteopathic Medicine, University of Medicine and Dentistry of New Jersey, Stratford, New Jersey, United States of America

Abstract

After decades of Alzheimer's disease (AD) research, the development of a definitive diagnostic test for this disease has remained elusive. The discovery of blood-borne biomarkers yielding an accurate and relatively non-invasive test has been a primary goal. Using human protein microarrays to characterize the differential expression of serum autoantibodies in AD and non-demented control (NDC) groups, we identified potential diagnostic biomarkers for AD. The differential significance of each biomarker was evaluated, resulting in the selection of only 10 autoantibody biomarkers that can effectively differentiate AD sera from NDC sera with a sensitivity of 96.0% and specificity of 92.5%. AD sera were also distinguishable from sera obtained from patients with Parkinson's disease and breast cancer with accuracies of 86% and 92%, respectively. Results demonstrate that serum autoantibodies can be used effectively as highly-specific and accurate biomarkers to diagnose AD throughout the course of the disease.

Citation: Nagele E, Han M, DeMarshall C, Belinka B, Nagele R (2011) Diagnosis of Alzheimer's Disease Based on Disease-Specific Autoantibody Profiles in Human Sera. PLoS ONE 6(8): e23112. doi:10.1371/journal.pone.0023112

Parkinson's Disease
A Multi-Disease Diagnostic Strategy!!

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PLoS one

Diagnosis of Parkinson's Disease Based on Disease-Specific Autoantibody Profiles in Human Sera

Min Han[1,2☯], Eric Nagele[3☯], Cassandra DeMarshall[1,2], Nimish Acharya[1,2], Robert Nagele[2,3*]

1 University of Medicine and Dentistry of New Jersey-Graduate School of Biomedical Sciences at the School of Osteopathic Medicine, Stratford, New Jersey, United States of America, 2 New Jersey Institute for Successful Aging, University of Medicine and Dentistry of New Jersey, Stratford, New Jersey, United States of America, 3 Durin Technologies, Inc. New Brunswick, New Jersey, United States of America

Abstract

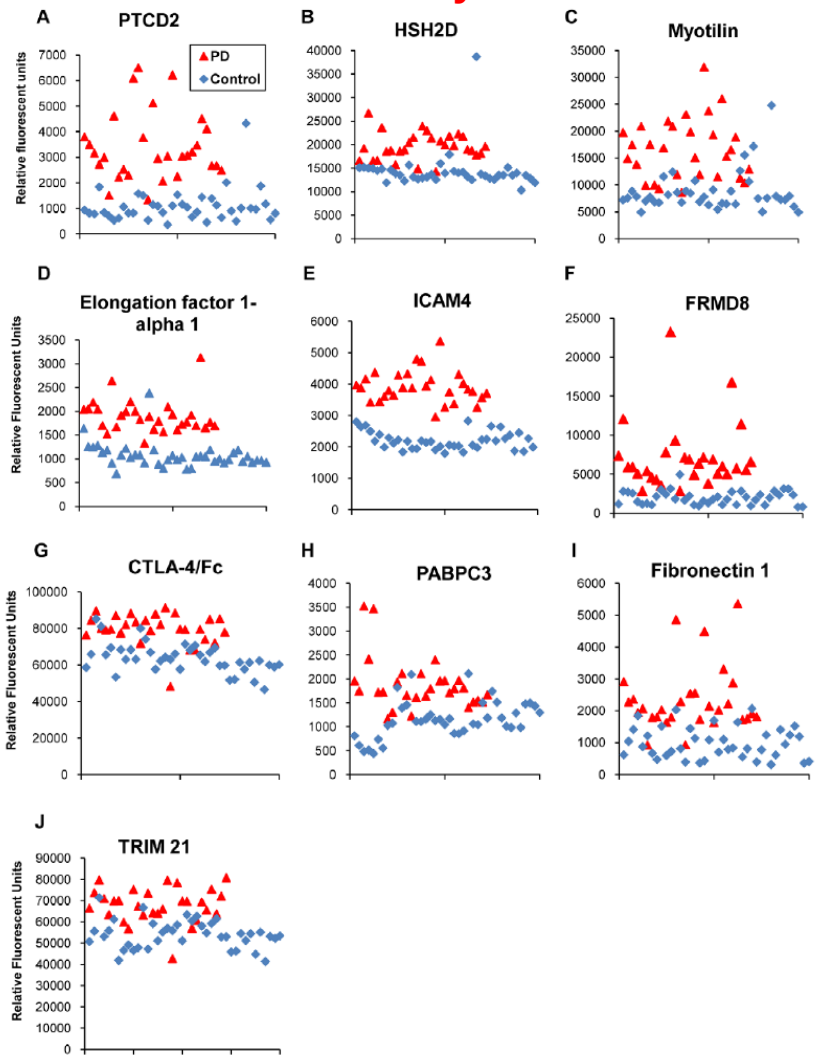
Parkinson's disease (PD), hallmarked by a variety of motor disorders and neurological decline, is the second most common neurodegenerative disease worldwide. Currently, no diagnostic test exists to identify sufferers, and physicians must rely on a combination of subjective physical and neurological assessments to make a diagnosis. The discovery of definitive blood-borne biomarkers would be a major step towards early and reliable diagnosis. Despite attention devoted to this search, such biomarkers have remained elusive. In the present study, we used human protein microarrays to reveal serum autoantibodies that are differentially expressed among PD and control subjects. The diagnostic significance of each of these autoantibodies was evaluated, resulting in the selection of 10 autoantibody biomarkers that can effectively differentiate PD sera from control sera with a sensitivity of 93.1% and specificity of 100%. PD sera were also distinguishable from sera obtained from Alzheimer's disease, breast cancer, and multiple sclerosis patients with accuracies of 86.0%, 96.6%, and 100%, respectively. Results demonstrate that serum autoantibodies can be used as highly specific and accurate biomarkers for PD diagnosis throughout the course of the disease.

Results:

Mild/moderate PD sera were differentiated from control sera with a **97.1% overall accuracy**; sensitivity of 93.1% and specificity of 100%

Differential Expression of Top 10 Biomarkers for Mild-Moderate PD

Microarray Data



Dot-blot confirmation

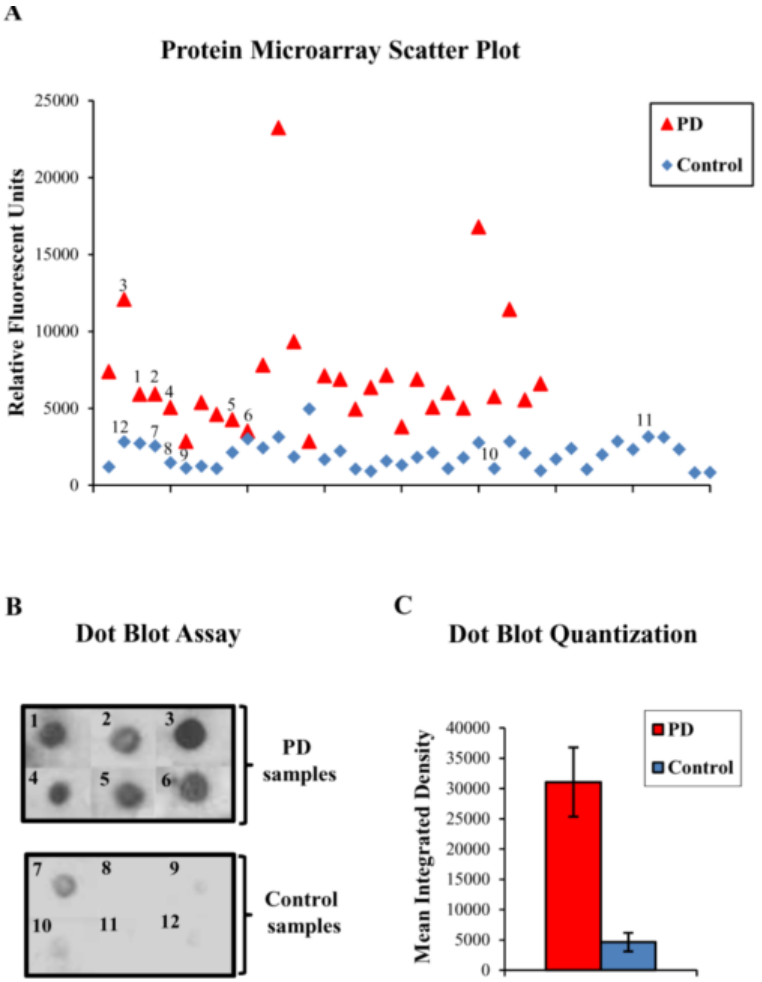


Figure 2. Differential expression of identified PD-specific autoantibody biomarkers in PD and control sera. Microarray fluorescence values reflecting individual serum autoantibody titers demonstrate the differences in the serum expression of the selected ten PD-specific autoantibody biomarkers in PD (n = 29) and control (n = 40) sera (A–I).
doi:10.1371/journal.pone.0032383.g002

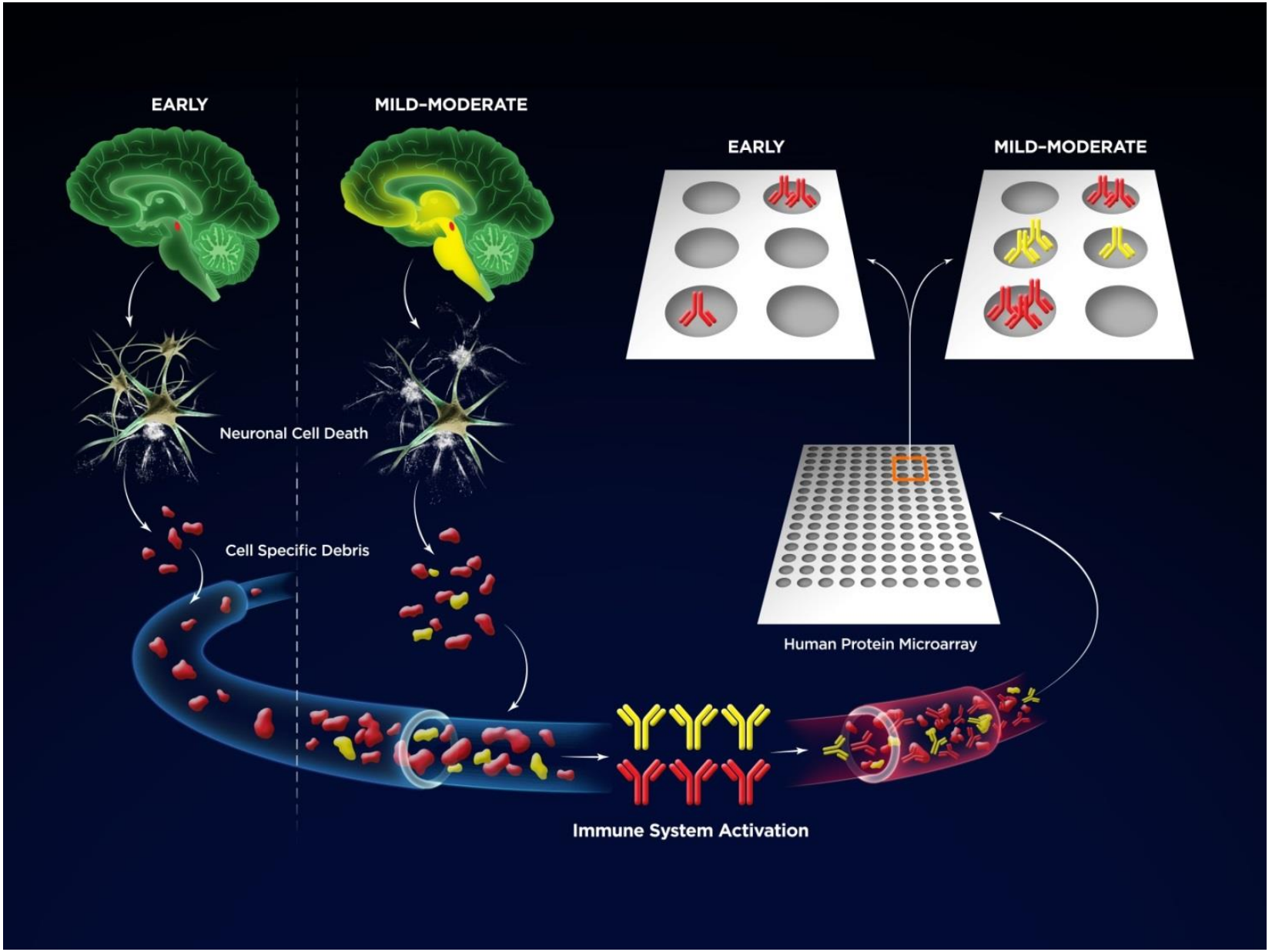
Early Detection of Parkinson's Disease

THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

In our first study, we achieved early detection of PD with **90.5% accuracy**!

Diagnosis of Early- and Mild-Moderate-Stage PD

Proposed origin of autoantibodies useful for PD diagnostics



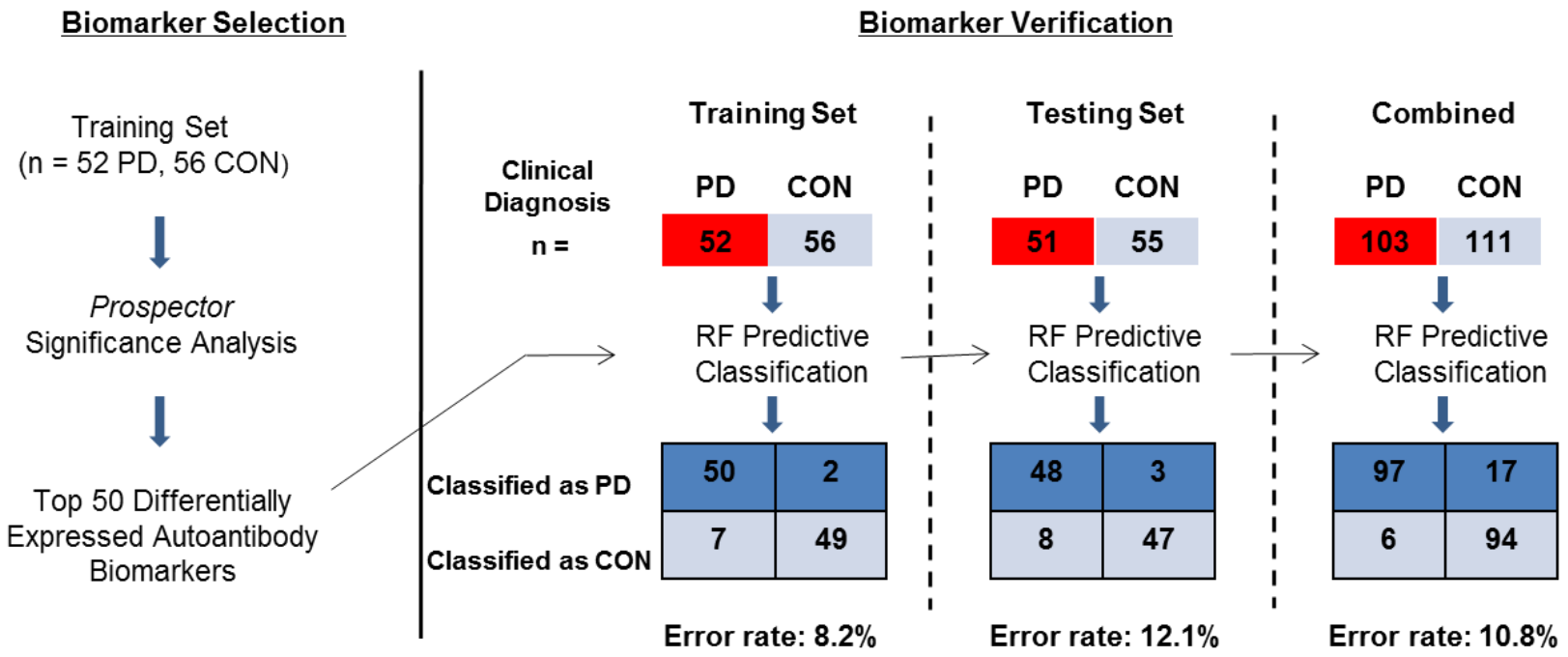
Subject Demographics for Early Parkinson's Study

Early-Stage PD Subjects Obtained From MJ Fox Foundation and Parkinson's Study Group

Group	n	Age		Sex	Ethnicity	UPDRS	Hoehn & Yahr
		(Years)	(Range)	(% Male)	(% Caucasian)		
Parkinson's disease	132	65.1 ± 10.3	37-88	57	89	-	-
-Early-Stage	103	62.7 ± 9.3	37-79	58	98	38.1 ± 16.8	2.1 ± 0.6
-Mild-Moderate	29	74.3 ± 9.0	53-88	55	55	-	-
Controls	156	55.0 ± 15.6	19-87	56	76	-	-
-Age-Matched	111	63.1 ± 8.4	51-87	56	78	-	-
-Non Age-Matched	45	34.9 ± 10.2	19-50	49	71	-	-
Alzheimer's disease	50	78.5 ± 8.8	61-97	42	88	-	-
Multiple Sclerosis	20	51.0 ± 9.2	36-67	33	97	-	-
Breast Cancer	30	46.9 ± 5.8	32-54	0	97	-	-

For each disease group the number of individuals (n), age, range of age, gender, and ethnicity are listed. For the early-stage PD subjects, the Unified Parkinson's Disease Rating Scale (UPDRS) and Hoehn and Yahr scores are included as indices of PD severity.

Early-Stage Parkinson's Disease
Biomarker Selection and Training/Testing Set Strategy



The total sample pool (n = 214) was randomly split into two groups: the Training Set and Testing Set. *Prospector* statistical analysis was performed on the Training Set to identify the top 50 most significant autoantibody classifiers of early stage PD. The diagnostic accuracy of these selected biomarkers was tested by using *Random Forest* to predict sample classification in the Training Set, Testing Set, and both sets combined.

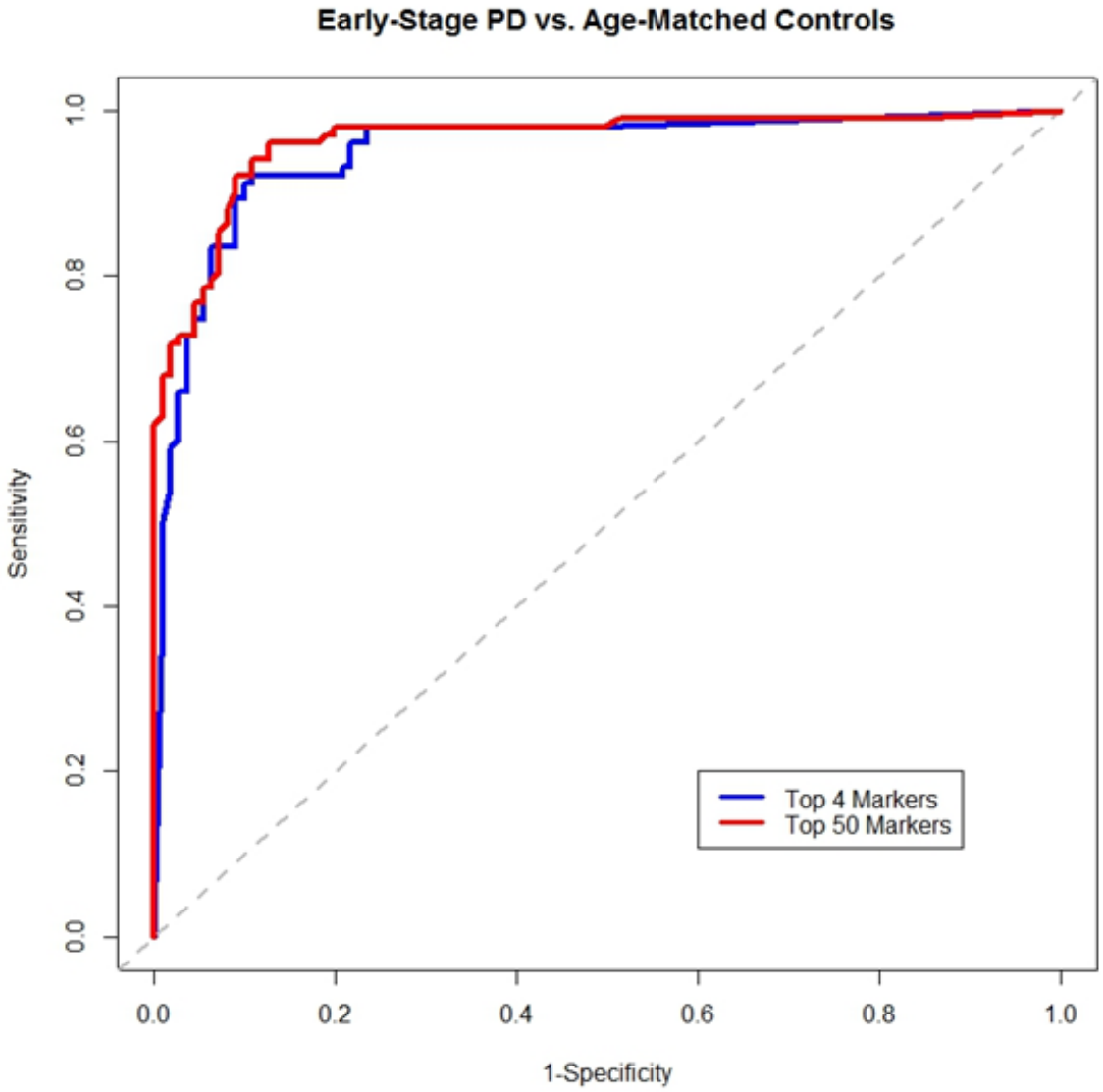
Diagnostic Results Using A Panel of 50 Early-Stage PD Biomarkers and *Random Forest (RF)*.

Early-Stage PD (n = 103) vs.	Age Matched Controls	Age Matched and Young Controls	Mild-Moderate PD	Mild-Moderate AD	Multiple Sclerosis	Breast Cancer
n	111	56	29	50	30	30
Sensitivity %	94.2	94.2	98.1	98.1	98.1	98.1
Specificity %	84.7	90.4	100.0	98.0	93.3	96.7
PPV %	85.1	86.6	100.0	99.0	98.1	99.0
NPV %	94.0	95.9	93.6	96.1	93.3	93.6
Overall Accuracy %	89.2	91.9	98.5	98.0	97.0	97.7
Overall Error %	10.8	8.1	1.5	2.0	3.0	2.3

The performance of the top 50 early-stage PD autoantibody biomarkers was assessed using *RF*. PPV, positive predictive value; NPV, negative predictive value.

Detection of Early-Stage Parkinson's Disease

ROC Curve Assessment of the Utility of PD Biomarkers for Detection of Early-Stage PD (n=103) vs. Age-matched Controls (n=111)



Comparison of early-stage PD vs. age-matched controls using a panel of 50 (**red line**) or 4 (**blue line**) biomarkers shows that these biomarker panels can be used to detect early-stage PD with a relatively high overall accuracy. Dashed line represents line of no discrimination.

ROC AUC = 0.93 (95% CI)
ROC AUC = 0.92 (95% CI)

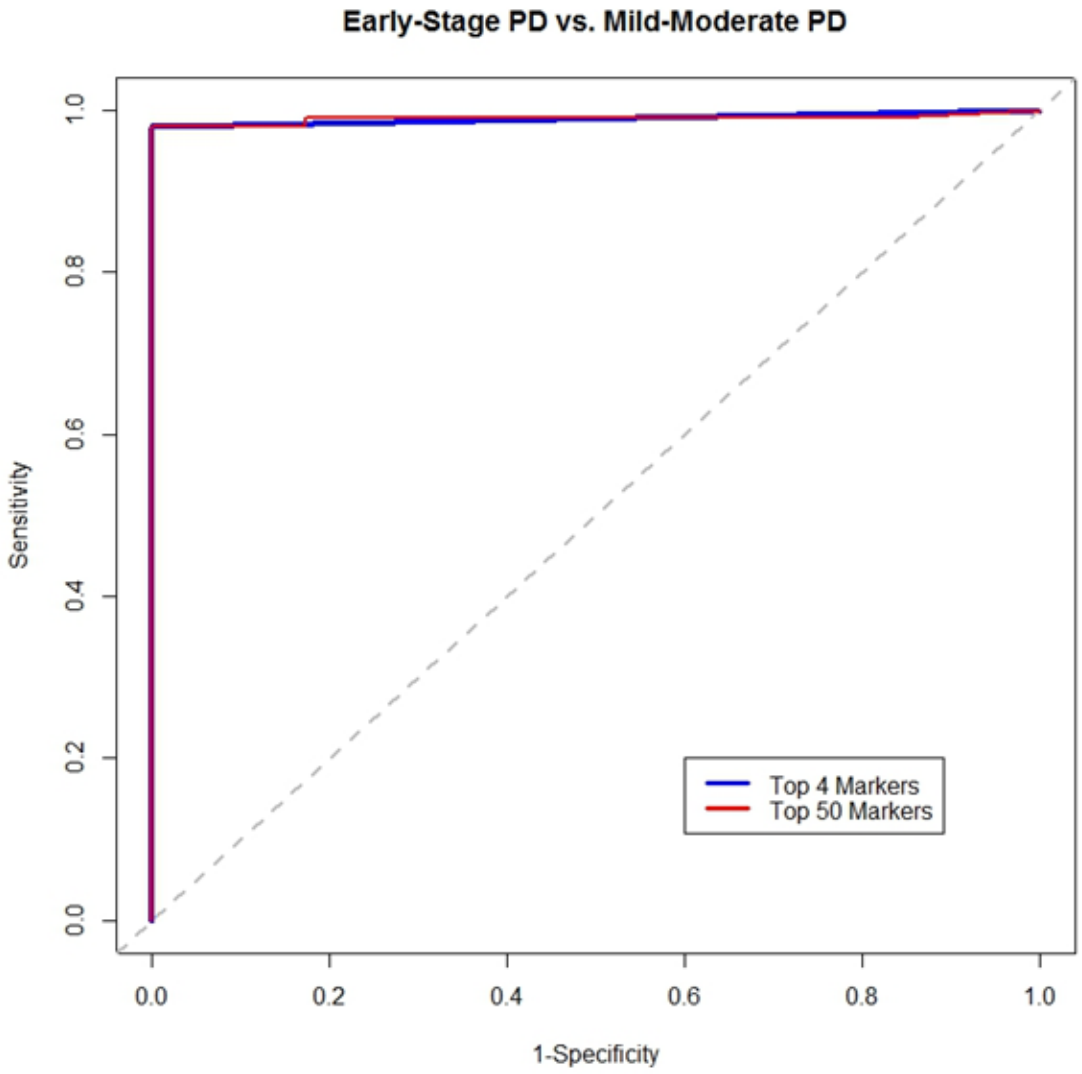
ROC Curve Analysis of Diagnostic Utility Using 50 or Only the Top 4 Early-Stage PD Biomarkers

	50 Markers			4 Markers		
Early-Stage PD (n=103) vs.	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	AUC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Age Matched Controls (n=111)	0.93 (.88-.99)	0.92 (.84-.98)	0.87 (.78-.94)	0.92 (.86-.97)	0.84 (.74-.94)	0.87 (.78-.94)
Age Matched and Younger Controls (n=156)	0.96 (.93-.98)	0.91 (.85-.96)	0.94 (.90-.97)	0.96 (.93-.98)	0.91 (.85-.96)	0.94 (.90-.97)
Mild-Moderate PD (n=29)	0.98 (.97-1)	0.98 (.95-1)	1.00	0.99 (.97-1)	0.98 (.95-1)	1.00
Mild-Moderate AD (n=50)	0.99 (.97-1)	0.98 (.95-1)	1.00	0.99 (.97-1)	0.98 (.95-1)	0.98 (.94-1)
Multiple Sclerosis (n=30)	0.98 (.97-1)	0.98 (.95-1)	1.00	0.99 (.97-1)	0.98 (.95-1)	1.00
Breast Cancer (n=30)	0.99 (.98-1)	0.98 (.93-1)	1.00	0.99 (.97-1)	0.98 (.95-1)	0.97 (.90-1)

ROC curve analyses was used to assess the diagnostic utility of the full panel of 50 or only the top 4 selected biomarkers for distinguishing early-stage PD subjects from age-matched controls from the subject groups listed. Areas under the curve (AUC) at 95% confidence are listed along with values for sensitivity and specificity derived from the ROC curve output data.

Staging of Parkinson's Disease

ROC Curve Assessment of the Utility of PD Biomarkers for Distinguishing Early-Stage vs. Mild-Moderate PD



Comparison of early-stage PD (n=103) vs. mild-moderate PD (n=29) using a panel of 50 (**red line**) or 4 (**blue line**) biomarkers showing that autoantibody biomarkers can be used to accurately distinguish different stages of PD progression.

ROC AUC = 0.98 (95% CI)
ROC AUC = 0.99 (95% CI)

Conclusions for the Early PD Detection Study

Using this diagnostic strategy, early-stage PD patients were correctly diagnosed with an overall accuracy of 89.2%, and sensitivity of 94.2% and a specificity of 84.7%.

These biomarkers were also capable of staging the disease, differentiating patients with early-stage PD from those with mild-moderate PD with an overall accuracy of 98.5%.

Early-stage PD autoantibody biomarkers are different from those that diagnose mild-moderate PD.

This appears to be a multi-disease diagnostic strategy, since it now seems to be useful for early-stage PD, mild-moderate PD, mild-moderate Alzheimer's disease, and mild cognitive impairment (MCI) driven by Alzheimer's disease.

This diagnostic strategy can be used to detect early stages of disease with minimal ongoing pathology.

Lots of Bad News Recently Regarding Failed Clinical Trials of Potential Alzheimer's Drugs

The Wall Street Journal
Lilly Alzheimer's Drug Disappoints in Trials
Aug. 24, 2012
The drug, **solanezumab**, failed to meet its primary goals in each study of slowing the erosion of memory and basic abilities

NY Times
Trials for Alzheimer's Drug Halted After Bapineuzimab Poor Results
Johnson & Johnson and Pfizer
August 6, 2012

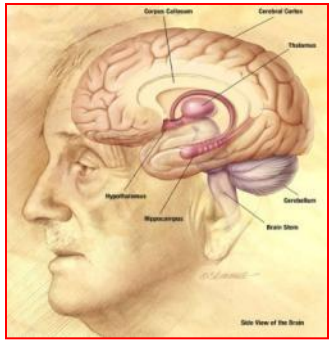
ABC News
Pfizer, Medivation Pull Plug on Alzheimer's Drug Dimebon
Jan 17. 2012
Another failure in phase III clinical testing. Dimebon finally sent to the trash heap

WHY?

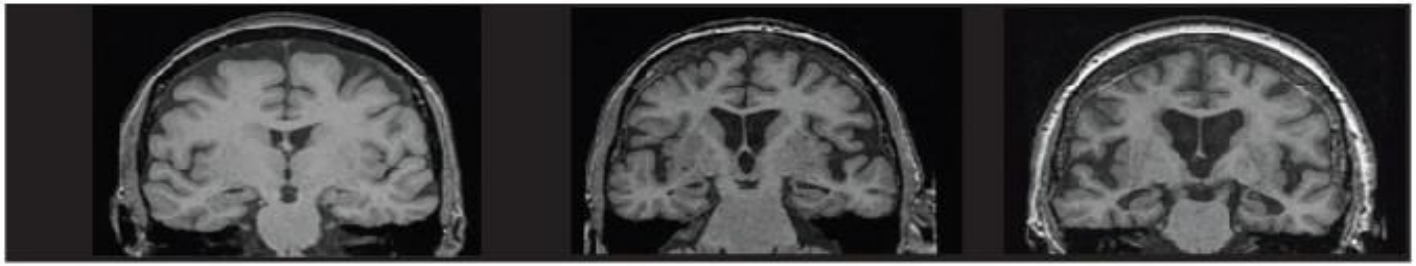
Answer: The disease is too far advanced. We need early diagnosis, so that early treatments become possible – early treatments are much more likely to be effective.

Detection of AD at the Mild Cognitive Impairment Stage

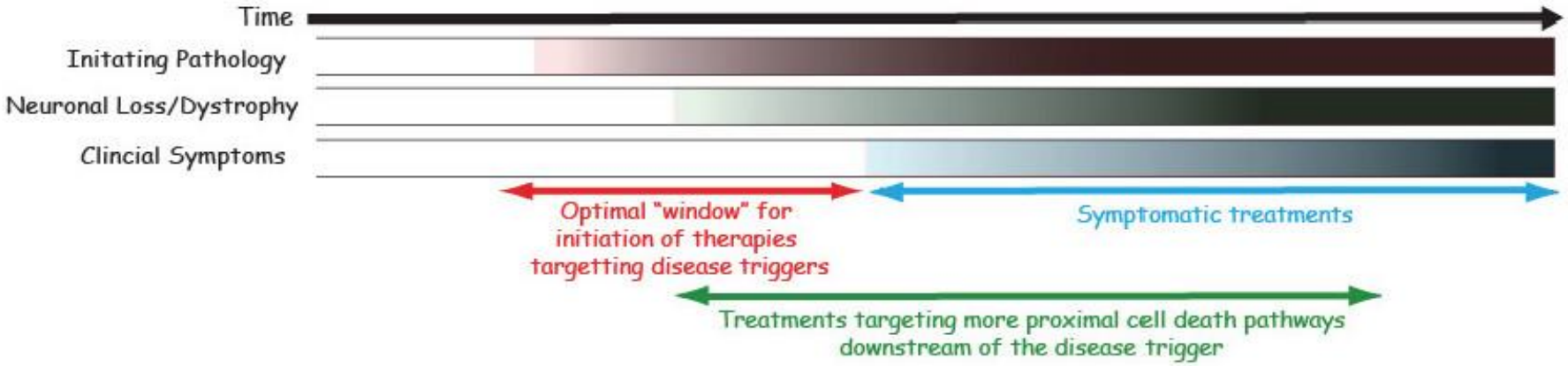
Our goal is to detect Alzheimer's disease in earlier, MCI and pre-symptomatic phases



Alzheimer's pathology is underway 8-10 years before symptoms appear



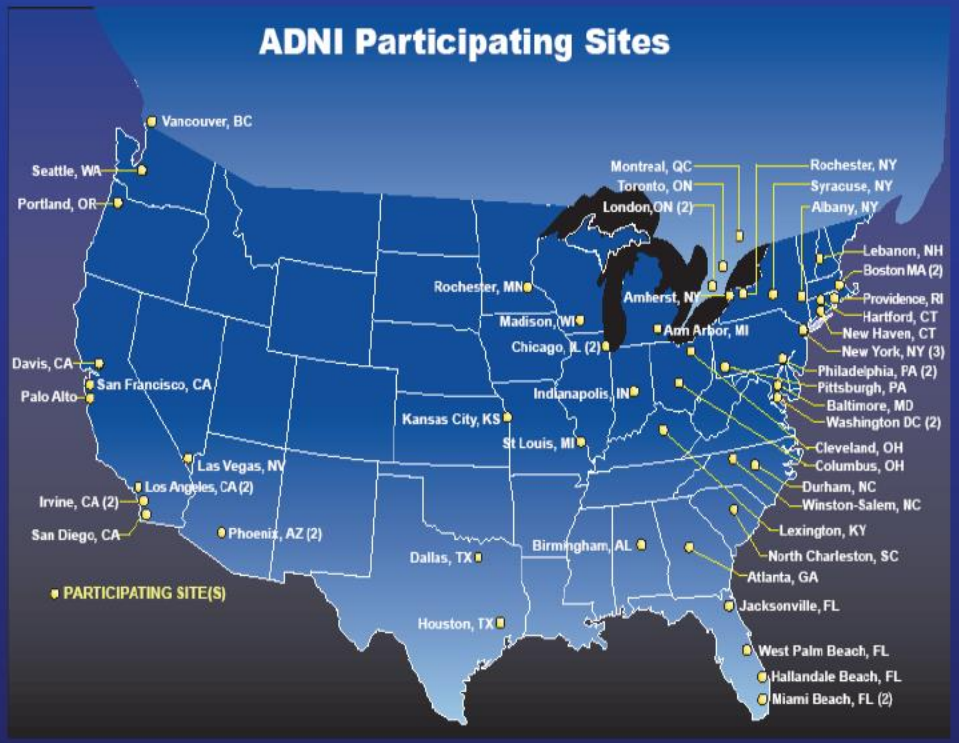
Normal | Initial Presentation with Functional Impairement | Rapidly Progressing Disease



Early Detection Allows Early Treatment (prior to appearance of symptoms)

Funded by the Osteopathic Heritage Foundation

ADNI-1: Naturalistic study of AD progression



- 200 NORMAL 3 yrs
- 400 MCI 3 yrs
- 200 AD 2 yrs
- Visits every 6 mo

- 57 sites
- Clinical, blood, LP
- Cognitive Tests
- 1.5T MRI

Some also have

- 3.0T MRI (25%)
- FDG-PET (50%)
- PiB-PET (approx 100)

All data in public database:
UCLA/LONI/ADNI
No embargo of data

Diagnosis of Mild Cognitive Impairment (MCI) in ADNI Patients with Low CSF Abeta42 Levels

Top 10 Biomarkers

All ADNI MCI patients had low CSF Abeta42 levels as surrogate biomarker for AD-related pathology

ADNI MCI (n=50)
vs.
Age-Matched Controls (n=35)

ADNI MCI ~74 yr old; controls ~73 yr old

Confusion matrix:

	CON	MCI	classification error
CON	34	1	0.02857143
MCI	0	50	0.00000000

Error rate: 1.18%
Sensitivity = 100.0%
Specificity = 97.1%
PPV = 98.0%
NPV = 100.0%

ADNI MCI (n=50)
vs.
All Controls (n=111)

ADNI MCI ~75 yr old; controls ~63 yr old

Confusion matrix:

	MCI	CON	classification error
MCI	49	1	0.02000000
CON	2	109	0.01801802

Error rate: 1.86%
Sensitivity = 98.0%
Specificity = 98.2%
PPV = 96.1%
NPV = 99.1%

Funded by The Osteopathic Heritage Foundation

Specificity of MCI Biomarkers and Staging of AD

MCI vs. Mild-Mod AD

(top 50 markers from training set)

OOB estimate of error rate: 0%

Confusion matrix:

	MCI	AD	classification error
MCI	50	0	0
AD	0	50	0

MCI vs. Early-Stage PD

(top 50 markers from training set)

OOB estimate of error rate: 2%

Confusion matrix:

	MCI	esPD	class.error
MCI	24	1	0.04
esPD	0	25	0.00

MCI vs. Multiple Sclerosis

(top 50 markers from training set)

OOB estimate of error rate: 0%

Confusion matrix:

	MCI	MS	classification error
MCI	50	0	0
MS	0	50	0

MCI vs. Breast Cancer

(top 50 markers from training set)

OOB estimate of error rate: 0%

Confusion matrix:

	MCI	BC	classification error
MCI	50	0	0
BC	0	50	0

Capabilities of Our New AD and PD Diagnostic Tests

Early Diagnosis
Patient Management
Test of Drug Efficacy

1. Early detection and diagnosis of diseases and traumatic injury (e.g., AD and PD).

2. Staging the disease - allows physicians to follow disease progress in individual patients.

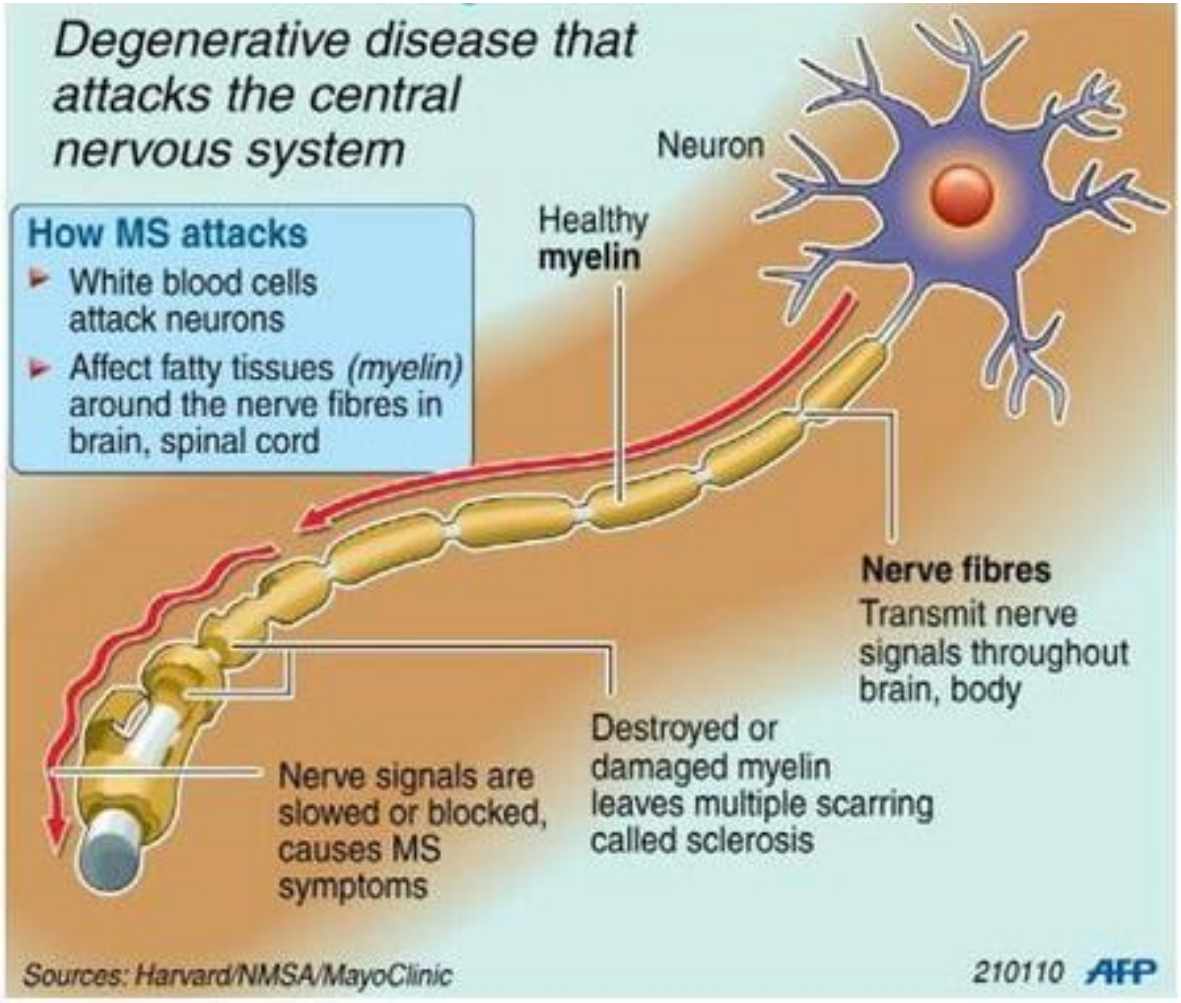
3. Evaluate patient response to drug therapy by monitoring patient progression through clinical stages.

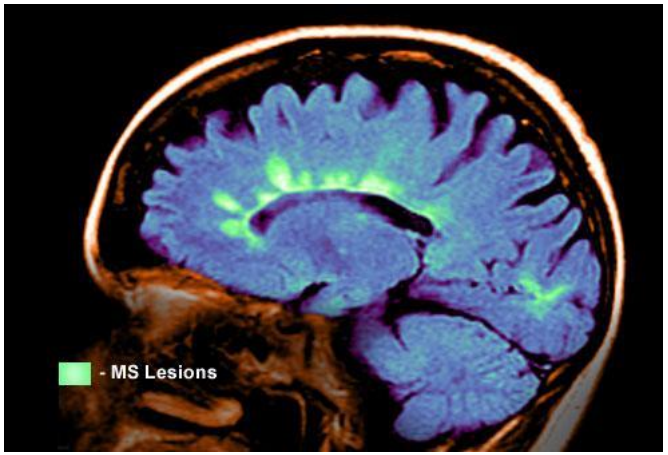
4. Confirmation of disease in subjects enrolling in clinical trials of new drugs.

5. Allows early enrollment of patients into clinical trials.

6. Evaluate patient response to therapy (drug efficacy) in clinical trials of new drugs.

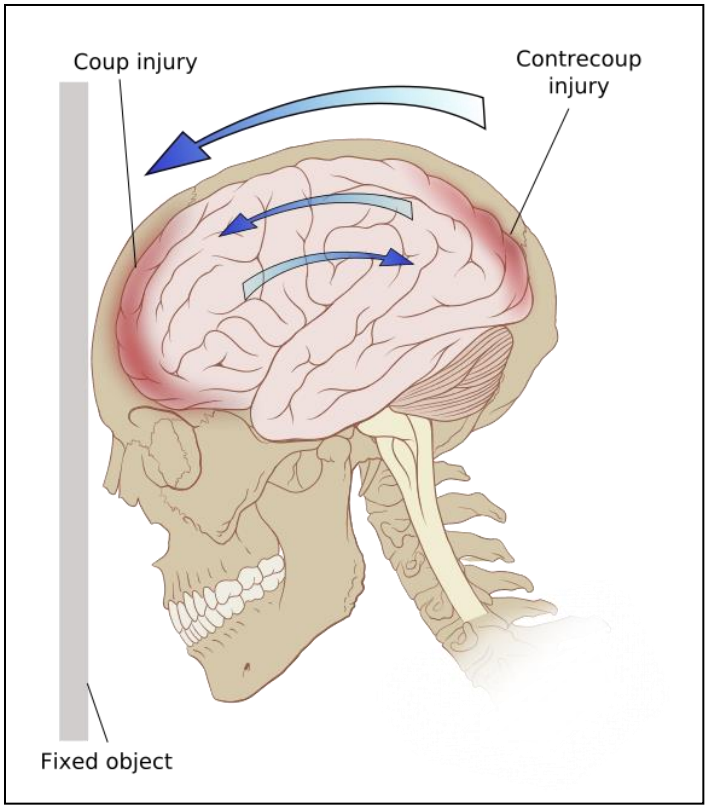
Multiple Sclerosis: Another autoimmune disease





In small patient group – 95% accuracy

Concussion and Traumatic Brain Injury

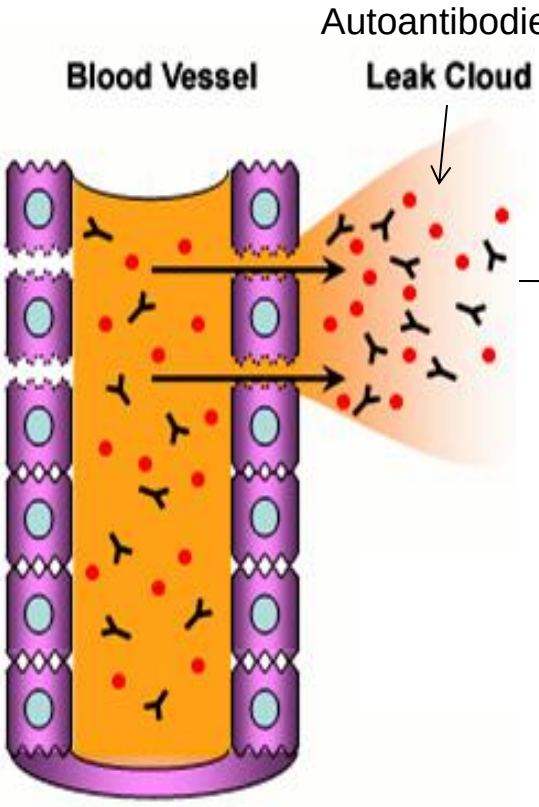


General Neurodegenerative Disease Biomarkers

- **Work Underway** -

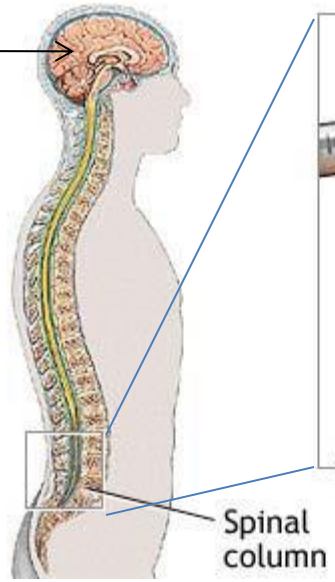
Detection of the Presence and Extent of BBB Breakdown In Post-Surgical Delirium Patients

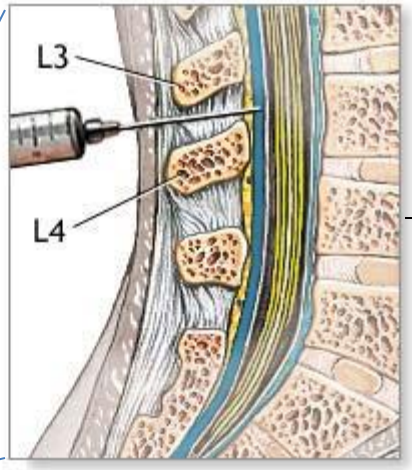
Detect Autoantibodies
in the Cerebrospinal Fluid (CSF)



Blood

→ Protein Microarray





CSF

→ Protein Microarray

READOUT

BBB Intact – No Abs in CSF
BBB Leak – Abs in CSF

Collaboration with F Sieber
at John's Hopkins.

Schizophrenia?

Neuropsychiatric disease relevance of circulating anti-NMDA receptor autoantibodies depends on blood–brain barrier integrity

C Hammer[1], B Stepniak[1], A Schneider[2,3,4], S Papiol[1,3], M Tantra[1,3], M Begemann[1], A-L Sirén[5], LA Pardo[6], S Sperling[1], S Mohd Jofrry[1], A Gurvich[1], N Jensen[1], K Ostmeier[1], F Lühder[7], C Probst[8], H Martens[9], M Gillis[10], G Saher[11], F Assogna[12], G Spalletta[12], W Stöcker[8], TF Schulz[10], K-A Nave[3,11] and H Ehrenreich[1,3]

In 2007, a multifaceted syndrome, associated with anti-NMDA receptor autoantibodies (NMDAR-AB) of immunoglobulin-G isotype, has been described, which variably consists of psychosis, epilepsy, cognitive decline and extrapyramidal symptoms. Prevalence and significance of NMDAR-AB in complex neuropsychiatric disease versus health, however, have remained unclear. We tested sera of 2817 subjects (1325 healthy, 1081 schizophrenic, 263 Parkinson and 148 affective-disorder subjects) for presence of NMDAR-AB, conducted a genome-wide genetic association study, comparing AB carriers versus non-carriers, and assessed their influenza AB status. For mechanistic insight and documentation of AB functionality, *in vivo* experiments involving mice with deficient blood–brain barrier ($ApoE^{-/-}$) and *in vitro* endocytosis assays in primary cortical neurons were performed. In 10.5% of subjects, NMDAR-AB (NR1 subunit) of any immunoglobulin isotype were detected, with no difference in seroprevalence, titer or *in vitro* functionality between patients and healthy controls. Administration of extracted human serum to mice influenced basal and MK-801-induced activity in the open field only in $ApoE^{-/-}$ mice injected with NMDAR-AB-positive serum but not in respective controls. Seropositive schizophrenic patients with a history of neurotrauma or birth complications, indicating an at least temporarily compromised blood–brain barrier, had more neurological abnormalities than seronegative patients with comparable history. A common genetic variant (rs524991, $P = 6.15E-08$) as well as past influenza A ($P = 0.024$) or B ($P = 0.006$) infection were identified as predisposing factors for NMDAR-AB seropositivity. The $> 10\%$ overall seroprevalence of NMDAR-AB of both healthy individuals and patients is unexpectedly high. Clinical significance, however, apparently depends on association with past or present perturbations of blood–brain barrier function.

Molecular Psychiatry advance online publication, 3 September 2013; doi:10.1038/mp.2013.110

Collaboration with Prof. H. Ehrenreich at Max Planck

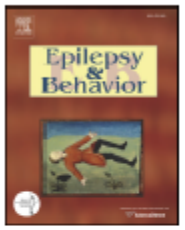
Psychosis?

Epilepsy & Behavior 36 (2014) 33–38

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh



Hypothesis

Epilepsy-related psychosis: A role for autoimmunity?

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[c] South London and Maudsley NHS Foundation Trust, UK
[d] Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, Oxford, UK

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N-methyl-D-aspartate receptor

ABSTRACT

Postictal psychosis (PIP) is a serious psychiatric complication of epilepsy that occurs in approximately 6% of patients following multiple complex partial or generalized seizures. The psychosis is classically described as having a pleomorphic phenomenology, including paranoid, grandiose, and religious delusions as well as multimodal hallucinations with prominent affective changes and agitation. Little is understood about the pathophysiology of the condition.

There has been a recent increase in interest in the relevance of autoimmunity to the pathogenesis of both epilepsy and psychosis. Studies have demonstrated the presence of antibodies directed against synaptic autoantigens (such as the N-methyl-D-aspartate receptor or the voltage-gated potassium channel complex) in approximately 10% of cases of sporadic epilepsy. These same autoantibodies are known to cause encephalopathy syndromes which feature psychiatric symptoms, usually psychosis, as a prominent part of the phenotype as well as other neurological features such as seizures, movement disorders, and autonomic dysfunction. It is beginning to be asked if these antibodies can be associated with a purely psychiatric phenotype.

Here, we hypothesize that PIP may be an autoimmune phenomenon mediated by autoantibodies against synaptic antigens. More specifically, we outline a potential mechanism whereby long or repeated seizures cause short-

Collaboration with TA Pollak at King's College London

Diagnosis of Stage 0 - 1 Beast Cancer Using Serum Autoantibodies

1. Experimental Design

Subjects	Gender	Sample size	Age
Breast Cancer	Female	30	47 ± 5.8
Control	Female	23	52 ± 16

Detected 301 autoantibodies with significant prevalence difference (P<0.01)

2. Diagnosis of breast cancer using the top 50 biomarkers

Training Error: 4.3% on average

Testing Error: 2.5% on average

	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	Trial 6	Trial 7	Trial 8	Trial 9	Trial 10	Average
Training Error	2.70%	2.70%	8.10%	5.41%	5.41%	2.70%	2.70%	5.41%	5.41%	2.70%	4.3%
Testing Error	1/16	0/16	0/16	0/16	0/16	1/16	0/16	0/16	1/16	1/16	2.5%

Overall Results for Early Stage Breast Cancer - >95% accuracy!

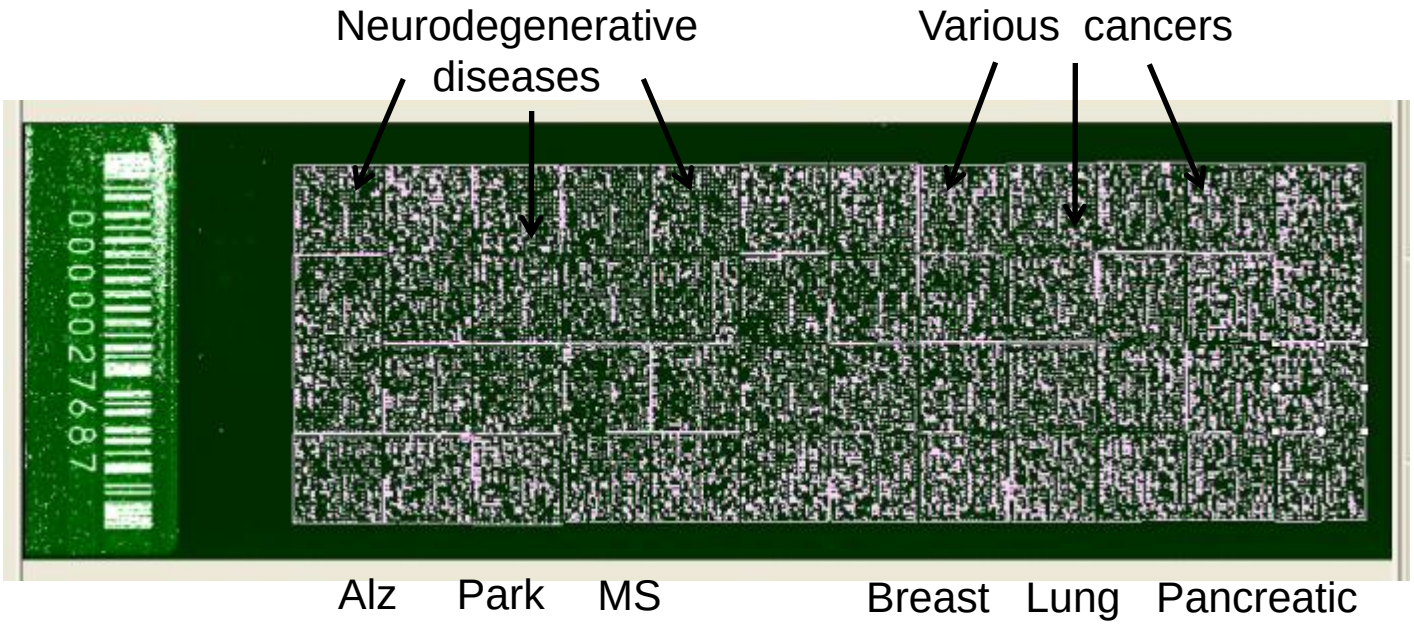
Future Plans and Directions

Short-Term Plans for MCI Diagnostic Test

1. Identify biomarkers for AD-driven MCI and patent the MCI biomarkers.
2. Complete a large-scale validation study of the MCI diagnostic using serum samples from the Alzheimer's Disease Neuroimaging Initiative (ADNI).
3. Seek FDA approval.

Long-term goal: Construct a Multi-Disease Diagnostic Blood Test

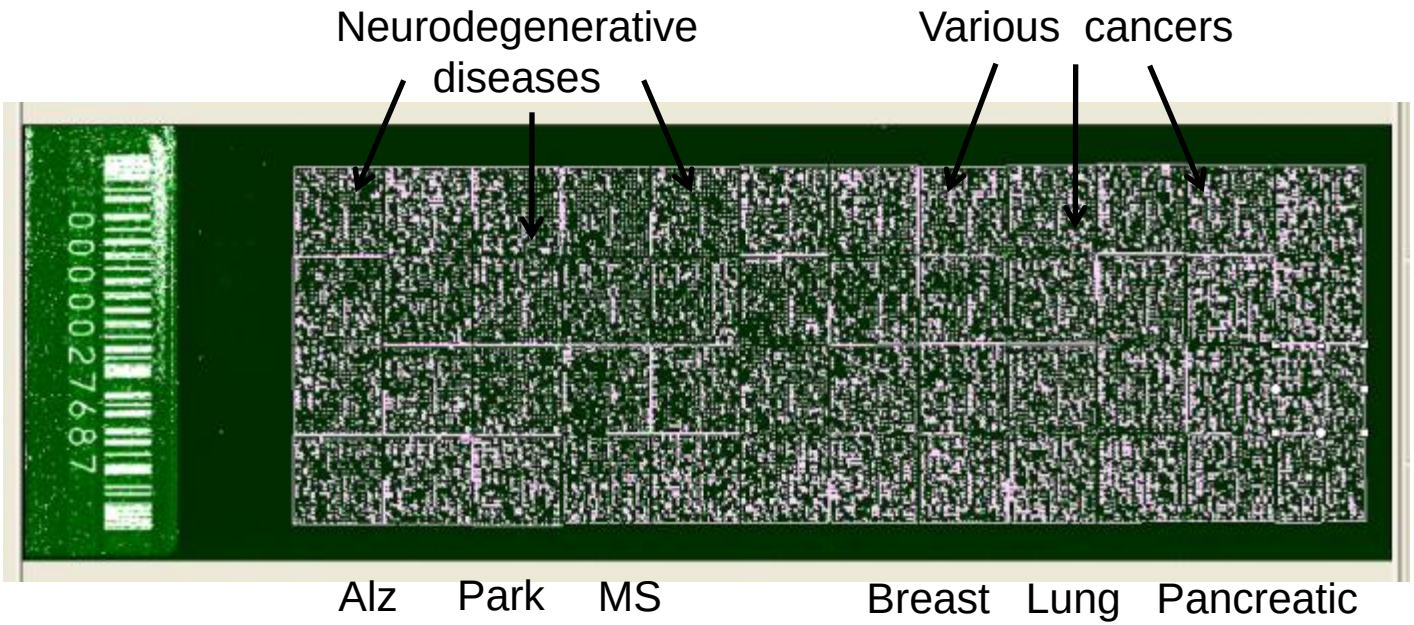
Only 20-50 autoantibodies are needed for each diagnostic.
Each array can currently hold over 20,000 protein targets.
There is plenty of room for hundreds of diagnostic tests on a single microarray.



Biomarkers of Therapeutic Efficacy

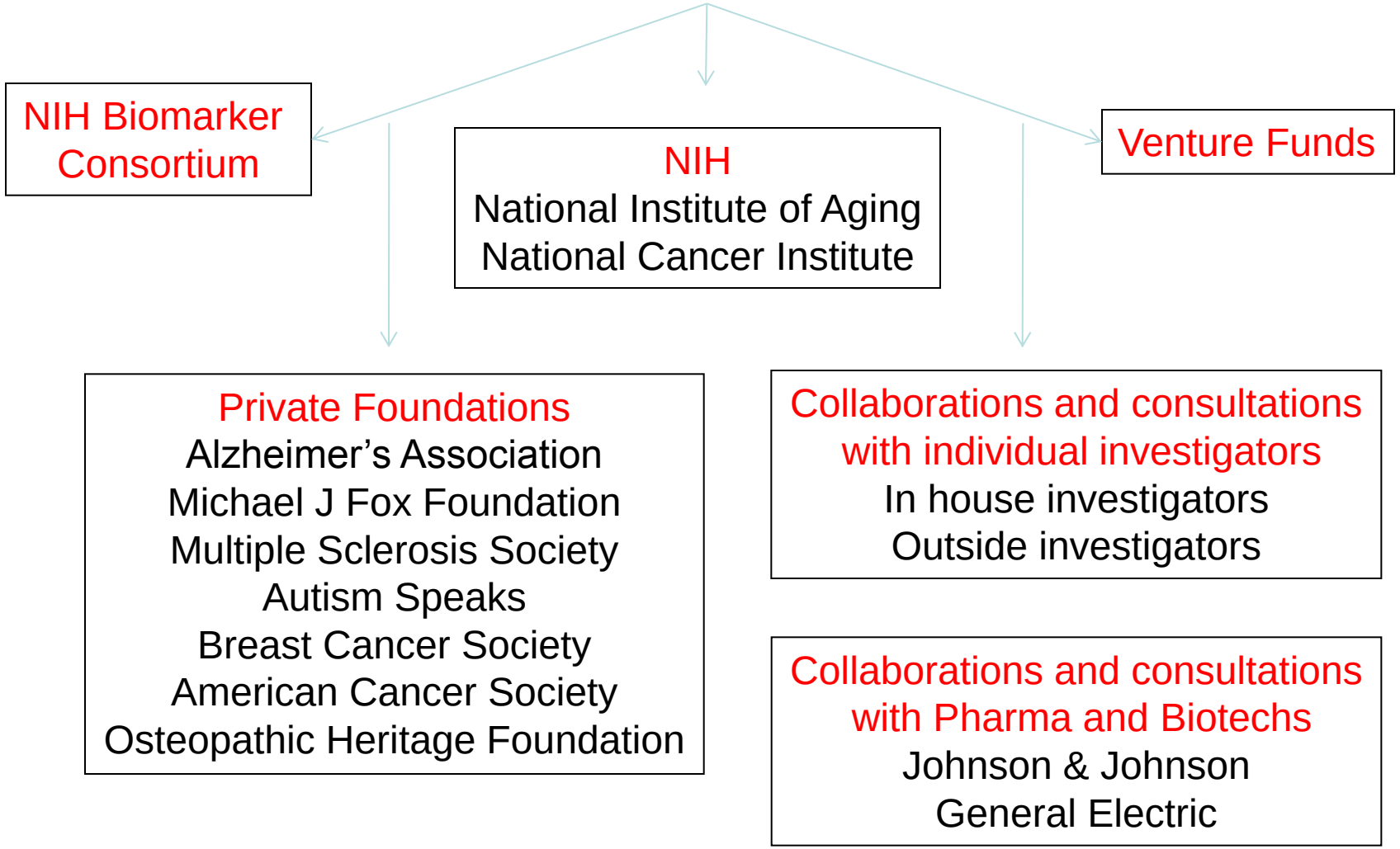
Concept

If treatments are effective, there should be less disease-associated debris production and a corresponding decrease in autoantibody biomarkers in the blood



Comparison of blood samples before and after drug treatment

RowanSOM NJISA's Biomarker Discovery Center



Some Members of My Laboratory Family

And The Osteopathic Heritage Foundation

Thank You

Osteopathic Ground Game

Sean R. Kerger, D.O., FAOASM
&
Richard G. Schuster, D.O.

Learning Objectives:

Explain the interrelationships of common complaints of the lower leg as they relate to the upper body from a musculoskeletal viewpoint.

Demonstrate the osteopathic considerations when diagnosing lower leg problems.

Demonstrate exemplary osteopathic techniques to address lower leg somatic dysfunctions.

An Osteopathic Ground Game

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Osteopathic Principles

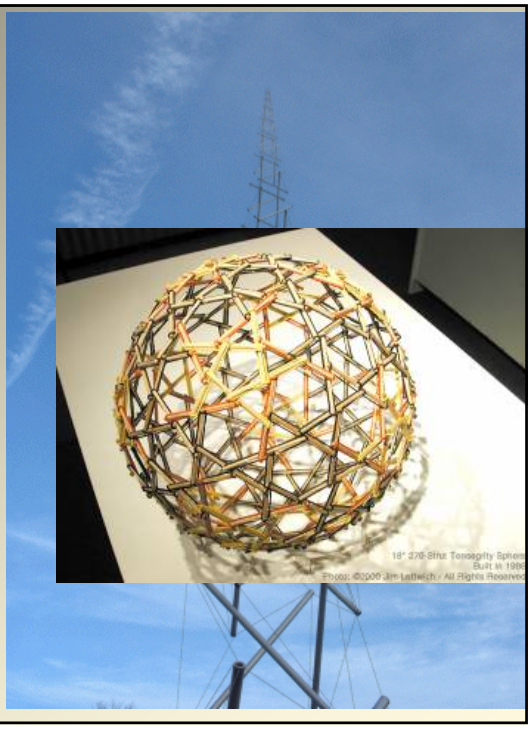
- The Osteopathic principles proposed by AT Still which most directly relate to our purposes here are:
  - "When all parts of the body are in line we have health."
  - "When complete, he is…in size & form to suit the duties he may have to perform."
  - "You as Osteopathic machinists …adjust the abnormal condition, in which you find the afflicted. Nature will do the rest."

Osteopathic Principles

- Or as restated by the faculty of the Kirksville College of Osteopathy & Surgery in 1953:
  - The body is a unit.
  - Structure & function are reciprocally interrelated.
  - The body is self-healing.

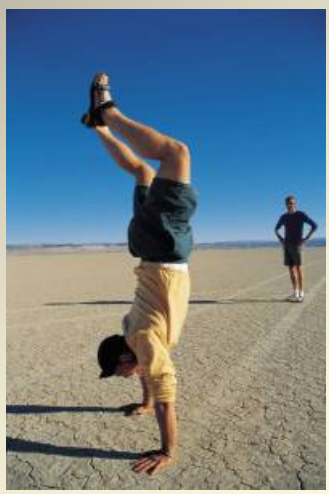
Tensegrity

- Still in development
- A self-stabilizing system in which tension is continuously transmitted across all elements
- Stability from distribution & balancing of mechanical forces
- Triangulated structures form the basis for this system
  - Tetrahedron
  - Octahedron
  - Icosahedron



Functional Anatomic Concepts: Muscle

- Kinetic chain - the sequencing of individual body segments & joints to accomplish a task
- Generally functions from a base of support proximally & then proceeds distally, but this is entirely dependant on the task at hand:
  - a bench press would follow the aforementioned path
  - a pushup reverses the mechanics even though the muscles engaged are similar, if not identical

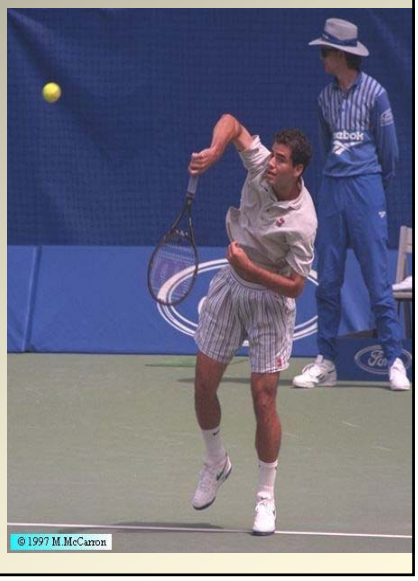


Kinetic Chain

'Catch-up' phenomenon

- compensation for dysfunction in the earlier (temporally speaking) components of the chain is not as productive a motion & can lead to injury in the later components, as the tissues either cannot handle the load or fire inappropriately

- Kibler



Compensation, Dysfunction and Motor Patterns

- Compensation can be a good thing – allows for us to perform *around* a hindrance.
- Or, it can result in dysfunction in which we are now impaired to a greater degree perhaps than the original hindrance!

Disturbed Motor Function

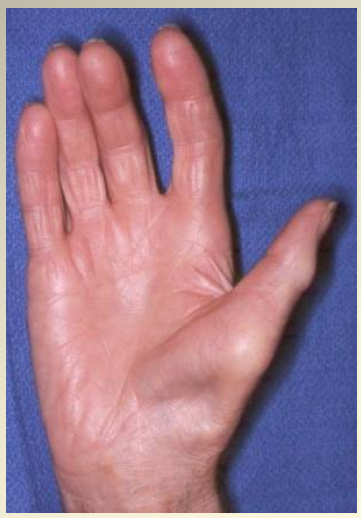
- Most important symptom ... PAIN!
- The area of the pain may not tell you where the problem is…
- Must learn to identify & treat underlying somatic dysfunction.

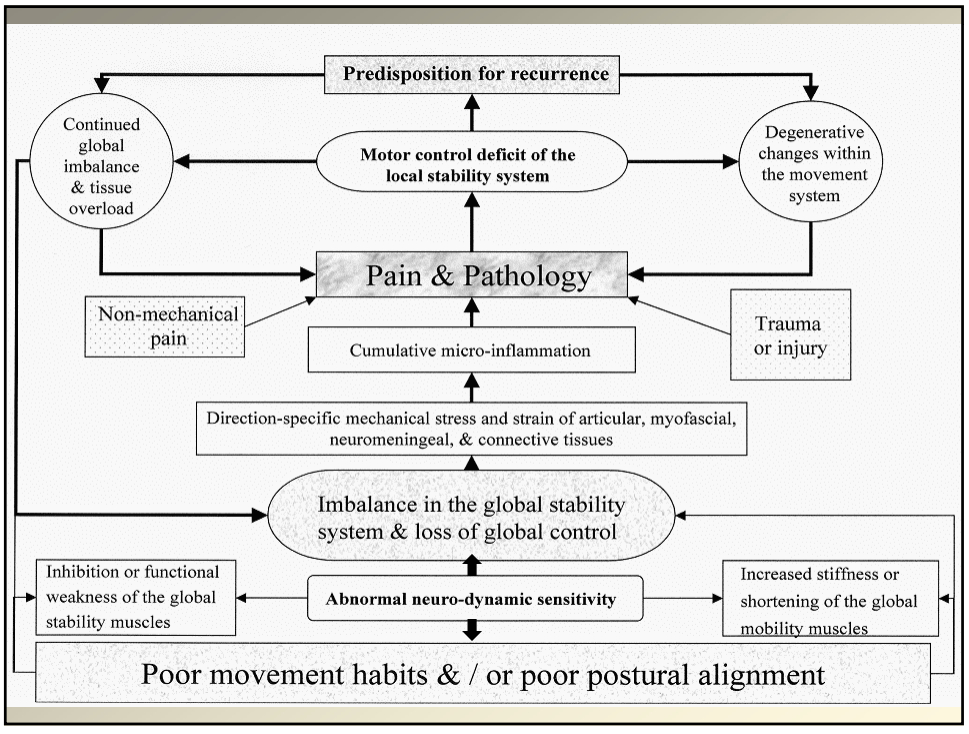
Somatic Dysfunction

- Impaired or altered function of related components of the somatic (body framework) system: skeletal, arthrodial, & myofascial structures, & related vascular, lymphatic, & neural elements.

Dysfunction

- **Logically, lack of use of a tissue (either due to injury, improper pain management, altered or improper technique, joint or soft tissue restrictions, etc.) will reverse the normal physiological processes.**
  - **Bone will become less dense**
  - **Joints will stiffen & ligaments will shorten**
  - **Muscles will atrophy & neuromuscular control will be negatively altered**
  - **Metabolic processes will revert to a lower energy (basal metabolic rate will drop), yet less exercise-tolerant, condition**





Gravitational Strain

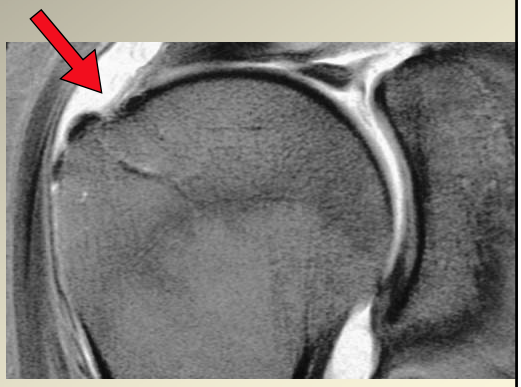
- Three Cardinal Bases of Support
  - The standing surface
  - The feet
  - The base of the sacrum

Gravitational Strain

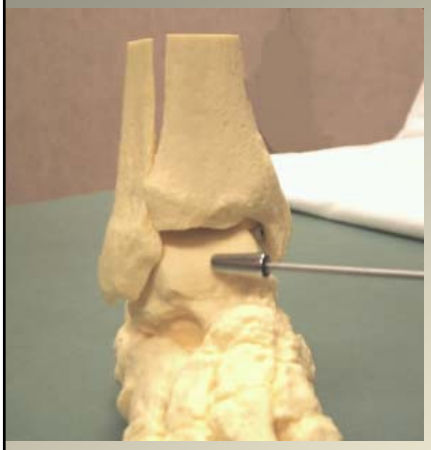
- Posture
  - Size , shape & attitude of the musculoskeletal system.
  - Departure from “ideal” posture results in increased mechanical stress.
  - Gravity *never* has an “off” day.

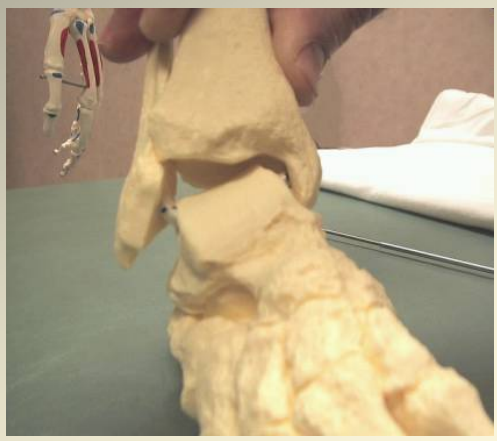
Functional Biomechanical Exam

- We'll assume you know how to diagnose the "itis" pathologies
- Now that we know *where* the problem is, the issue becomes *why* is it there?



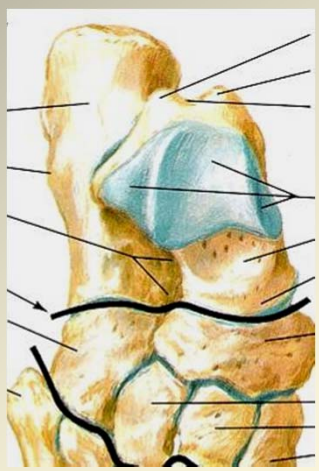
Inversion Ankle Sprain





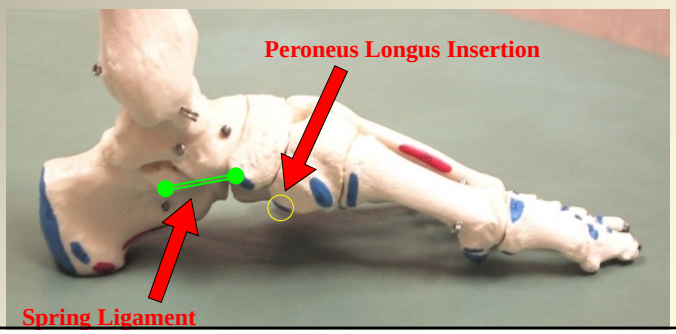
Inversion Ankle Sprain

- Typically with plantar flexion
  - Thin posterior portion of talus offers little ankle stability, relying primarily on soft tissue support
- Peroneal muscles eccentrically loaded rapidly
- Weight of body coming down 'jams' talus into the crural (distal tib/fib) articulation



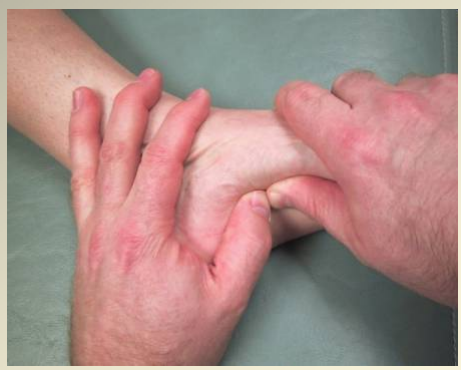
Navicular Dysfunction

- Peroneus longus tendon inserts on medial cuneiform bone - with inversion, it pulls inferiorly & "collapses" the arch via the navicular-cuneiform ligament
- Can be acute or chronic
- Can also occur due to dysfunction elsewhere (hamstrings, sacrum, etc.)



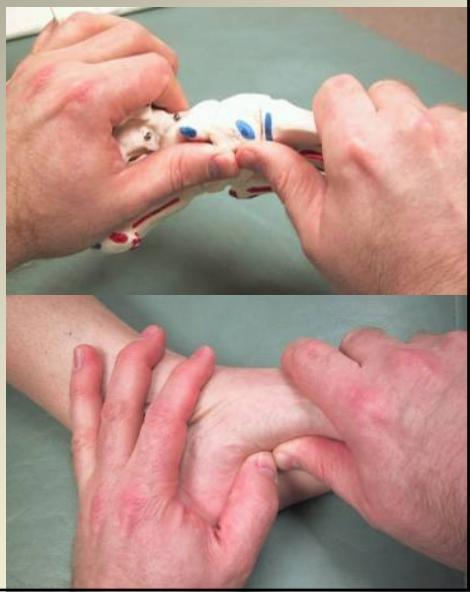
Navicular Dysfunction

- Palpation of arch reveals a more prominent (& usually tender) navicular bone in arch medially
- Pronation may be noticeable in standing examination



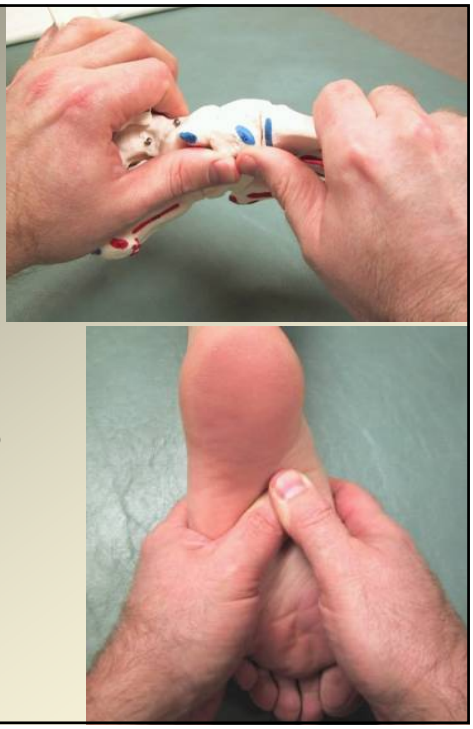
Navicular Dysfunction

- Restore arch by gapping superior aspects of navicular & cuneiform bones & applying plantar → dorsal pressure
  - Can be done with one rapid action or with slow steady pressure
- Recheck findings



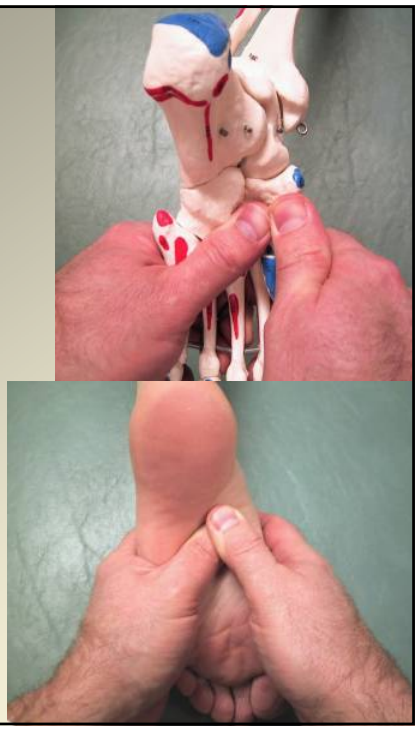
Navicular Dysfunction

- Can also be treated successfully with strain-counterstrain
  - Find most tender point in tissues over navicular
  - With pt prone, greatly flex forefoot & invert/evert forefoot until tender point 70% (& can go for more) gone
  - Maintain position with pt stabilized passively for 90 seconds
  - Return (passively) to neutral
- Recheck findings



Navicular "Whip"

- With patient prone & leg relaxed, place thumbs over plantar aspect of navicular bone
- While plantar flexing the foot, apply a valgus motion to the ankle as you 'snap' or 'whip' the navicular bone dorsally
- Recheck your findings



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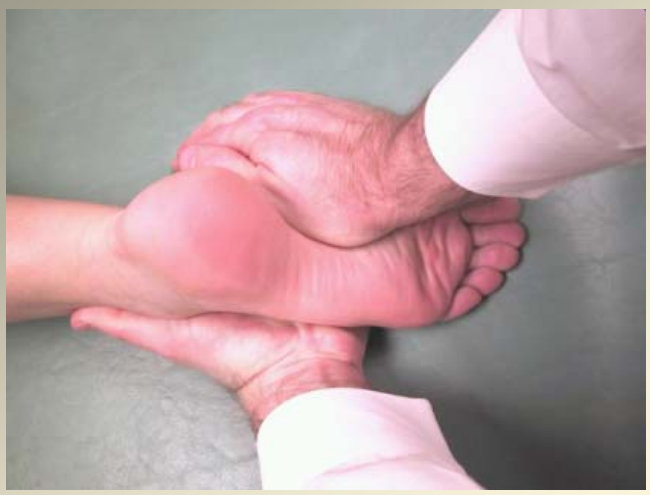
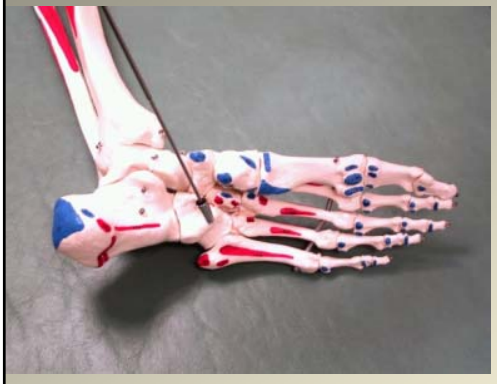
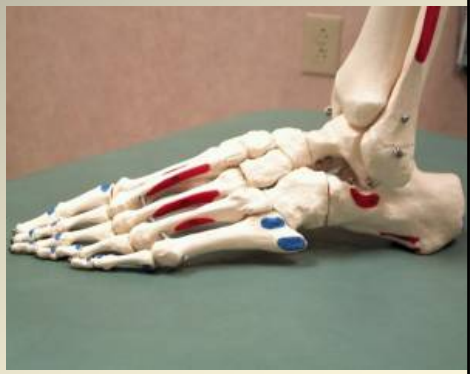


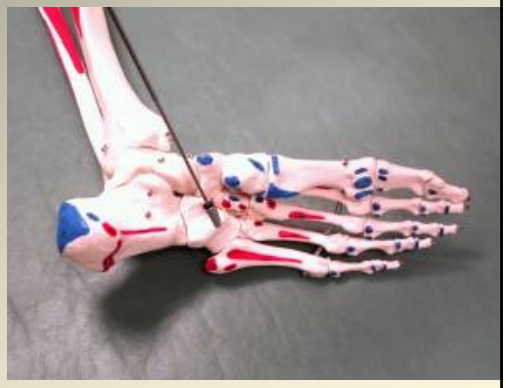
Cuboid Dysfunction





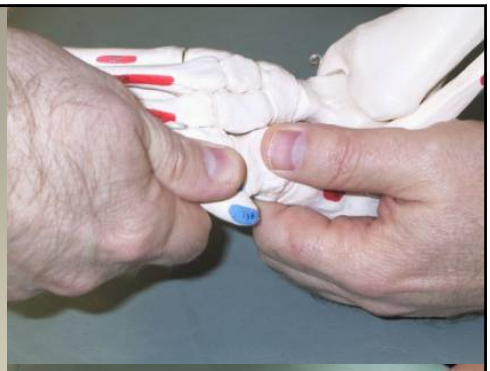
Cuboid Dysfunction

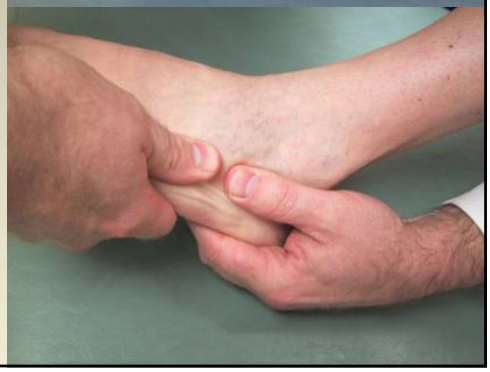
- Palpation of arch reveals a more prominent (& usually tender) cuboid bone in arch laterally
- Pronation may be noticeable in standing examination, but due to guarding, patient may exhibit supination



Cuboid Dysfunction

- Can be treated in a mirror fashion as navicular, but also may be addressed by grasping cuboid snugly & 'chalking' the 5th metatarsal head onto the cuboid gently, or the cuboid onto the calcaneus.





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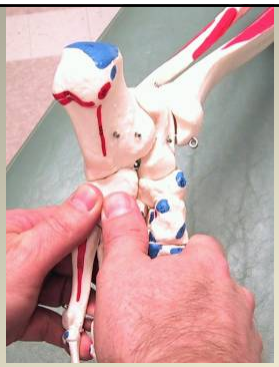
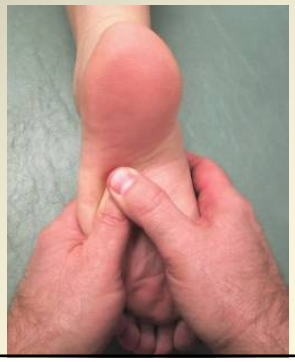
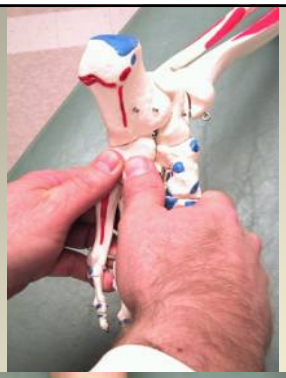
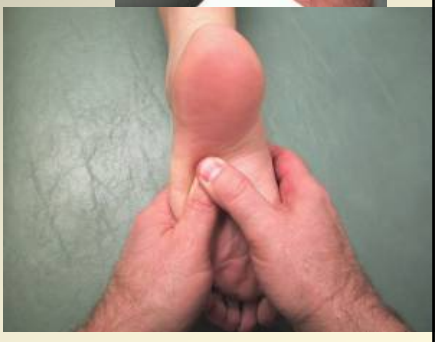




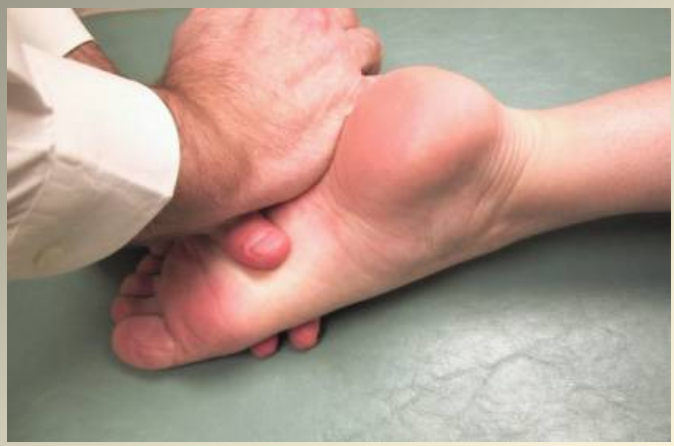
Cuboid "Whip"

- With patient prone & leg relaxed, place thumbs over plantar aspect of cuboid bone
- While plantar flexing the foot, apply a varus motion to the ankle as you 'snap' or 'whip' the cuboid dorsally
- Recheck your findings



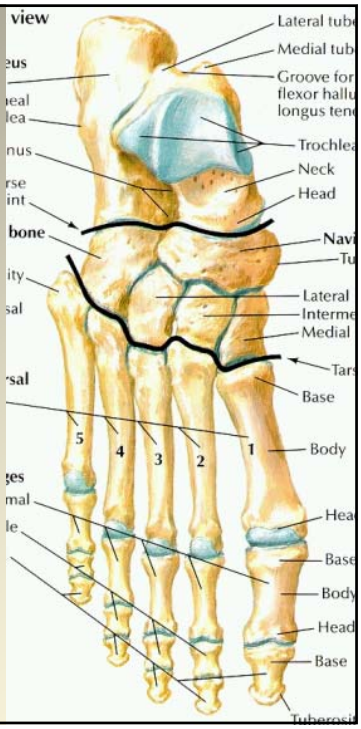


Cuboid Dysfunction



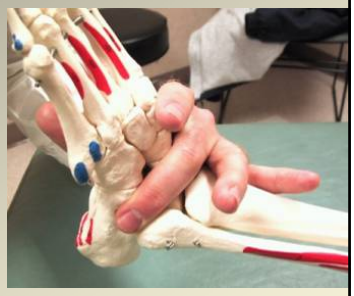
Articular Techniques for Talus

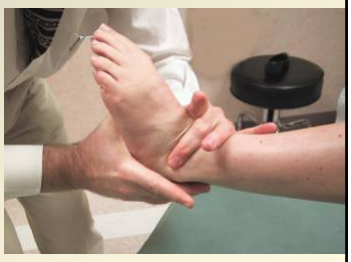
- Commonly restricted anteriorly, or impacted. May also present as an anterior fibular head!
- Usually secondary to a traumatic inversion mechanism at the ankle, but can also be due to chronically tight posterior calf muscles.
- Can be associated with plantar fasciitis.
- Pt will complain of anterior talar pain or 'jamming' with attempted dorsiflexion, & possibly of reduced calf stretch when attempted.



Articular Techniques for Talus

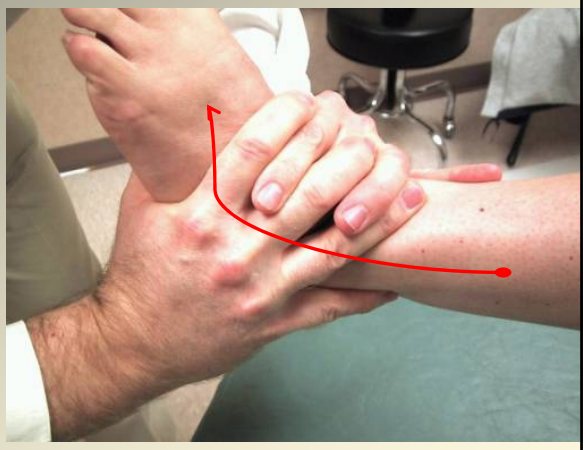
- Place ipsilateral middle or ring finger over the superior aspect of the talus, below the tib-fib joint.
- Dorsiflex ankle to the barrier, while cradling the calcaneus with the contralateral hand. You may fine tune with inversion & eversion to maximize dorsiflexion.
- With the patient relaxed, either:
  - tug the foot quickly with a moderate force in a caudal direction,
  - or with a traction force caudally, rock the calcaneus & talus as a unit in an inversion/eversion plane.





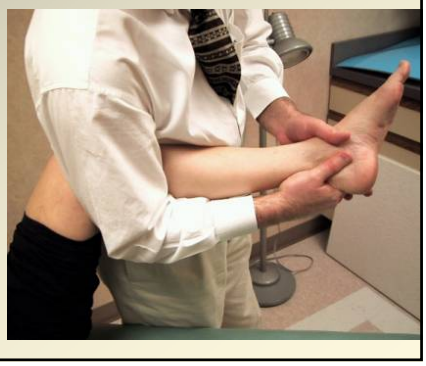
Talar Tug – Alternate Hold

- Need to pull & dorsiflex at the same time – makes a 'J' pattern movement when viewed this way



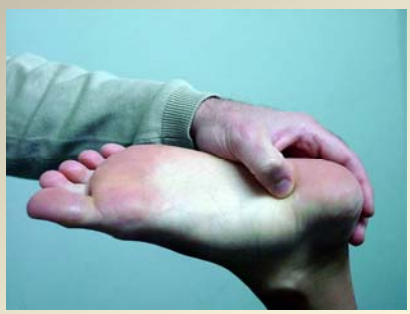
Talar Release

- Pt supine with knee & hip flexed to 90º & hip slightly abducted, nestle your elbow against the mid-hamstring area while forming a ring with your thumbs & forefingers around the talus.
- Slowly, but firmly, flex the knee while maintaining the ring around the talus. You should feel a traction force building.
- Maintaining the tension, either exert a quick thrust with the talus or gently rock the talus into dorsiflexion with a little inversion/eversion until you feel a release, pop, or clunk.



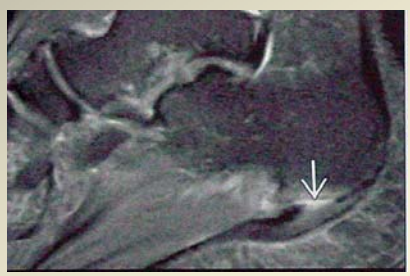
Plantar fasciitis - the problem:

- Too much tension on the plantar fascia. Why?
  - Arches not able to support themselves:
    - Navicular rotated
    - Weak intrinsic foot muscles
    - Weak or fatigued tibialis posterior, flexor digitorum longus, flexor hallucis longus
  - Tightness of Achilles



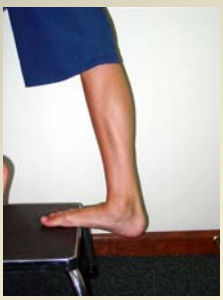
Differential diagnosis

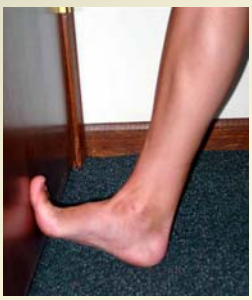
- **Fat pad contusion/atrophy**
- **Achilles tendonitis**
- **Retrocalcaneal bursitis**
- **Subcalcaneal bursitis**
- **Rupture of plantar fascia**
- **Medial calcaneal nerve entrapment**
- **Stress fracture of the calcaneus**
- **Tarsal tunnel syndrome (posterior tibial nerve)**
- **Enthesopathy (seronegative spondyloarthropathies)**
- **Paget's disease**
- **S1,2 radiculopathy**



Standard treatment

- Relative rest
- Stretching
- Intrinsic foot muscle strengthening
- Physical therapy
- Injection
- Tension night splint
- Orthotics
- Surgery



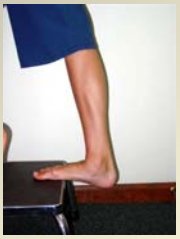


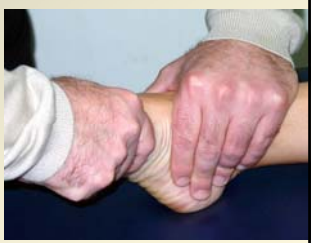
What does an osteopath offer?

- Does being an osteopath bring anything else to the table?
  - Understanding the functional anatomy, and dysfunctional physiology, might lead to improved results.
- Therefore, what is the function of the anatomy? How may it be influenced? Does this change our treatment? How does it influence our standard treatment.
- I would argue that largest benefit comes from an osteopathic understanding of the problem.

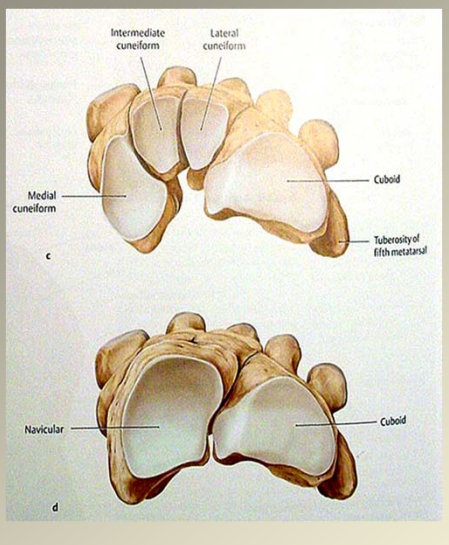
The osteopathic advantage

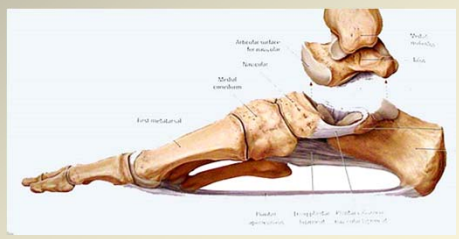
- **Therefore, the goal of treatment must be to re-establish normal function:**
  - **Maintenance of the medial arch**
    - **Relieve pressure from the ligaments**
      - **OMT, arch support**
    - **Improve strength of intrinsic foot muscles**
      - **exercises**
    - **Correct tightness of the Achilles**
      - **OMT, stretching**
    - **Improve proprioceptive function**
      - **OMT, specific proprioceptive retraining**
- ***But don't forget that there is still pathology that must heal!***



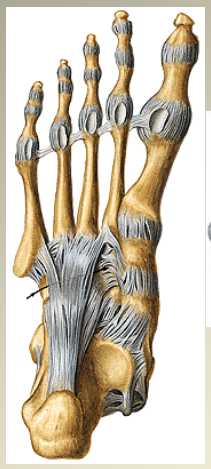


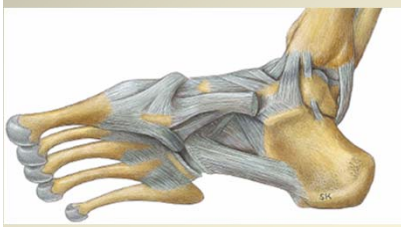
Arches



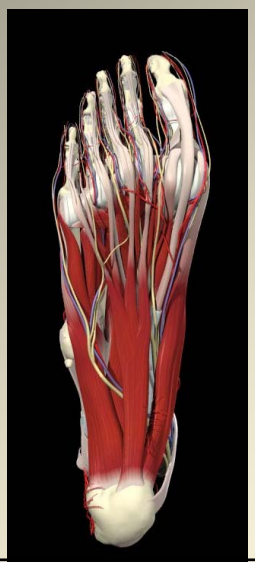
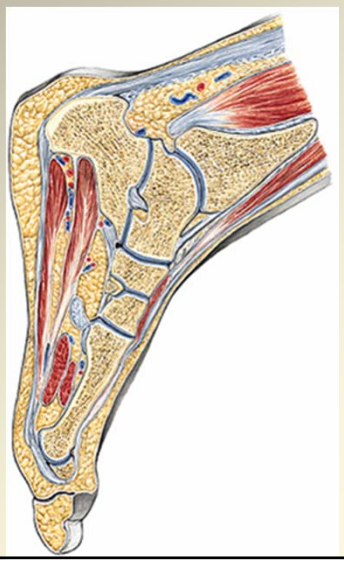


Arches: deep ligaments

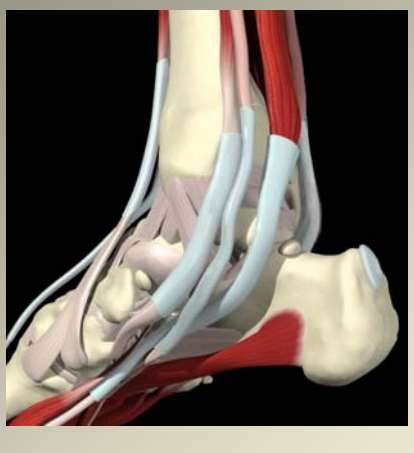
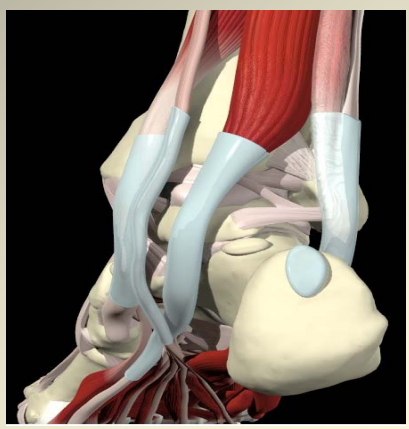




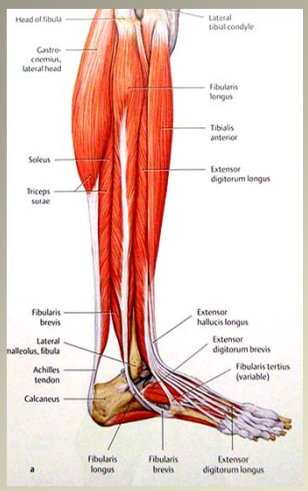
Intrinsic foot muscles

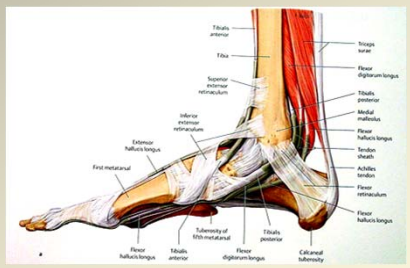




Tibialis posterior, flexor hallucis longus, flexor digitorum longus

Achilles Tendon





The treatment

- Regardless of how you choose to affect the problem, certain things must be consistently done in order to treat the problem, and prevent its recurrence.
  - Remember that there is pathology here.
- Inquire regarding changes in activity, footwear:
  - Often patients present after it has been present for months—ask specifically.
  - Look at the shoes and the insoles.

Common aspects of treatment

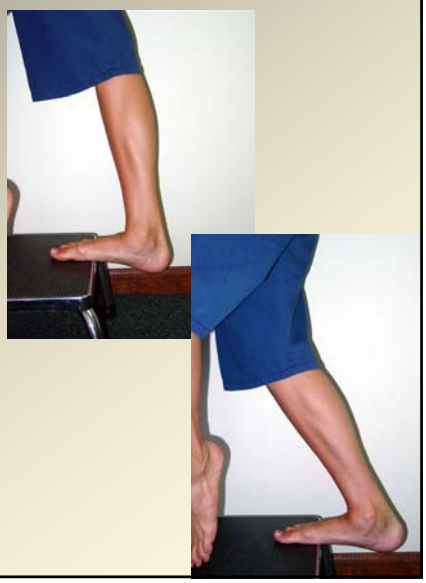
- You must take pressure off the plantar fascia:
  - Easiest way to do this is with a heel lift:
    - Typically 5-10mm is sufficient.
  - Treat both sides.
- Stretch the Achilles tendon, both gastrocnemius and soleus.
- Stretch the plantar fascia.
- Strengthen the intrinsic foot muscles.

Unload the plantar fascia

- Very important to relieve the tension on the plantar fascia.
- Can be done multiple ways, but heel lift is often easiest:
  - This drops the forefoot during weight bearing, shortening the distance between the metatarsals and calcaneus
  - Secondarily relieves tension on the Achilles
- Should be done from a horizontal, not sloping (such as a high-heeled shoe would do), position.

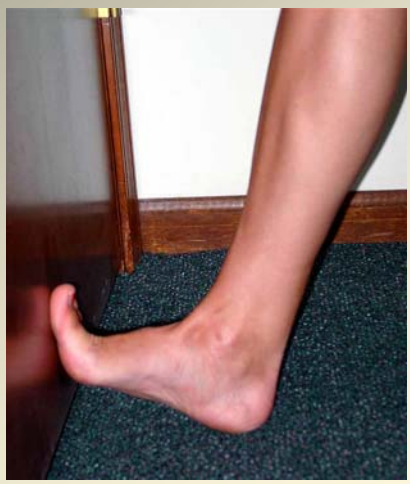
Stretch the Achilles tendon

- Possibly the most important aspect of treatment.
- Remember to stretch both gastroc (knee straight) & soleus (knee bent)
- Stretches should be held for 20-30s, repeated three times, both sides, regardless of symptoms.
- Consider using a step &/or activated stretching (muscle energy)



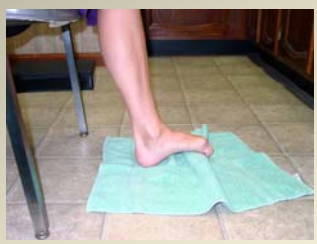
Plantar fascia stretch

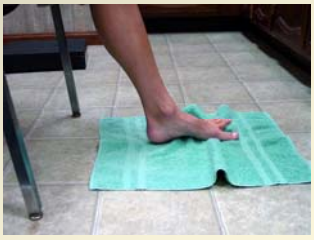
- Direct stretching of plantar fascia is often recommended
- I am not always sure how beneficial this is, or if the therapeutic benefit is really in stretching the fascia, or in some of the associated muscles supporting the arch.
- Stretch held same as previous ones.



Strengthen intrinsic foot muscles

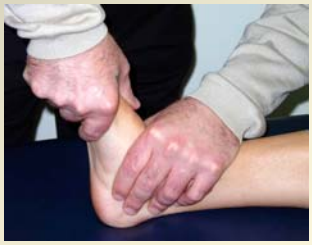
- I find this very helpful in reconditioning muscles to help support the arch.
- Does more than just intrinsic muscles, also includes the flexor hallucis longus, flexor digitorum longus, and maybe tibialis posterior.





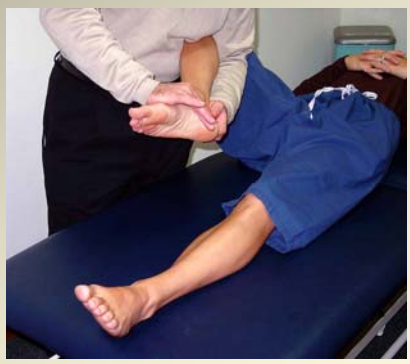
OMT: navicular/cuboid

- Correct dysfunction of the arch, especially the navicular, which tends to be rotated medially.
- Functional approach:
  - Start from position of ease.
  - Add compressive force.
  - Take joint to, and through, the original barrier, maintaining the compressive force.



OMT: tibiotalar joint

- Often also restricted with talus held in relatively valgus position.
- Many ways to do this: this is an articulatory technique:
  - Contralateral elbow in popliteal fossa
  - Hand grasp calcaneus and anterior process of talus.
  - Lean cephalad, elbow acting as fulcrum to distract the talus from the mortise.
  - Gently rock the talus until articulation and release occurs.



OMT: tibial torsion

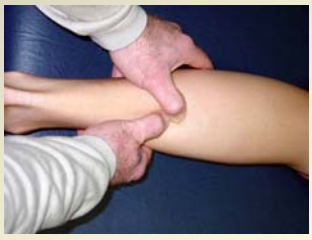
- Notice that we are working up the kinetic chain. Obviously any somatic dysfunction should be treated, especially in the lumbar spine and pelvis.
- Functional technique:
  - Start from position of ease, typically ext rot.
  - Apply compressive force.
  - Move tibia to and through barrier while extending the knee.

Fascial stripping

- This is something that has been modified from Steven Typaldos, DO.
- It is very painful, but very effective, and they often stand up feeling much better.
- Treatment is done once per week, and typically takes ~6 treatments, sometimes less.

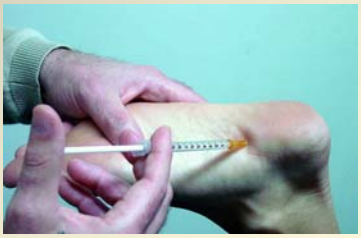
Fascial stripping



So what do we do?

- Make sure it is plantar fasciitis!
- Treat the existing somatic dysfunction on the first visit.
- Heel lift.
- HEP consisting of stretching and strengthening as described.
- Then either:
  - Fascial stripping protocol
  - Injection protocol



E Cigarettes:
The Good, The Bad and The Ugly

Tracey O'Neal Hooker, D.O., MHA

Learning Objective:

Discover FDA approved smoking cessation devices and the implications of recommending non-approved devices.

Discuss public health concerns as well as personal health concerns with respect to E-cigarettes.

Reveal how marketing and "big tobacco" has shaped perceptions of E-cigarettes.

References

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American Cancer Society (2014) Regulating E-cigarettes. *Cancer*. Retrived from http://onlinelibrary.wiley.com/doi/10.1002/cncr.28872/abstract

Burstyn, I. (2013) Peering through the mist: What does the chemistry of contaminants in electronic cigarettes tell us about health risks. Technical report. Retrieved from http://www.google.com/url?url=http://publichealth.drexel.edu/~/media/files/publichealth/ms08.pdf&rct=j&frm=1&q=&esrc=s&sa=U&ei=HCJBVNGbA63bsAT2lIKABw&ved=0CBQQFjAA&usg=AFQjCNHE2_iwvPxhWJyHMxP9uxXru8pJdA

Harrison, B. (2014). Here Come Electronic Cigarettes, and What's Old is New Again. Non-published but received at a CSOEM conference in Spring 2014

Kandra K. et al (2014) Physcians' Attitudes and use of E-cigarettes as cessation devices, North Carolina, 2013. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/25072466

Palazzolo, D. (2013) Electronic Cigarettes and Vaping: A New Challenge in Clinical Medicine and Public Health. A Literature Review. *Frontiers in Public Health.* Retrieved from: http://www.ncbi.nlm.nih.gov/pubmed/24350225

Benign Prostatic Hyperplasia Update

Salvador E. Peron, M.D.

Learning Objective:

Discuss the clinical manifestations of benign prostatic hyperplasia (BPH).

Discuss diagnosis of BPH.

Discuss treatment of BPH.

NOTES

SUNDAY, NOVEMBER 15, 2014

7:00 a.m.	Registration
7:00 a.m.-9:00 a.m.	Breakfast Buffet Served – ***West Pathway***
7:50 a.m.-8:00 a.m.	Opening Remarks - ***Orange/Nile Rooms***
8:00 a.m.-9:00 a.m.	Improving Adherence in Type 2 Diabetes Mellitus *Allison M. Petznick, D.O.*
9:00 a.m.-10:00 a.m.	Advancements in Concussion Management *Matthew C. Petznick, D.O.*
10:00 a.m.-11:00 a.m.	Skin and Soft Tissue Infections *Michael S. Blank, M.D.*
11:00 a.m.-12:00 p.m.	Breast Cancer Update 2014 *Helen Mabry, M.D.*

Or

8:00 a.m.-1:00 p.m.	ACLS/BLS Recertification ***- Aloeswood Room*** *Brent C. DeVries, D.O. & Dave Degnan, Fire Chief*

Improving Adherence in Type 2 Diabetes Mellitus

Allison M. Petznick, D.O.

Learning Objectives:

Provide evidence for importance of high glucose control.

Identify barriers preventing glucose control.

Define interventions for improving glucose control.

Improving Adherence in Type 2 Diabetes Mellitus

ALLISON PETZNICK DO
NOMS FAMILY MEDICINE
SANDUSKY, OH

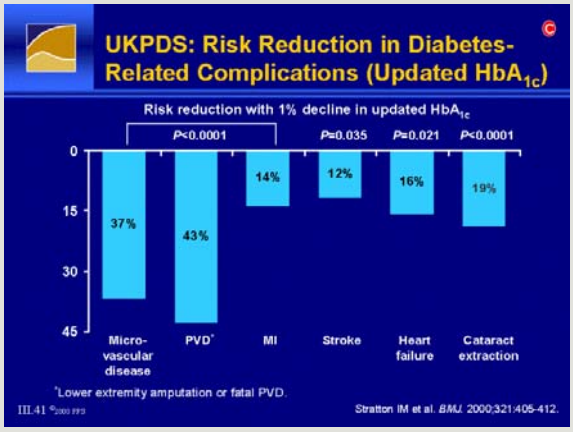
Objectives

Evidence for importance of tight glucose control

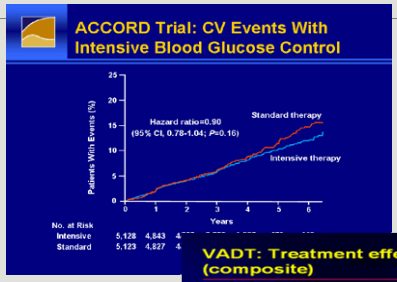
Barriers preventing glucose control

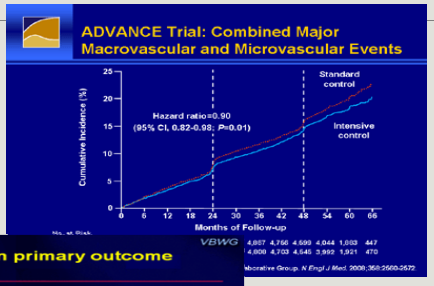
Interventions for improving glucose control

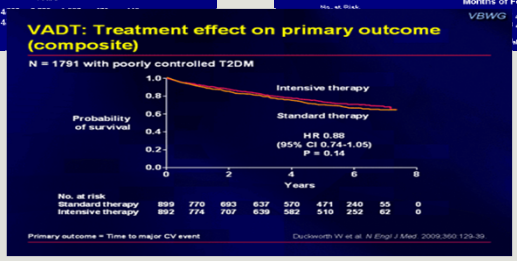
UKPDS Trial



ACCORD, ADVANCE, VADT







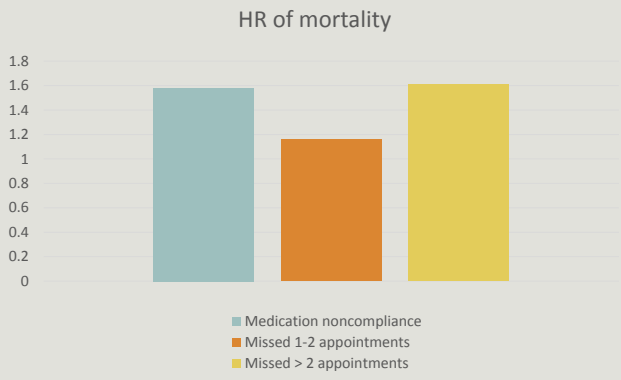
Barriers to achieving glucose control

Physican related	Patient related
Concern for side effects Time constraints Insurance denial of medication use	Difficulty with transportation Cost of medications Lack of education or understanding Stress in social/work life Inconvenience or complexity of regimen Side effects from medications Memory issues and lack of routine Depression Lack of trust with their provider or medications

Impact of treatment non-compliance on mortality

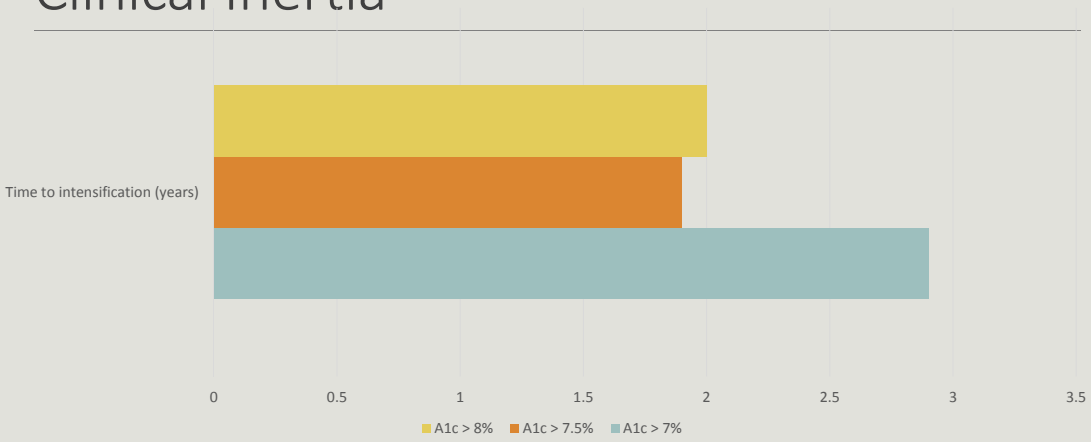
15,984 patients with type 2 diabetes

- 39% patients missed at least one appointment



Currie CJ. The impact of treatment non-compliance on mortality in people with type 2 diabetes mellitus. *Diabetes Care.* 2012; 35: 1279-1284

Clinical Inertia



Khunti K. Clinical inertia in people with type 2 diabetes. *Diabetes Care.* 2013;

DAWN study

85% patients experience severe stress at the time of diagnosis and 50% still have considerable stress 15 years after diagnosis

Only 19.4% (DM-1) patients and 16.2% (DM-2) report they completely carried out all recommendations the provider had given them

However 88.8% rated quality of relationship with physician as good

SO WHAT IS THE PROBLEM????

Funnell MM. The diabetes attitudes, wishes, and needs (DAWN) study. *Clinical Diabetes*. 2006; 24: 154-155.

Too much is not a always a good thing…..

Overwhelming physicians and patients with goal oriented care

A1c < 7%

Exercise

Eye exam

Smoking cessation

BP < 140/80

Healthy diet

Foot exam

Influenza vaccine

LDL < 100

Weight

Pneumonia vaccine

PVR

HDL > 40 (male) > 50 female)

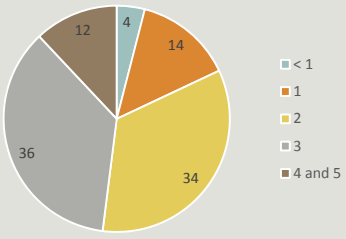
Depression screening

Cost

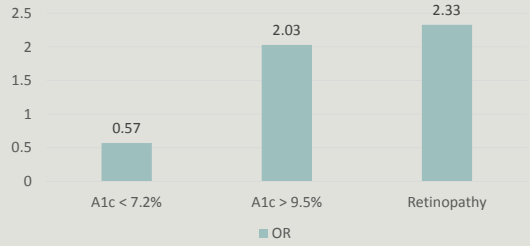
Health literacy

The degree to which individuals have the capacity to obtain, process, and understand basic health information needed to make appropriate health decisions and services needed to prevent or treat illness.

% US adults health literacy



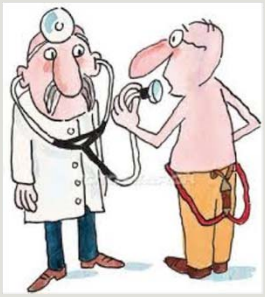
Odds ratio with inadequate health literacy



Schillinger D et al. Association of health literacy with diabetes outcomes. *JAMA*. 2002; 288: 475-482.
CDC US adults literacy scale 2003

Patient centered approach

"Providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions"



Inzucchi et al. Management of hyperglycemia in type 2 diabetes: a patient centered approach. *Diabetes Care.* 2012; 35: 1364-1379.

Patient centered measures

Health behaviors
- Healthy eating, medication taking, physical activity, not smoking

Quality of life
- Emotional and physical health

Self management goals
- Set specific goals

Patient centered care
- Patient engagement, shared decision making, patient preferences

Glasglow et al. Where is the patient in diabetes performance? The case for including patient centered and self management measures. *Diabetes Care*. 2008; 31: 1046-1050.

5C Intervention

Construct a problem definition
- What is the patient's concern/problem area?

Collaborative goal setting
- Set specific, measurable, action oriented, and realistic goals

Collaborative problem solving
- Identify barriers and formulate a strategy for success

Contracting for change
- Track outcomes and reward successes

Continuing support

Peyrot M et al. Behavioral and psychosocial interventions in diabetes: a conceptual review. *Diabetes Care* 2007: 30; 2433-2440

Motivations, Goals, Barriers

Focus on ACTIONS, not outcomes

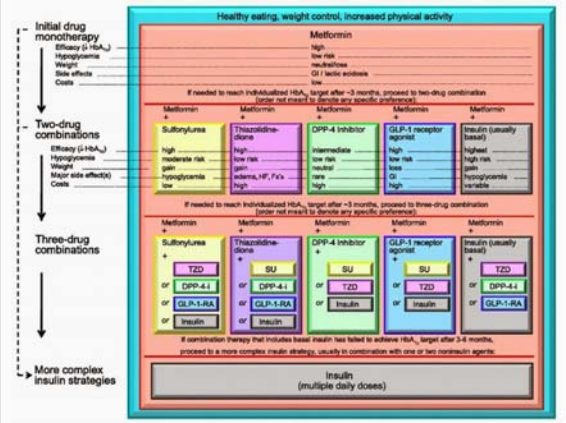
Define barriers

Verbalize goals

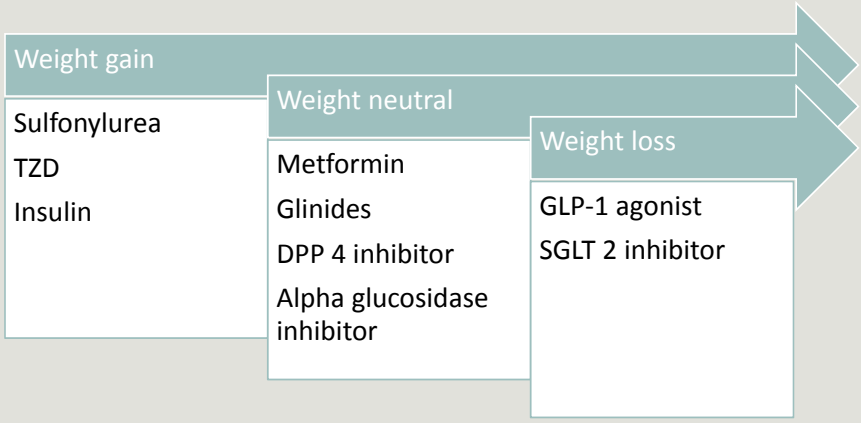
Provide reinforcement and follow up

Funnell MM et al. The diabetes attitudes, wishes, and needs study (DAWN). *Clinical Diabetes*. 2006; 24: 154-155.

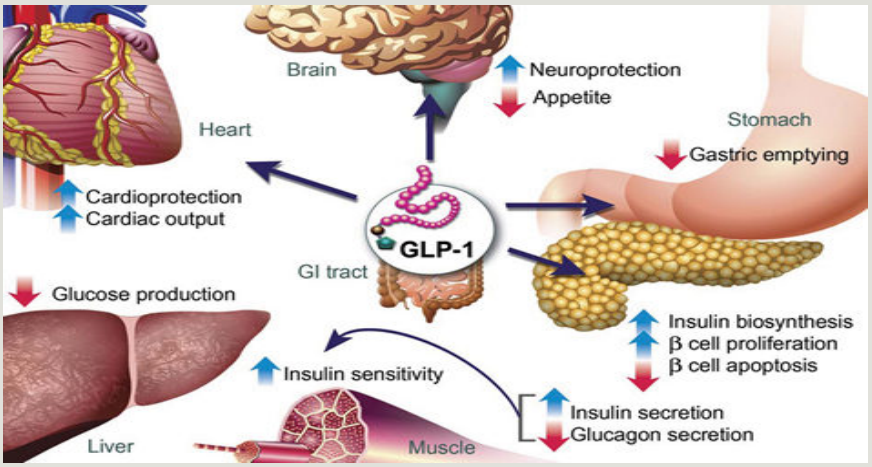
Simplify the regimen



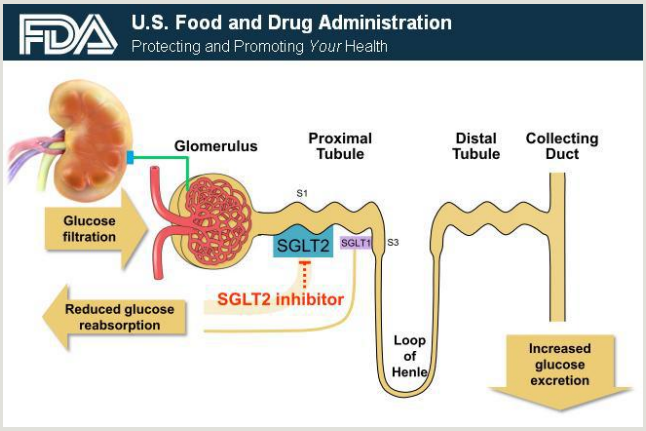
New classes of diabetes medications



GLP-1 agonists



SGLT 2 inhibitors



Take home points

Intensive glucose control is associated with decreased risk for diabetes related complications
- Goal should be tailored to the patient (A1c 6-8%)

This is only effective if the patient understands and adheres to treatment plan

Don't allow yourself or the patient to be overwhelmed by health measures

Focus on ACTIONS… Not outcomes

Simplify the treatment regimen if possible

Advancements in Concussion Management

Matthew C. Petznick, D.O.

Learning Objectives:

Identify the current hypothesis of concussion pathophysiology.

Gain the ability to diagnose and predict protracted recovery from a concussion.

Discuss current concepts in concussion recovery and treatment.

ADVANCMENTS IN CONCUSSION MANAGEMENT

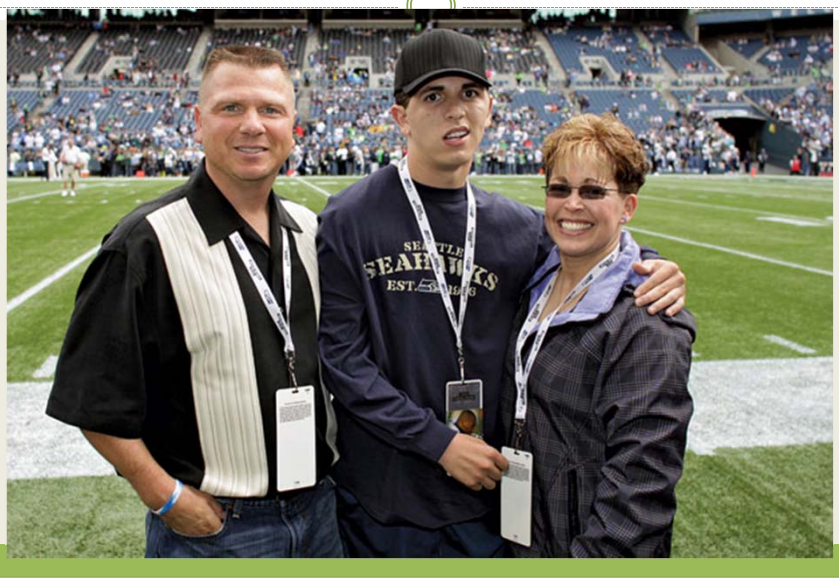
DR MATTHEW PETZNICK D.O
BOARD CERTIFIED SPORTS MEDICINE
BOARD CERTIFIED FAMILY MEDICINE

OBJECTIVES

- IDENTIFY THE CURRENT HYPOTHESIS OF CONCUSSION PATHOPHYSIOLOGY
- GAIN THE ABILITY TO DIAGNOSE AND PREDICT PROTRACTED RECOVERY
- DISCUSS CURRENT CONCEPTS IN CONCUSSION RECOVERY AND TREATMENT

HOW DID WE GET HERE

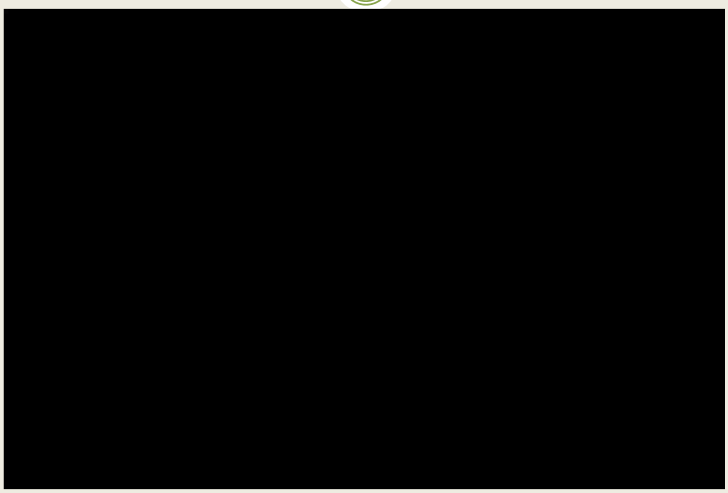
ZACHERY LYSTEDT



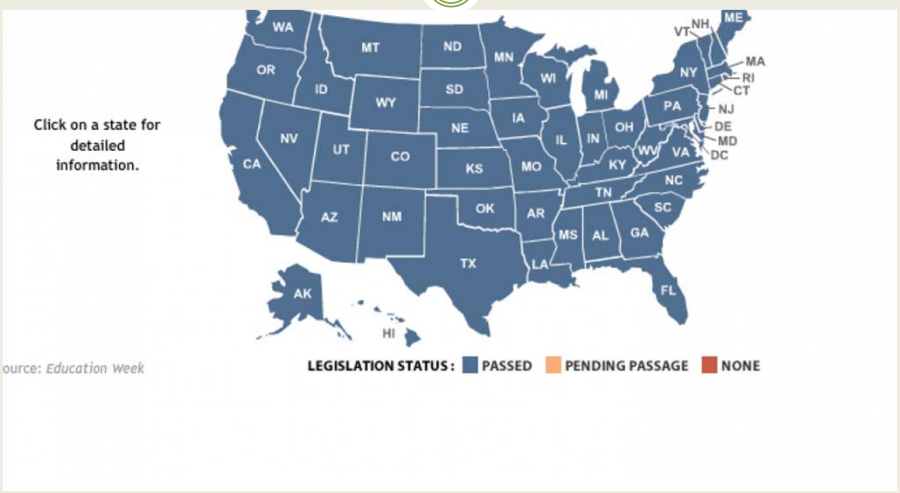
ZACHERY'S STORY

- 2006 in Junior High School
- Multiple concussions in one game
- Sustained Second Impact Syndrome during a game
- Left with significant comorbidities
  - 7 days life support
  - Unable to speak for 9 months
  - 2 years of feeding tube
- May 16, 2009 first state to pass Lystedt Law
  - Washington State

PLAY THAT CHANGED EVERYTHING



CURRENT LAWS PASSED



OHIO LAW

- Ohio Bill 143
- April 26, 2013
- Online training for Coaches and referees
- Information provided to parents
- No return to sport same day of diagnosis/suspected of concussion
- MD or DO for clearance

NFL making changes

NCAA Follows NFL Lead

- December 2010
  - NCAA now making changes in response to what NFL has done
    - No return to play same day of concussion
    - Must be cleared my doctor

HEIGHTENED AWARENESS

- More
  - CDC-
  - Coach
- Media
  - Local
  - Natio
- Better

USA TODAY

Testing helps change the ga youth cc

Updated 5h 56m ago

By Erik Brady, USA

FAIRFAX, Va. – knocked in the h Fairfax High Sch until passing a c evaluation that i showing she wa function, same a Washington Red

Athletes at the 25 Fairfax County, a Washington, take used by NFL play one tool doctors use to tell when i field. That's cruci concussion wher first one is dange

THURSDA

concussior p.m. ET

But baseline test because they ge more quickly, say administrator of t training program. trainers must err students away fr

"The NFL is in th Almquist says. "V business."

PBS NEWSHOUR

Q&A: Should soccer players wear helmets? Top neurosurgeon weighs in on concussion risks

BY PBS NEWSHOUR *October 25, 2014 at 12:19 PM EDT*

Dr. Robert Cantu, one of the nation's top experts on youth concussions says collisions and hard falls sustained during soccer games are problematic because kids' brains are still developing. Credit: NewsHour

Member (NCAA) athletes online T

The stud Harvard determi manage report ol in place.

"As scie short- a the need authors

Newsw

In April establist every m to be pu

One of the nation's leading experts on concussions in youth sports, Dr. Robert Cantu, chief of neurosurgery at Emerson Hospital and co-director of Boston University's Center for the Study of Traumatic Encephalopathy, has teamed up with World Cup champion Brandi Chastain to advocate the end of headers in youth soccer for kids aged 14 and under.

While Cantu acknowledges the science connecting soccer with brain injury is limited, he still

STATISTICS

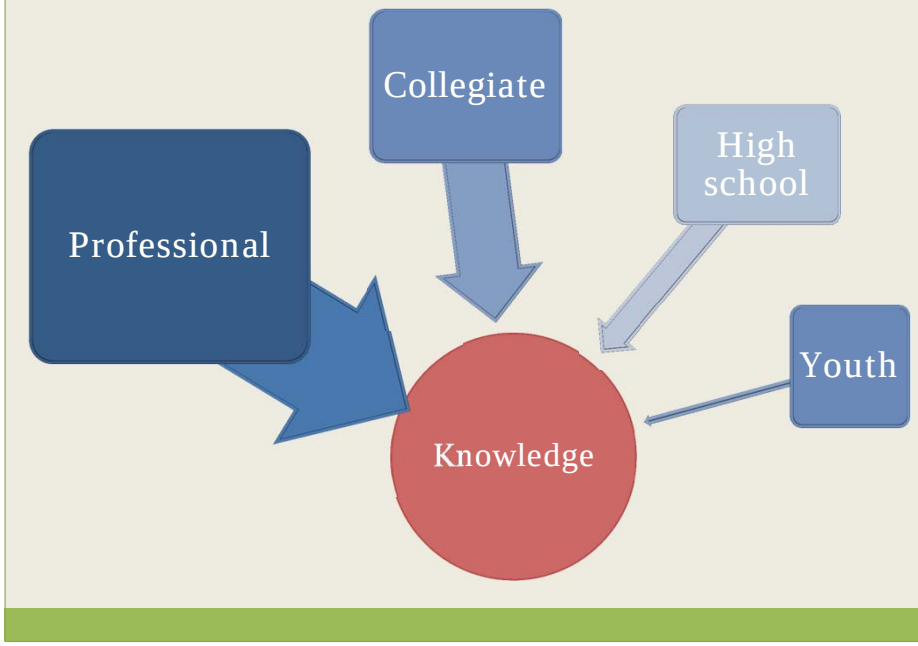
- 1.6-3.8 million concussions a year (kutcher 2010 sports health)
- 5-9% of all sports related injuries (AMSSM)
- As many of 50% go unreported (AMSSM position statement 2012)
- 2-5.8 x increase risk of another concussion

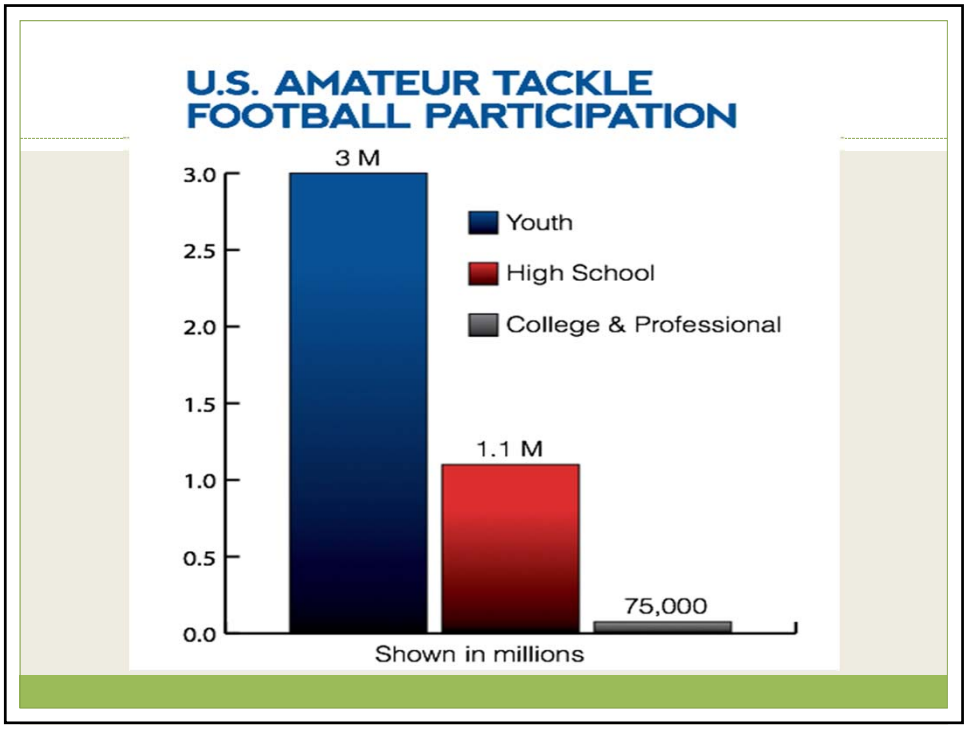
KNOWLEDGE

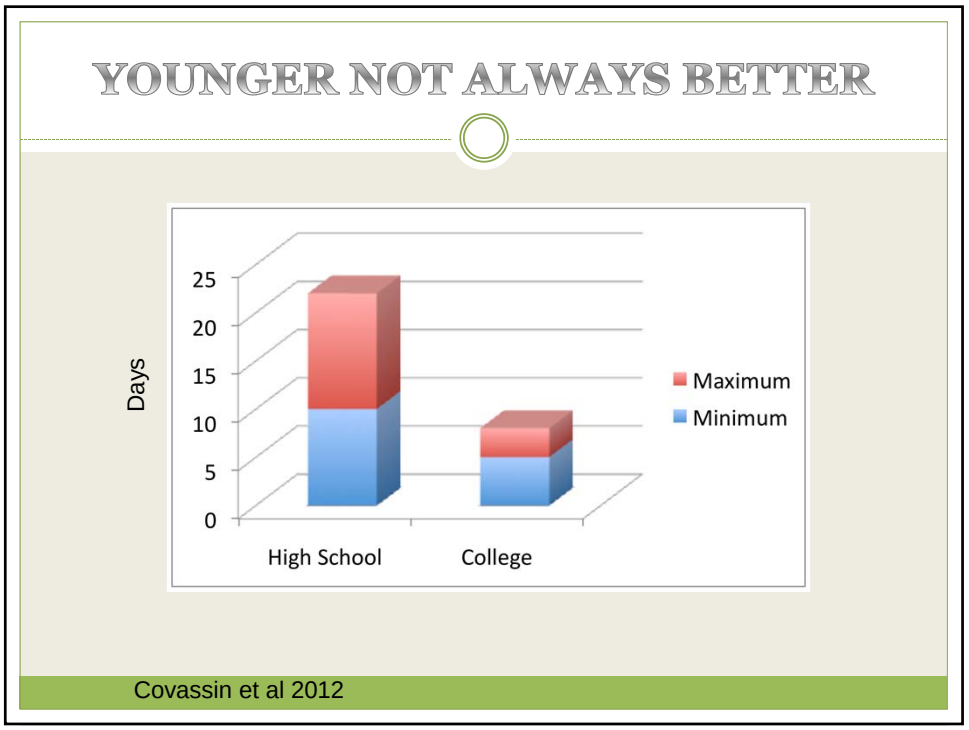
CONCUSSION RATES PER SPORTS

Table 2 Concussion rates per 1000 athlete exposures

Sport	Powell 1999	Schultz 2004	Hootman 2007	Gessel 2007	Lincoln 2011	Marar 2012
Level	High school	High school	College	High school	High school	High school
Years studied	1995–1997	1996–1999	1988–2004	2005–2006	1997–2008	2008–2010
Baseball	0.05	0.11	0.07	0.05	0.06	0.05
Softball	0.10	0.10	0.14	0.07	0.11	0.16
Boys' basketball	0.11	0.10	0.16	0.07	0.10	0.16
Girls' basketball	0.16	0.17	0.22	0.21	0.16	0.21
Boys' soccer	0.18	0.23	0.28	0.22	0.17	0.19
Girls' soccer	0.23	0.13	0.41	0.36	0.35	0.34
Football	0.59	0.33	0.37	0.47	0.60	0.64
Field hockey	0.09	NR	0.18	NR	0.10	0.22
Volleyball	0.02	NR	0.09	0.05	NR	0.06
Wrestling	0.25	0.09	0.25	0.18	0.17	0.22
Ice hockey			0.41			0.54
Overall		0.17	0.28	0.43	0.24	0.24




U.S. AMATEUR TACKLE FOOTBALL PARTICIPATION
3 M
1.1 M
75,000
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Youth
High School
College & Professional
Shown in millions


YOUNGER NOT ALWAYS BETTER
Days
25
20
15
10
5
0
High School
College
Maximum
Minimum
Covassin et al 2012

IS STARTING YOUNG APPROPRIATE

Proper Training- skills gained

Team building

Exposure game situations

YOUTH FOOTBALL

Hammer or the Nail?

- Vianno 2007

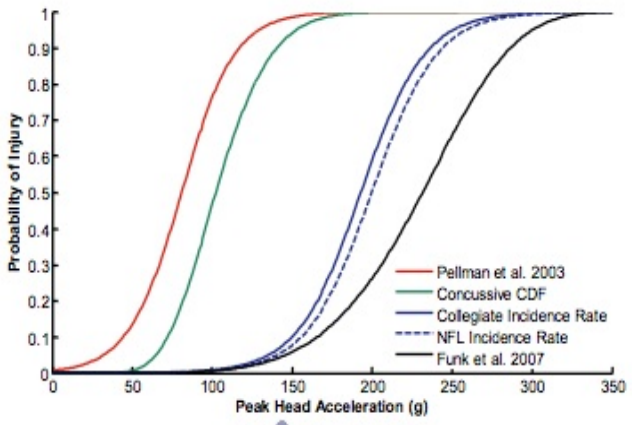
Struck

Striki

PATHOPHYSIOLOGY of CONCUSSION

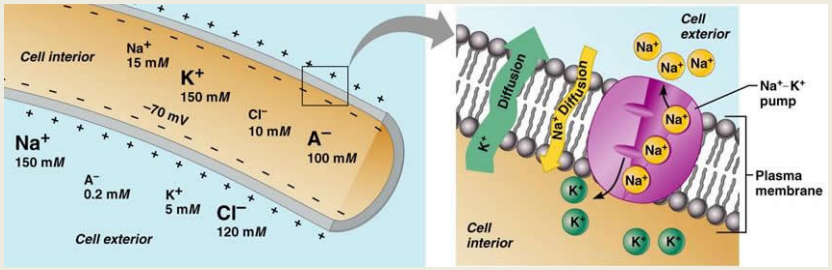
FORCES TO CAUSES CONCUSSION

Concussion Risk R(a) = Collegiate Incidence Rate Curve



VT Helmet Study
http://www.sbes.vt.edu/nid.php

NORMAL AXON GRADIENT



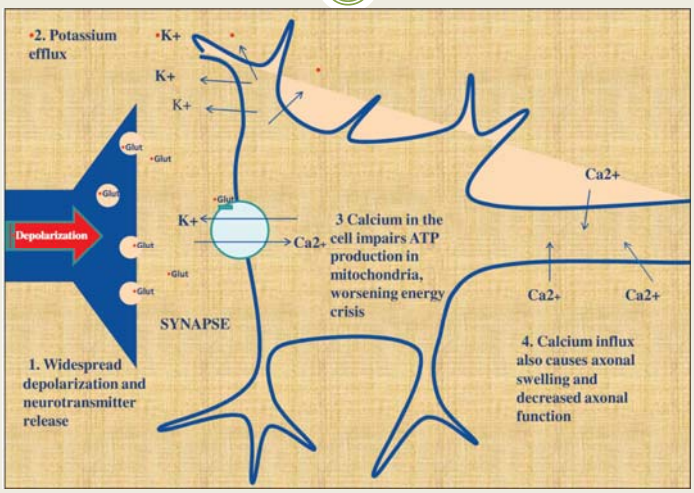
LEADING HYPOTHESIS

Injury
- Rotational deformity leading to membrane deformation
- Pressure wave

Nerve
- Na+ moves into cell, K+ out
- Glutamate release (excitatory NT) – binds to NMDAr causing calcium to accumulate

Random Depolarization
- Spreading depression
- Ca++ increases inside cell
- more glutamate release
- Mitochondrial dysfunction (calcium overload)

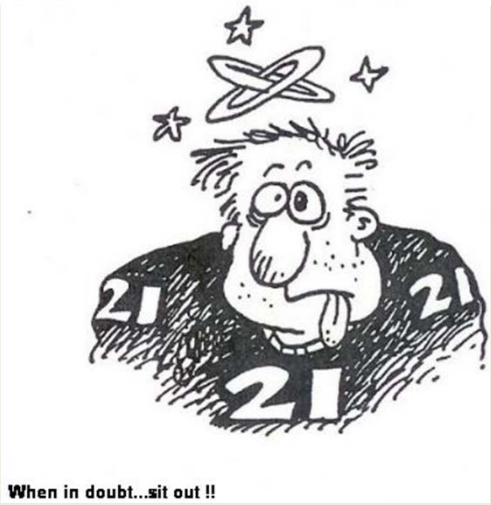
Miss-Match
- Decrease blood flow and unable to re-establish gradient
- No glucose
- Rely on glycolysis



ON-FIELD PRESENTATION

SYMPTOMS

- HA (MC)
- Fogginess
- Dizzy
- Nausea
- Amnesia
- LOC <10%
- Change mood
- Confusion
- Vision issues

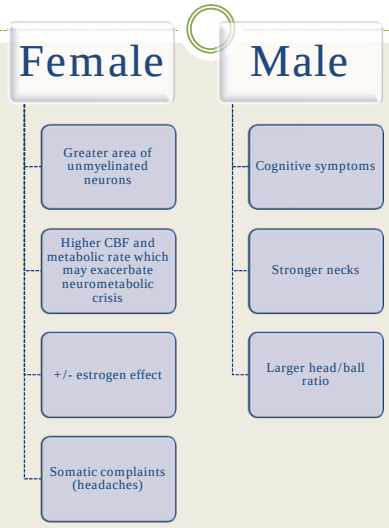


ON-FIELD SYMPTOM

- Dizziness
  - Highest predicted symptoms for protracted recovery (>10 days)
- LOC and amnesia, confusion, vomiting not significant predictor

Lau, Kontos, Collins 2011 AJSM

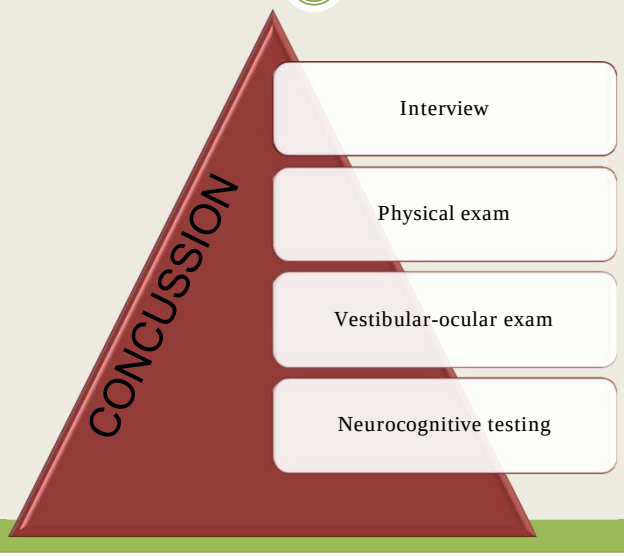
MALES VS FEMALES



Covassin et al Transl. Stroke Res. 2013

OFFICE SETTING

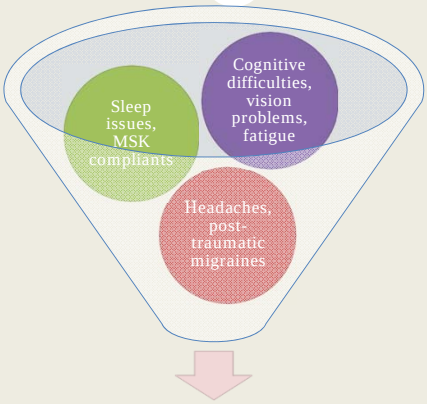
Comprehensive Approach



INTERVIEW

- Detailed
- PHMx:
  - Migraines, LD/ADHD, prior concussions, grades, motion sickness, etc
- FHX:
  - History of migraines
  - Memory issues

FIRST WEEK AFTER CONCUSSION



Kontos et al 2012 AJSM

NAME:_____ DOB:_____

SEVERITY RATING None 0 Mild 1 2 Moderate 3 4 Severe 5 6	POST-CONCUSSION SYMPTOM SCALE Modified from ImPACT			
SYMPTOMS:	DATE:	DATE:	DATE:	DATE:
HEADACHE				
NAUSEA				
VOMITING				
BALANCE				
DIZZY				
LIGHTHEADEDNESS				
SENSITIVITY TO LIGHT				
SENSITIVITY TO SOUND				
NUMBNESS OR TINGLING				
VISUAL PROLBEMS				
DROWSINESS				
FATIGUE				
FEELING SLOWED DOWN				
FOGGY				
DIFFICULTY CONCENTRATING				
DIFFICULTY REMEMBERING				
SLEEPING MORE THAN USUAL				
IRRITABILITY				
SADNESS				
NERVOUSNESS/ANXIOUS				
FEELING MORE EMOTIONAL				
TROUBLE SLEEPING				

4 SUBSETS OF SYMPTOMS


Cognitive


Sleep

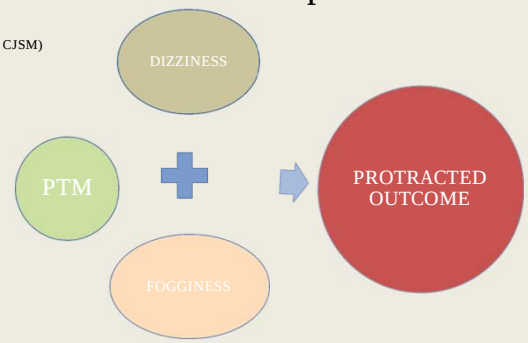

Headache/PTM

Psych Issues

Collins et al 2013 Applied Neuropsych.

SYMPTOM PREDICTORS

- Headache, nausea, photo/phonophobia 7.29 odds ratio of protracted outcome vs no headache (kontos AJSM)
- PTM protracted outcome when compared to HA
- **Fogginess** (LAU 2009 CJSM)



BIOMARKERS

BIOMARKERS

- Neuron Proteins:
  - Neuron Specific Enolase
  - Cleaved Tau proteins
- Glial Cells:
  - S-100
  - CKBB
  - Glial fibrillary acidic protein
  - Myelin basic protein

Biomarkers, Genetics, Risk factors for concussion PMR 2011

EXAM

- Neurologic exam
  - Cranial nerves
  - Memory
  - BESS Testing
- Vestibular ocular system
  - Accommodative insufficiency
  - Convergence insufficiency
  - VOR
    - Keep images in the center of the retina
- Musculoskeletal system

The Balance Error Scoring System (BESS)

Obtain Preseason Baseline Score; Compare with Post-Concussion Score[25,26]

The Balance Error Scoring System[25,26] provides a portable, cost-effective and objective method of assessing static **postural stability**. The BESS can be used to assess the effects of mild head injury on static postural stability. Information obtained from this clinical balance tool can be used to assist clinicians in making return to play decisions following mild head injury. The BESS can be performed in nearly any environment and takes approximately 10 minutes to conduct.

The balance-testing regime consists three stances on two different surfaces. The three stances are **double leg stance**, **single leg stance** and **tandem stance**. The two different surfaces include both a **firm** (ground) and **foam** surface. **Athletes' stance should consist of the hands on the iliac crests, eyes closed and a consistent foot position depending on the stance**. Shoes should not be worn.

In the **double leg stance**, the feet are flat on the testing surface approximately pelvic width apart.

In the **single leg stance** position, the athlete is to stand on the non-dominant leg with the contralateral limb held in approximately 20° of hip flexion, 45° of knee flexion and neutral position in the frontal plane.

In the **tandem stance** testing position, one foot is placed in front of the other with heel of the anterior foot touching the toe of the posterior foot. The athlete's non-dominant leg is in the posterior position. Leg dominance should be determined by the athlete's kicking preference.

Administering the BESS: Establish baseline score prior to the start of the athletic season. After a concussive injury, re-assess the athlete and compare to baseline score. Only consider return to activity if scores are comparable to baseline score. Use with Standardized Symptom Scale Checklist.

Scoring the BESS: Each of the trials is **20 seconds.** Count the number of errors (deviations) from the proper stance. The examiner should begin counting errors only after the individual has assumed the proper testing position.

Double Leg Stance Firm Surface | Single Leg Stance Firm Surface | Tandem Stance Firm Surface | Double Leg Stance Foam Surface | Single Leg Stance Foam Surface | Tandem Stance Foam Surface

Errors:
- **Moving the hands off the hips**
- **Opening the eyes**
- **Step, stumble or fall**
- **Abduction or flexion of the hip beyond 30°**
- **Lifting the forefoot or heel off of the testing surface**
- **Remaining out of the proper testing position for greater than 5 seconds**

The maximum total number of errors for any single condition is 10.

If a subject commits multiple errors simultaneously, only one error is recorded.

B.E.S.S. SCORECARD

Count Number of Errors max of 10 each stance/surface	FIRM Surface	FOAM Surface
Double Leg Stance (feet together)		
Single Leg Stance (non-dominant foot)		
Tandem Stance (non-dominant foot in back)		
TOTAL SCORES: total each column		
B.E.S.S. TOTAL: (Firm+Foam total)		

Airex™ Foam Balance Pads available at www.power-systems.com or through most sporting goods stores.

Vestibular-Ocular Screening

- Ocular:
  - Smooth pursuits
  - Saccades- horizontal, vertical
  - Convergence
  - Accommodation
- Vestibular:
  - Vestibular ocular reflex- horizontal, vertical
  - Cytokinetic screening

NEUROCOGNITIVE TESTING

ImPACT™
The Best Approach to Concussion Management
www.impacttest.com

Concussion Vital Signs®

CogSport

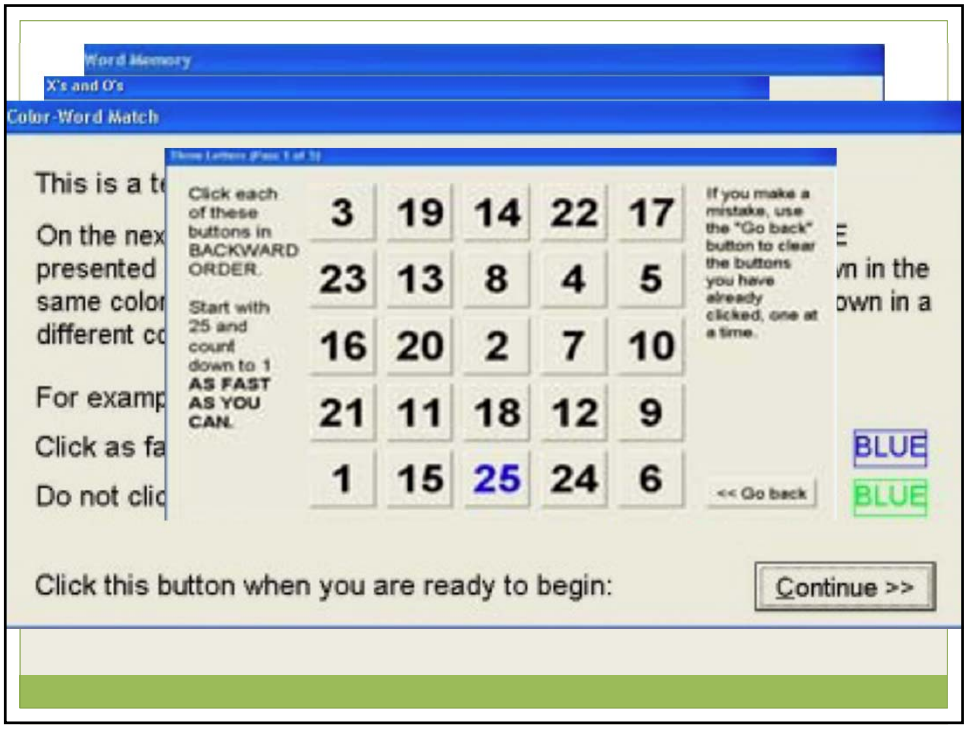
ImPACT™ Clinical Report

Sample Student

Exam Type	Baseline	Post-Injury 1	Post-Injury 2		
Date Tested	07/14/2009	08/25/2010	08/31/2010		
Last Concussion		08/23/2010	08/23/2010		
Exam Language	English	English	English		
Test Version	2.0	2.0	2.0		

Composite Scores								
Memory composite (verbal)	90	80%	**72**	17%	94	88%		
Memory composite (visual)	79	69%	**55**	8%	71	39%		
Visual motor speed composite	29.08	33%	**19.65**	<1%	33.17	34%		
Reaction time composite	0.55	93%	**0.79**	4%	0.59	56%		
Impulse control composite	8		13		13			
Total Symptom Score	0		**31**		0			

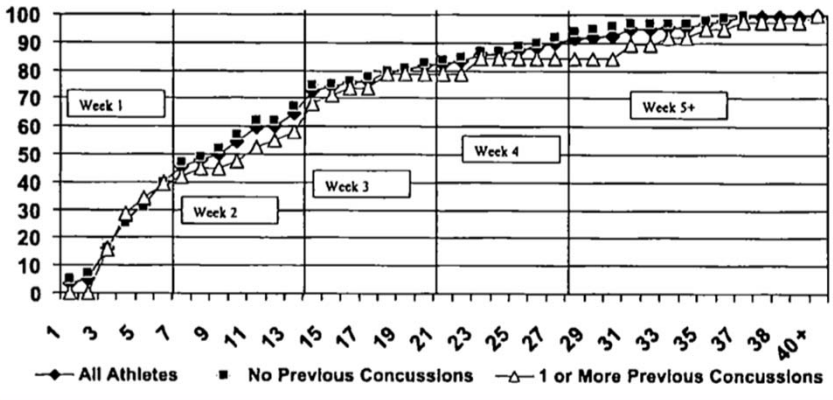
Scores in **bold RED** type exceed the Reliable Change Index (RCI) when compared to the baseline score. However, scores that do not exceed to RCI index may still be clinically significant. Percentile scores if available are listed in small type.


Word Memory
X's and O's
Color-Word Match
This is a te
On the nex
presented
same color
different co
For examp
Click as fa
Do not clic
Click each of these buttons in BACKWARD ORDER.
Start with 25 and count down to 1 AS FAST AS YOU CAN.
3 19 14 22 17
23 13 8 4 5
16 20 2 7 10
21 11 18 12 9
1 15 25 24 6
If you make a mistake, use the "Go back" button to clear the buttons you have already clicked, one at a time.
<< Go back
wn in the
own in a
BLUE
BLUE
Click this button when you are ready to begin:
Continue >>

TREATMENT


CONCUSSION SYMPTOMS: HA, fatigue, sleep, MSK, balance issues, etc
Cognitive
Sleep
Headache/PTM
Psych Issues
Vestibular/Ocular
MSK

RECOVERY AVERAGES



80% recovery in 3 weeks
20% >3 weeks (prolong recovery)

Reddy, Collins 2009

POST-TRAUMATIC MIGRAINE

Post-Traumatic Migraine

- Most common symptom reported from concussion
- Can at times be delayed (bus ride home)
- Will worsen with physical and mental activity
- Always think of other causes- cervical, vestibular-ocular, rebound medication

PTM Treatments

- Vitamins
  - Magnesium oxide 500 mg daily
  - Vitamin B2 (riboflavin) 200-400 mg daily
  - Omega fatty acids (2-4 grams daily)

Table 1 Classification of migraine preventive therapies (available in the United States)

Level A: Medications with established efficacy (≥2 Class I trials)	Level B: Medications are probably effective (1 Class I or 2 Class II studies)	Level C: Medications are possibly effective (1 Class II study)	Level U: Inadequate or conflicting data to support or refute medication use	Other: Medications that are established as possibly or probably ineffective
Herbal preparations, vitamins, minerals, and other	NSAIDs	NSAIDs	NSAIDs	Probably not effective
Petasites	Fenoprofen[a]	Flurbiprofen[a]	Aspirin	Leukotriene receptor antagonist
	Ibuprofen[a]	Mefenamic acid[a]	Indomethacin[a]	Montelukast
	Ketoprofen[a]	Herbal preparations vitamins, minerals, and other	Herbal preparations vitamins, minerals, and other	
	Naproxen[a]	Co-Q10	Omega-3	
	Naproxen sodium[a]	Estrogen	Other	
	Herbal preparations, vitamins, minerals, and other	Antihistamine	Hyperbaric oxygen	
	Magnesium	Cyproheptadine		
	MIG-99 (feverfew)			
	Riboflavin			
	Histamines			
	Histamine SC			

Abbreviation: NSAID = nonsteroidal anti-inflammatory drug.
[a] Indicates classification based on original guideline and new evidence not found for this report.

PTM Treatment

- Abortive- triptans
- Preventive
  - Antidepressants
    - Amitriptyline 10-30 mg
    - Venlafaxine
    - Sertaline
  - Anticonvulsants
    - Topamax, valproic acid
  - Beta-blockers
    - Use if unable to use antidepressants

COGNITIVE

COGNITIVE

- Think of when headaches progress/worsen as day progresses
- Fogginess, concentration, school issues
- Trying to increase dopaminergic transmission

MEDICATION

- Amantadine:
  - 100 mg qd 5 days then bid with meals
  - Must wean off
  - Efficacy of Amantadine Journal of head trauma 2013
    - 25 athletes; protracted recovery
    - Looked at ImPACT data as end point (3-4 weeks)
- Methyphendiate
  - Recommended for treatment of attention and processing speed (Meehan clinic of sports med 2011)

MOOD ISSUES

Mood Problems

- Depression/Anxiety
  - Sadness (removal from playing)
  - Stress about the future
  - Not active
- Psychotherapy
- Anti-depressants
  - SSRIs
  - Amitriptyline
  - SNRIs
- Benzo's
  - Klonopin (vestibular component)

SLEEP ISSUES

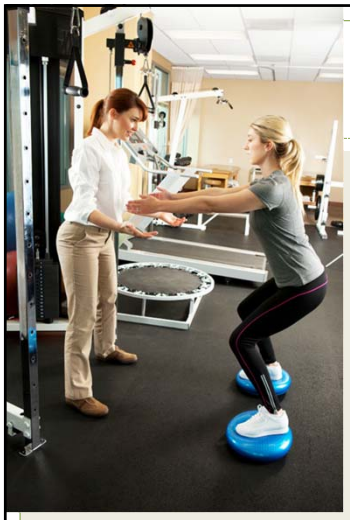
Sleep Disturbances

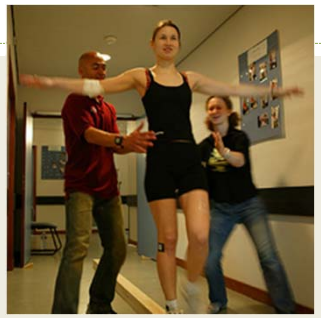
- Problems staying asleep (thoughts, HA), initiating sleep
- Think about environment
- Schedule of sleep- sleep hygiene
- Medication
  - Anti-depressants (amitriptyline)
  - Melatonin- 3-5 mg qhs
  - Anti-histamine SE
  - Non-benzodiazepine

VESTIUBULAR

Vestibular

- Dizziness, fogginess, feeling detached, motion discomfort, problems in crowded moving places, Problems in moving crowds heights
- Optokinetic hypersensitivity
- Balance= vision, somatic, vestibular
- Bess scoring
  - Tends to recover quicker in concussion than other concussive symptoms





Ocular

- Blurry vision, reading/math problems (subjects that require visual aspect)
- Smooth pursuits, saccades, accommodation, convergence

RETURN TO PLAY

CONCUSSION PROGRAM — GUIDELINES FOR POST-CONCUSSION REHAB

Stage of Rehabilitation	Physical Therapy Program	Recommended Exercises
Stage 1 Target Heart Rate : 30-40% of maximum exertion *(Max HR- Rest. HR X .30)+Rest. HR Recommendations: exercise in quiet area (treatment rooms recommended); no impact activities; balance and vestibular treatment by specialist (prn); limit head movement/ position change; limit concentration activities; 10-15 minutes of light cardio exercise.	-Very light aerobic conditioning -Sub-max isometric strengthening and gentle isotonic -ROM/ Stretching - low level balance activities	Stationary Bike; Seated Elliptical; UBE; Treadmill walking: (10-15 min) Quad sets; Ham sets; (UE) light hand weights; resistive band rowing; (LE) SLR's, Resistive bands ankle strengthening Cervical ROM exercise, Trap/LS stretching, Pec stretching, Hamstring stretching, Quad stretching, Calf stretching Romberg exercises (feet together, tandem stance, eyes open-closed); single leg balance
Stage 2 Target Heart Rate : 40-60% of maximum exertion * (Max HR- Rest. HR X .40)+Rest. HR Recommendations: exercise in gym areas recommended; use various exercise equipment; allow some positional changes and head movement; low level concentration activities (counting repetitions); 20-30 minutes of cardio exercise. (stage 1 exercises included, as appropriate)	-Light to Moderate aerobic conditioning -Light weight PRE's -stretching (active stretching initiated) -Moderate Balance activities; initiate activities with head position changes	Treadmill; Stationary Bike; Elliptical (upright or seated); UBE; (20-25 min) Light weight strength exercise (Nautilus style equipment); resistive band exercises (UE/LE); wall squats, lunges, step up/downs Any stage 1 stretching, active stretching as tolerated (Lunge walks, side to side groin stretching, walking hamstring stretch) Romberg exercises, VOR exercise (walking with eyes focused with head turns); Swiss ball exercises; single leg balance exercises
Stage 3 Target Heart Rate: 60-80% of maximum exertion *(Max HR- Rest. HR X .65)+ Rest HR Recommendations: any environment ok for exercise (indoor, outdoor); integrate strength, conditioning, and balance/proprioceptive exercise; can incorporate concentration challenges (counting exercises, MRS equipment/ visual games) (stage 1&2 exercises included, as appropriate)	-Moderately aggressive aerobic exercise -All forms of strength exercise (80% max) -active stretching exercise -Impact activities running, plyometrics (no contact) -Challenging proprioceptive/ dynamic balance (integrated with strength and conditioning); challenging positional changes.	Treadmill (jogging); Stationary Bike; Elliptical (upright or seated); UBE (25-30min) Resistive weight training including free weights; MRS/ Functional Squat; Dynamic Strength activities Active stretching (Lunge walks, side to side groin stretching, walking hamstring stretch) Initiate agility drills (zig zag runs, side shuffle, ect…), Jumping on tramp/blocks. Higher level balance activities: ball toss on plyo floor, balance discs, trampoline; squats and lunges on BOSU ball
Stage 4 (Sport Performance Training) Target Heart Rate: 80% of maximum exertion *(Max HR- Rest. HR X .80)+ Rest HR Recommendations: continue to avoid contact activity, but resume aggressive training in all environments	-Non-contact physical training -Aggressive strength exercise -Impact activities/ plyometrics -Sport Specific Performance Training	Program to be designed by Sport Performance Trainers Graded Treadmill testing Interval training Sport Specific drills/training
Stage 5 (Sport Performance Training) Target Heart Rate: Full exertion Recommendations: Initiate contact activities as appropriate to sport activity; full exertion activities for sport activities	-Resume full physical training activities with contact -Continue Aggressive strength/ conditioning exercise -Sport specific Activities	Program to be designed by Sport Performance Trainers Practice and game intensity training Sport specific activities

* Target Heart Rates calculated by Karvonen's equation : Max HR (220-Age) – Resting HR X Target Percentage + Resting HR

HOW MANY IS TOO MANY

HOW MANY IS TOO MANY

- Prior concussion possibly lower threshold for future concussions
  - 2-5.8 x risk for subsequent concussions
- >2 concussion demonstrate longer return to baseline then history of athlete with 1 concussion (elbin et al 2013 transl. stroke res.)
- Prior history of concussions leads to decrease NCT
- >2 concussions higher number of baseline symptoms
- Neuroimaging return to baseline about 30 days (N acetyelasparate) (Zafonate JAMA 2011)

PREVENTION

NOTHING HAS BEEN PROVEN TO PREVENT CONUSSION

- Helmets/helmet add-ons
  - Protect skull fracture
- Mouth guards:
  - Dental protection

Skin and Soft Tissue Infections

Michael S. Blank, M.D.

Learning Objectives:

Review common skin and soft tissue infections.

Provide guidance in managing SSTI.

Review antibiotics and discuss newer antibiotics available.

Skin and Soft Tissue Infections

Michael Blank, MD

Objectives

- Review common skin and soft tissue infections
- Provide guidance in managing SSTI
- Review antibiotics and discuss newer antibiotics available

Skin and Soft Tissue Infections

Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America

Dennis L. Stevens,[1] Alan L. Bisno,[2] Henry F. Chambers,[3] E. Patchen Dellinger,[4] Ellie J. C. Goldstein,[5] Sherwood L. Gorbach,[6] Jan V. Hirschmann,[7] Sheldon L. Kaplan,[8] Jose G. Montoya,[9] and James C. Wade[10]

Clinical Practice Guidelines by the Infectious Diseases Society of America for the Treatment of Methicillin-Resistant *Staphylococcus Aureus* Infections in Adults and Children

Catherine Liu,[1] Arnold Bayer,[3,5] Sara E. Cosgrove,[6] Robert S. Daum,[7] Scott K. Fridkin,[8] Rachel J. Gorwitz,[9] Sheldon L. Kaplan,[10] Adolf W. Karchmer,[11] Donald P. Levine,[12] Barbara E. Murray,[14] Michael J. Rybak,[12,13] David A. Talan,[4,5] and Henry F. Chambers[1,2]

Skin and Soft Tissue Infections

- Cellulitis
- Impetigo
- Erysipelas
- Abscess
- Animal bite*
- Human bite*
- Surgical site infection*
- Necrotizing fasciitis*

* Not to be covered in this lecture

Cellulitis

- Non necrotizing inflammation of the skin and subcutaneous tissues, usually from acute infection
- Cellulitis usually follows a breach in the skin, although a portal of entry may not be obvious; the breach may involve microscopic skin changes or invasive qualities of certain bacteria
- Cellulitis has been classically considered to be an infection without formation of abscess (nonpurulent), purulent drainage, or ulceration

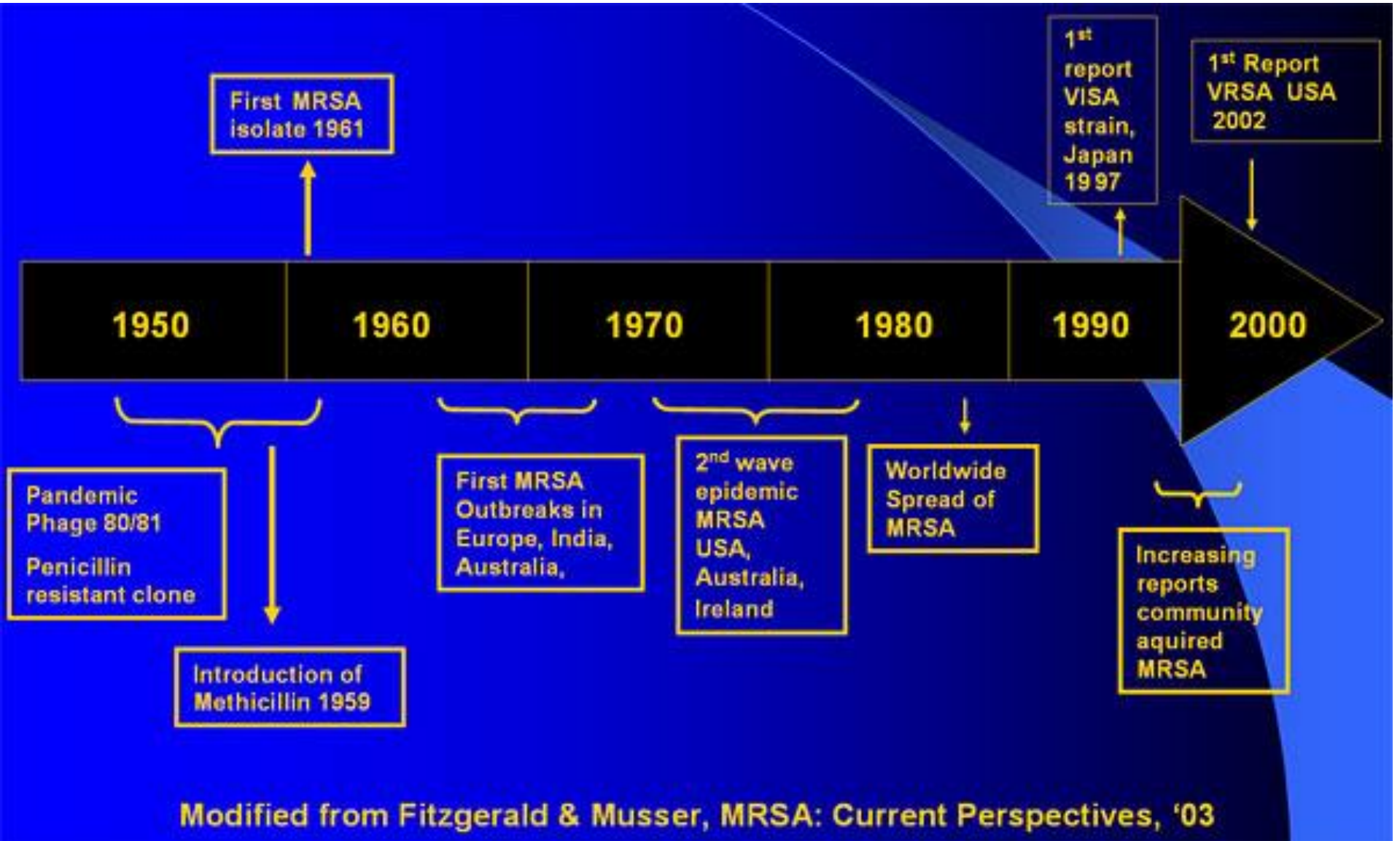
Risk Factors for Cellulitis

- Diabetes
- Elderly
- Immunodeficiency
- Cancer
- Venous stasis
- Chronic liver disease
- PAD
  - Venous insufficiency
  - Lymphatic obstruction
- CKD
- Obesity
- Inflammatory dermatoses – eczema
- Repeated cellulitis

Background

- MRSA first outbreak in a hospital in 1968
- MRSA infections were identified only in patients with recent hospitalization, surgery, renal dialysis, residence in long-term-care facilities, or IV drug use
- Past decade isolates of *S. aureus* have been found in patients without risk factors for nosocomial disease

MRSA Timeline



Community Associated MRSA [CA-MRSA]

- Genetically different from Healthcare associated MRSA [HA-MRSA]
  - Contains SCCmec IV resistance chromosome
  - Less resistant, more susceptible to more classes of antibiotics
- Carries the Panton Valentine Leukocidin (PVL) gene
  - Allows production of necrotizing cytotoxin
  - May be responsible for increased invasiveness of the organism

Characteristics of CA-MRSA

- Typically causes skin and soft tissue infections
  - Early lesions look like spider bites
  - Often present with boils, abscesses or cellulitis
- Can also cause more serious infections such as bacteremia, pneumonia, wound and surgical site infections

Comparison of HA-MRSA and CA-MRSA

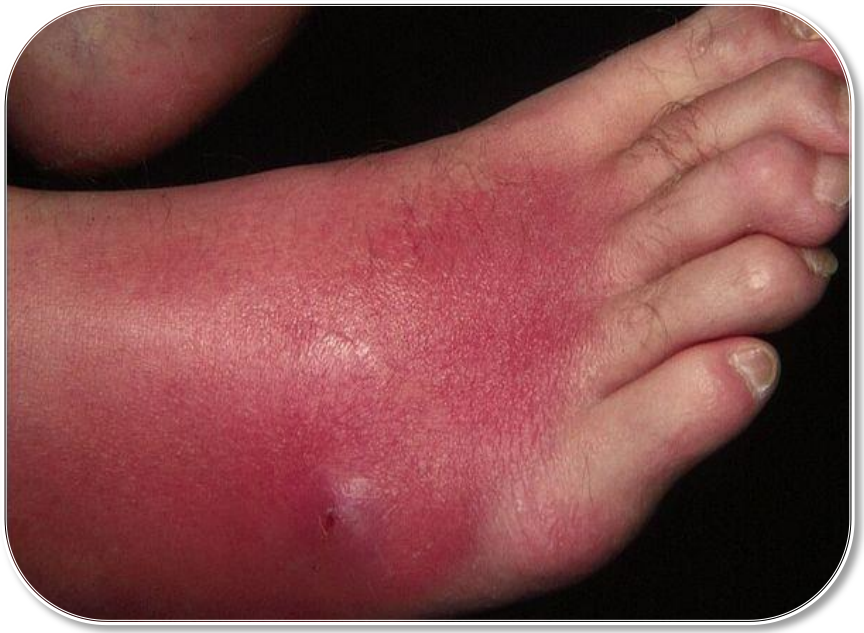
	HA-MRSA	CA-MRSA
Health care contact	Yes	No
Mean age at infection	Older	Younger
Skin and soft tissue infections	35%	75%
Antibiotic resistance	Many agents	Some agents
Resistance gene	SCC*mec* Types I, II,III	SCC*mec* Type IV, V
Strain type	USA 100 and 200	USA 300 and 400
PVL toxin gene	Rare (5%)	Frequent (almost 100%)

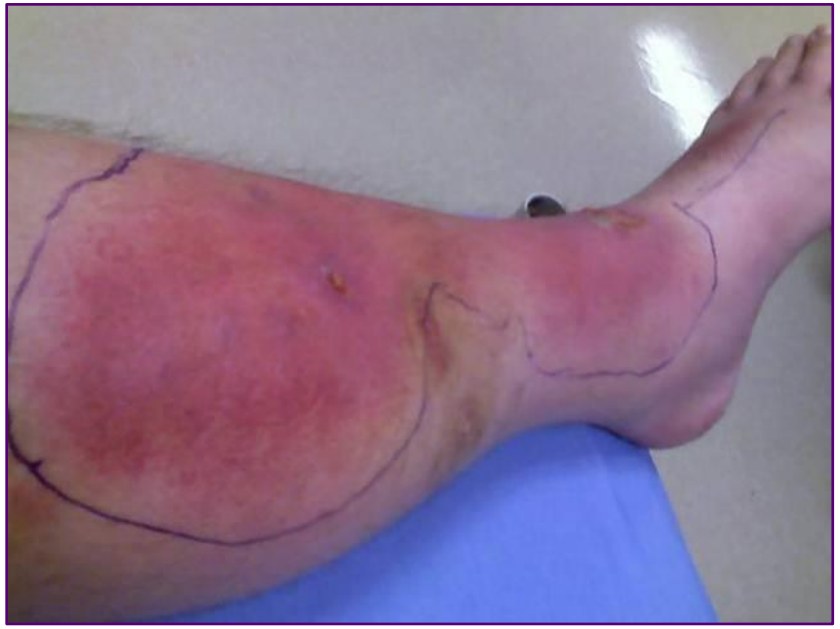
"Community Associated Methicillin Resistant StaphyococcusAureus (CA MRSA) –Guidelines for Management and Control of Transmission", PPH 42160, October 2005, Wisconsin DFHS

Purulent vs. Non purulent Cellulitis

- Non-Purulent Cellulitis
  - Cellulitis
  - Erysipelas
  - Necrotizing infection
- Purulent Cellulitis
  - Furuncle
  - Carbuncle
  - Abscess

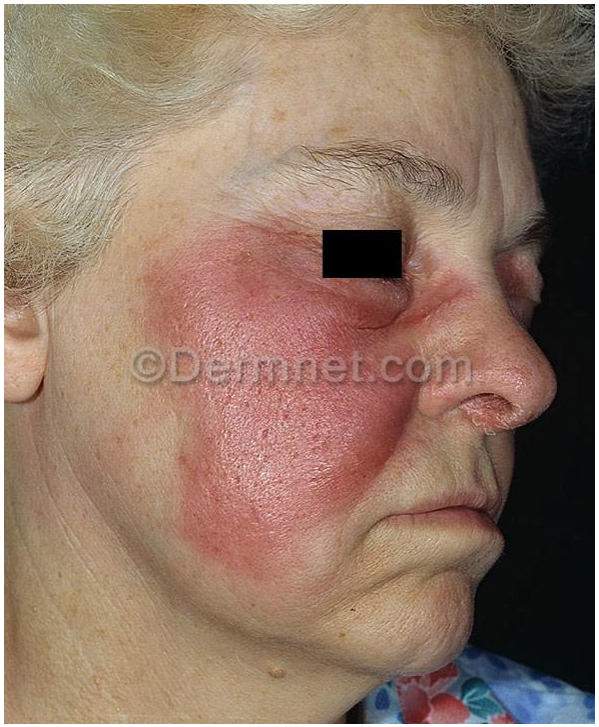
Non-purulent Cellulitis

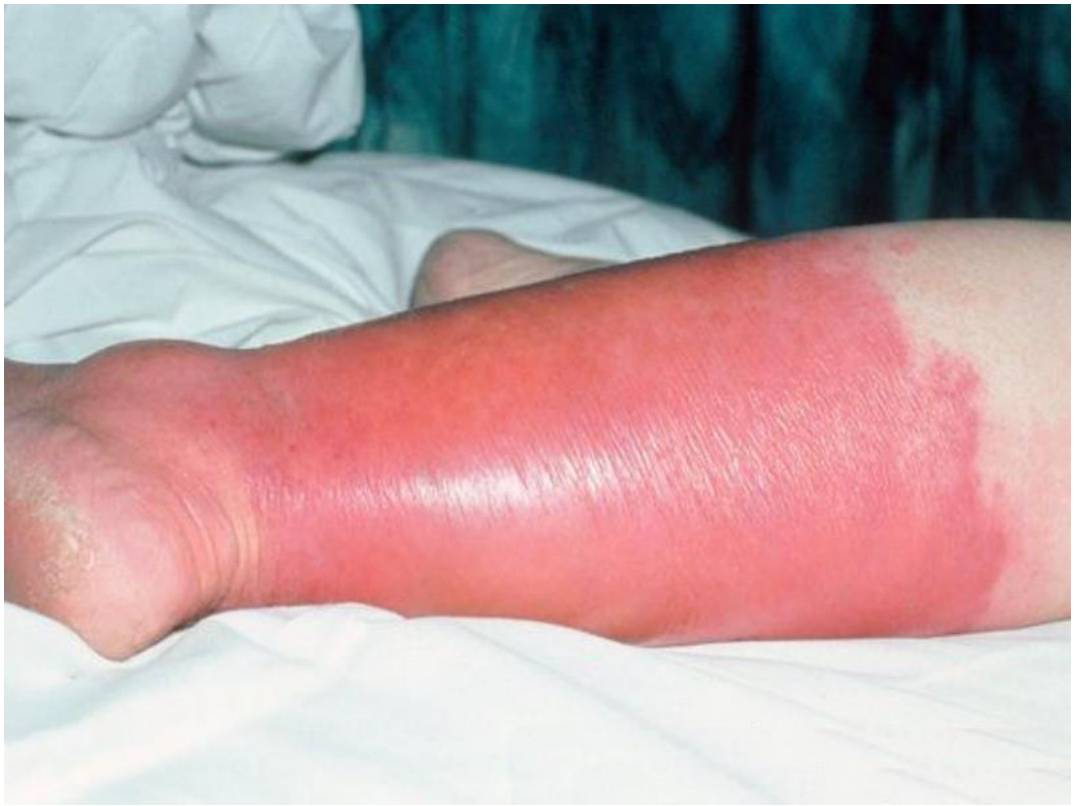




Non-purulent Cellulitis

- Erysipelas

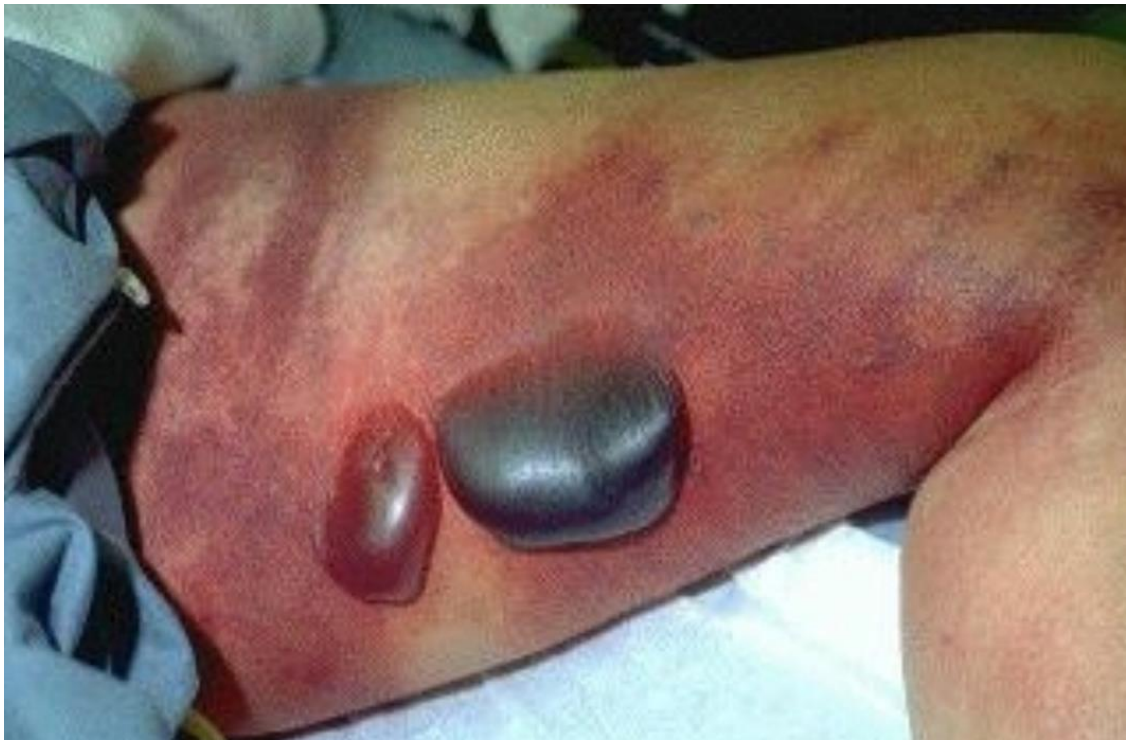


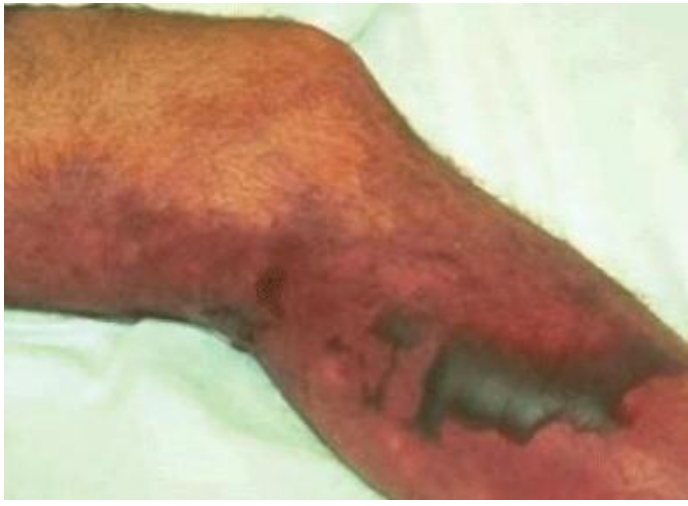


Cellulitis vs. Erysipelas

- Cellulitis
  - Dermal and sub-dermal
  - Ill-defined
  - Indolent
  - Less systemic symptoms
- Erysipelas
  - Dermal lymphatics
  - Well-demarcated
  - Acute onset
  - More systemic symptoms

Necrotizing Infection

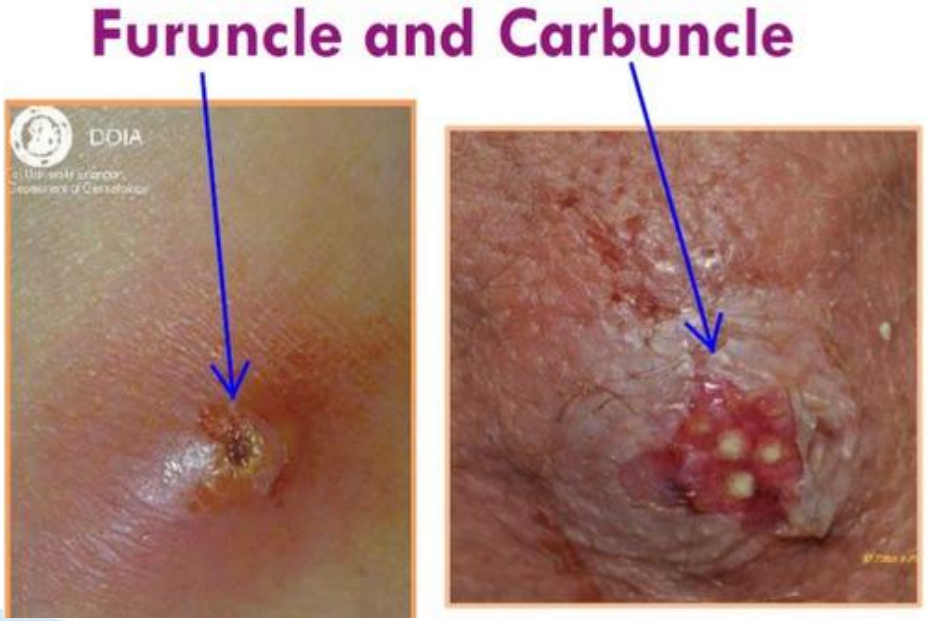


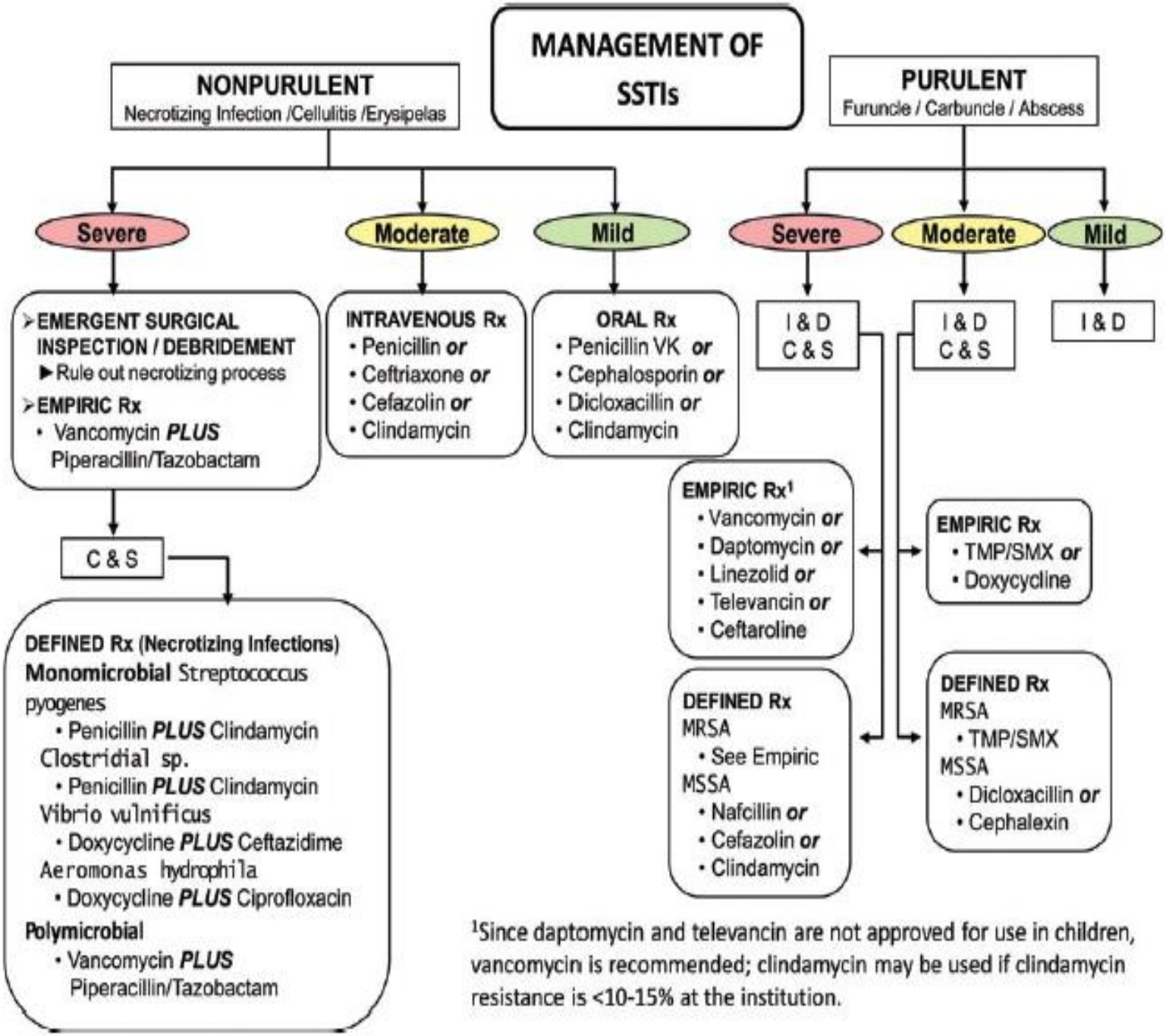


Purulent Cellulitis

- Folliculitis
  - Localized to hair follicle

- Furuncle
  - Infection of pilosebaceous unit
- Carbuncle
  - Multiple furuncles

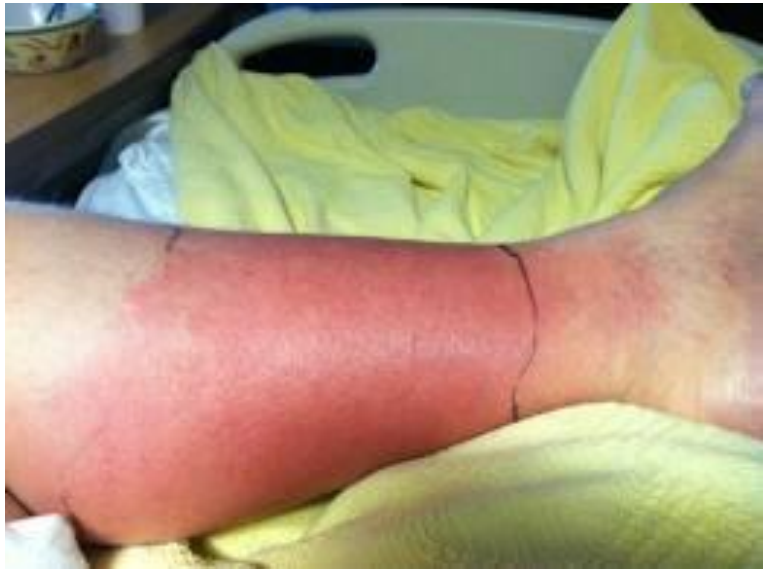




[1]Since daptomycin and televancin are not approved for use in children, vancomycin is recommended; clindamycin may be used if clindamycin resistance is <10-15% at the institution.

Case 1

28 year old woman presents with erythema of her left leg over past 48 hours. There is no purulent drainage, exudate or abscess. No evidence of joint or bursa involvement.



T 37.0 BP 132/70
P 78

What is the appropriate management of this patient?

A. Clindamycin 300 mg PO tid

B. Cephalexin 500 mg QID, monitor clinically with addition of TMP/SMX if no response

C. Cephalexin 500 mg QID *and* TMP/ SMX 2 DS tab PO bid

Nonpurulent Cellulitis: β-hemolytic strep vs. *S. aureus*?

- Empiric Rx for β-hemolytic strep recommended
  - Prospective study[1], 248 hospitalized pts
    - 73% due to β-hemolytic strep (diagnosis by serologies for ASO and anti-DNAse-B, blood cultures); 27% with no identified cause.
    - Overall 96% response rate to β-lactam antibiotic.
  - Retrospective study[2]
    - ↑ treatment failures with TMP-SMX vs. β-lactam or clindamycin
- Empiric Rx for MRSA if fails to respond to β-lactam
  - Consider in patients with systemic toxicity

[1]Jeng et al Medicine 2010; 89:217-26

[2]Elliott et al Pediatrics 2009; 123:e959-66

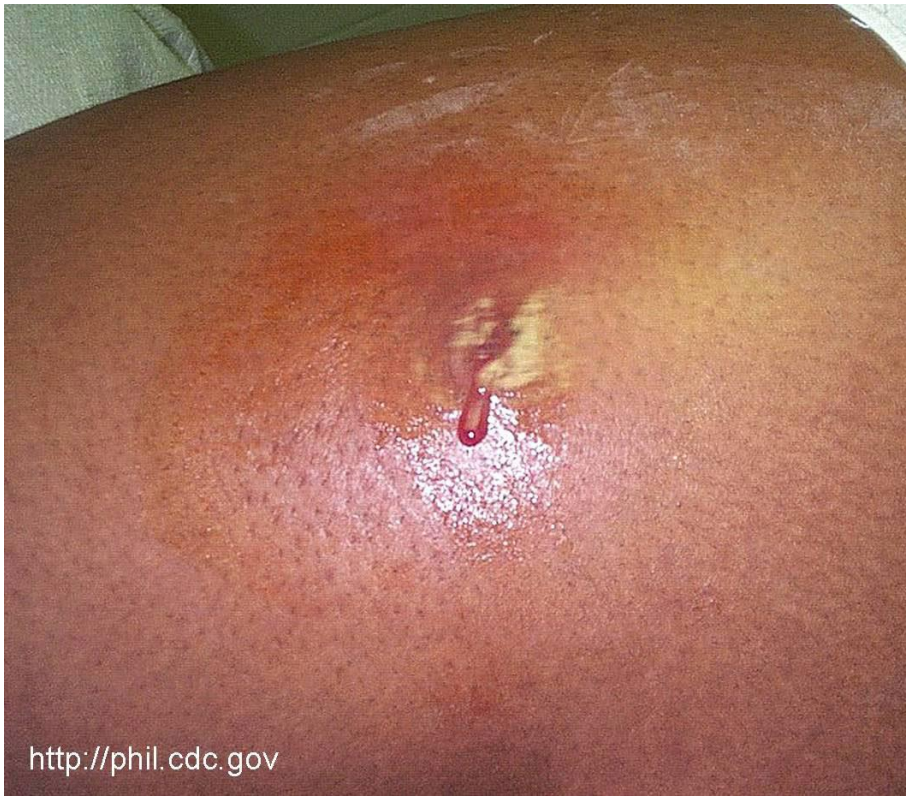
Outpatient nonpurulent cellulitis: Empiric Rx for β-hemolytic streptococci +/- MRSA

Drug	Adult Dose
Cephalexin	500 QID
Dicloxacillin	500 QID
Clindamycin*	300-450 TID
Linezolid*	600 BID
*Also have activity against CA-MRSA	

Case 2

32 y/o M with 3 days of an enlarging, painful lesion on his L thigh that he attributes to a “spider bite”

T 36.9 BP 118/70 P 82



What is the appropriate management of this patient?

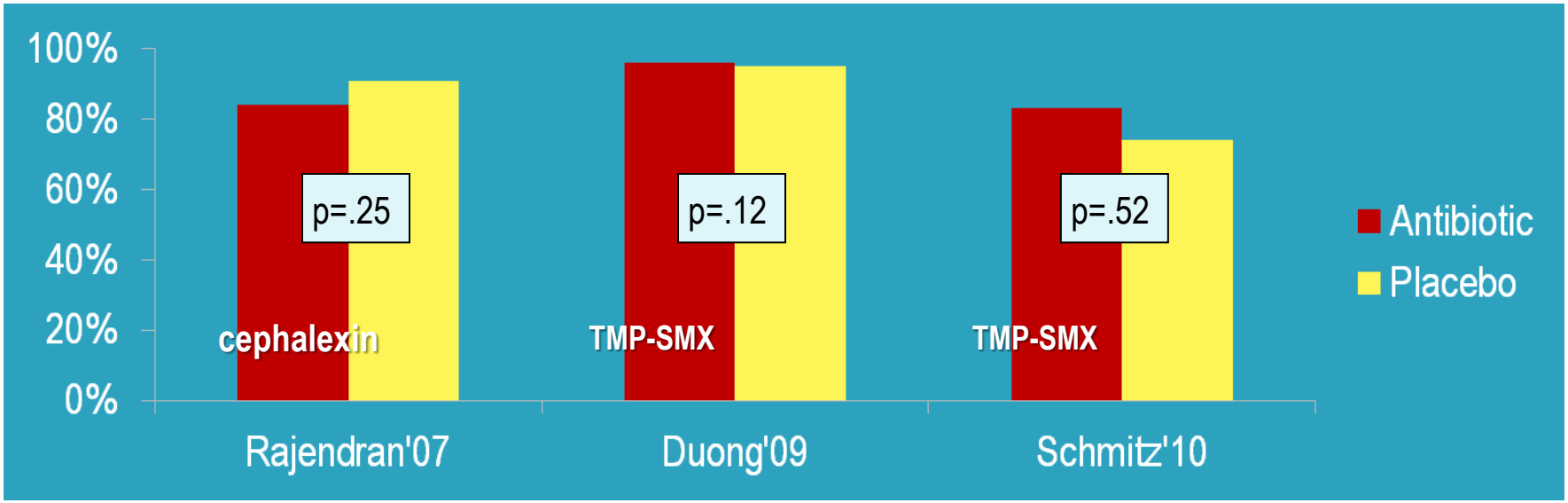
A. Incision and drainage alone

B. Incision and drainage plus oral anti-MRSA antimicrobial agent

C. Oral anti-MRSA antimicrobial agent

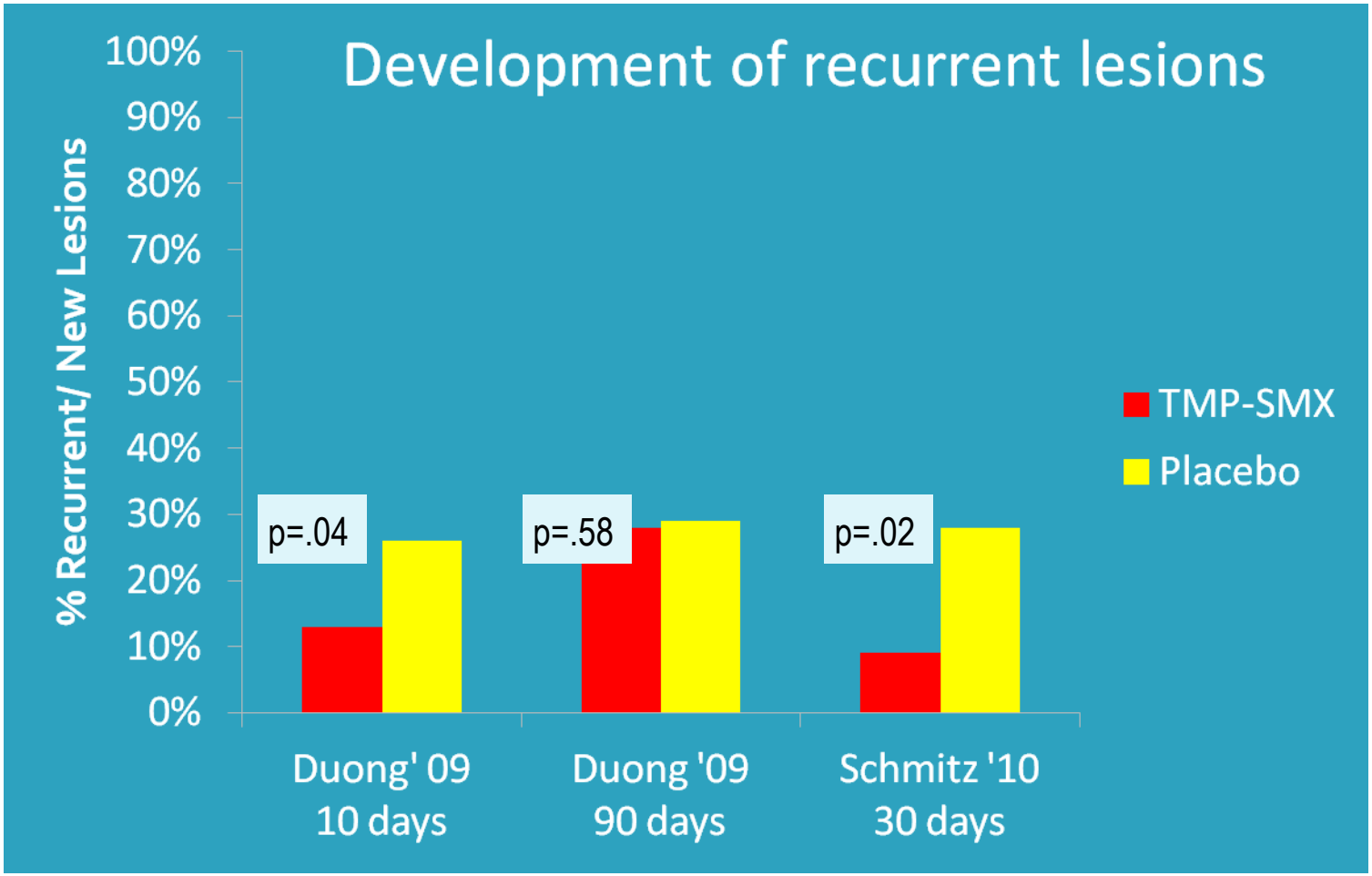
Abscesses

- Incision and drainage is the primary treatment
  - For simple abscesses or boils, I&D alone likely adequate
- Do antibiotics provide additional benefit?
  - Multiple, observational studies: high cure rates with or without abx
  - 3 RCTs of uncomplicated skin abscesses; 2 large NIH trials ongoing



Rajendran AAC 2007; 51:4044-8; Duong Ann Emerg Med 2009;55:401-7; Schmitz Ann Emerg Med 2010; 56:283-7

Is clinical cure the only important endpoint?



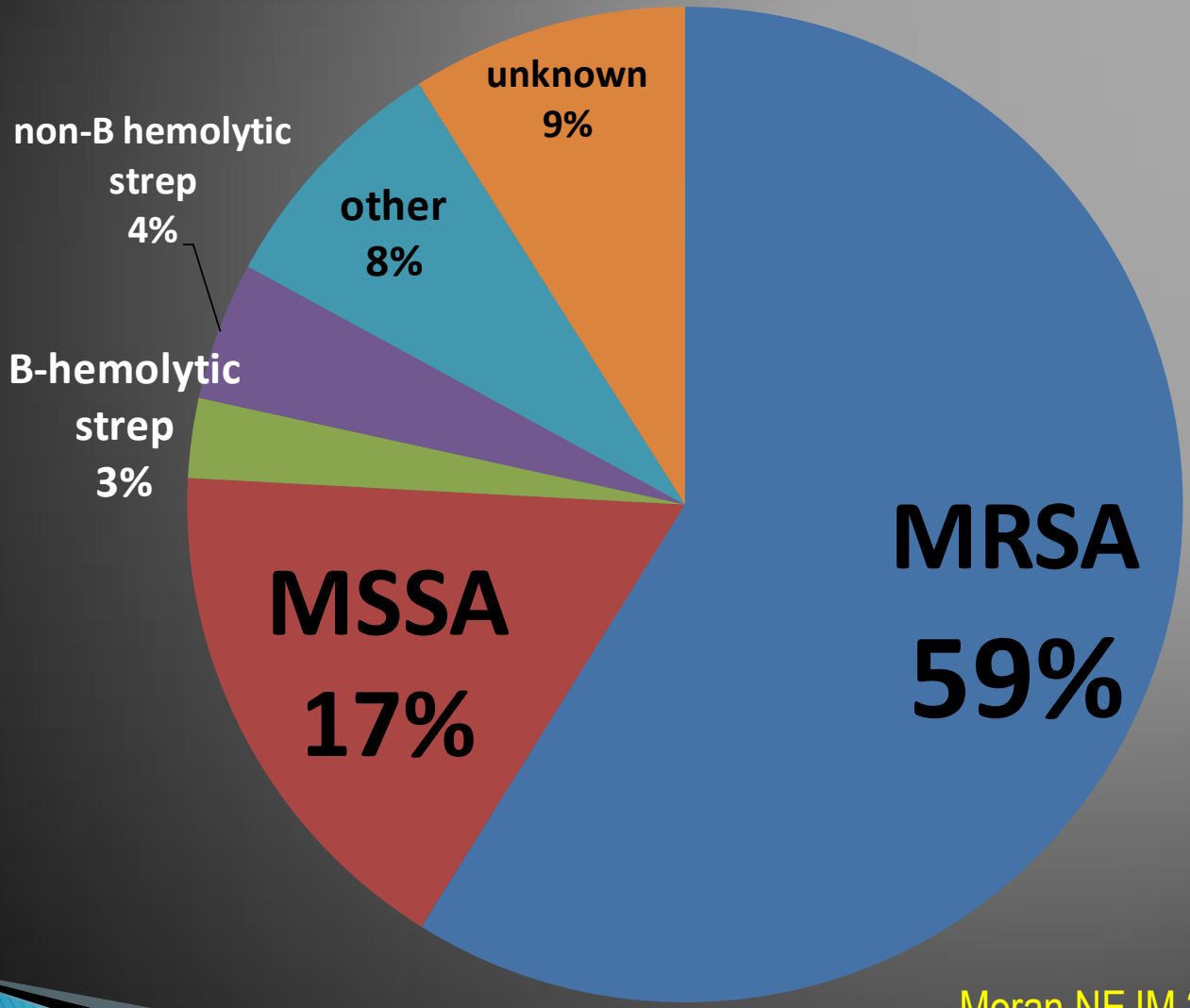
Duong Ann Em Med 2009;55:401-7; Schmitz Ann Em Med 2010; 56:283-7; Talan Ann Em Med 2010; 55:412-14;

Spellburg Ann Em Med 2011; 57:183-4.

Antibiotic therapy is recommended for abscesses associated with:

- Severe, extensive disease, rapidly progressive with associated cellulitis or septic phlebitis
- Signs & sx of systemic illness
- Associated comorbidities, immunosuppressed
- Extremes of age
- Difficult to drain area (e.g. face, hand, genitalia)
- Failure of prior I&D

Microbiology of Purulent SSTIs



Moran NEJM 2006; 355: 666-74

Purulent Cellulitis: *S. aureus* >>> β-hemolytic strep

- Cellulitis associated with purulent drainage or exudate without a drainable abscess
  - Empiric Rx for CA-MRSA is recommended
  - Empiric Rx for β-hemolytic strep unlikely needed
  - Duration of therapy: 5-10 days, individualize based on clinical response

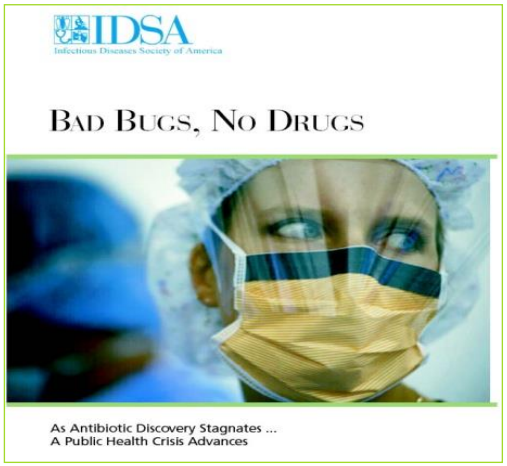
Outpatient purulent cellulitis: Empiric Rx for CA-MRSA

Drug	Adult Dose
TMP-SMX	1-2 DS BID
Doxycycline Minocycline	100 BID
Clindamycin	300-450 TID
Linezolid	600 BID

Antibiotics for MRSA

- Vancomycin
- Linezolid
- Daptomycin
- Tigecycline
- Quinupristin/Dalfopristin
- Trimethoprim/Sulfamethoxazole
- Clindamycin
- Ceftaroline
- Telavancin

IDSA Policy Initiatives



2004
BAD BUGS, NO DRUGS

2010
BAD BUGS, NEED DRUGS
The 10 x '20 initiative

Combating Antimicrobial Resistance:
Policy Recommendations to Save Lives

Infectious Diseases Society of America (IDSA)*

2011
IDSA PUBLIC POLICY
CID 52 (Suppl 5):S397, 2011

ABOUT THE GAIN ACT OF 2012 09/09/2014

Recognizing the growing problem of antibiotic resistance and lack of new antibiotics reaching patients, Congress introduced the Generating Antibiotics Incentives Now (GAIN) Act which was signed into law by President Barack Obama as part of the Food and Drug Administration Safety and Innovation Act on July 9, 2012.

GAIN includes several incentives for antibiotic research and development.

Under the GAIN Act, antibiotics intended to treat serious or life-threatening infections, including those caused by drug-resistant pathogens, may be designated as "Qualified Infectious Disease Products" or QIDPs. provision."

QIDPs are eligible for two U.S. Food and Drug Administration programs:

- fast track status (an expedited development pathway) and
- priority review (shortened review time for marketing applications)
- Upon approval, QIDPs receive five-years of data exclusivity where they are free from generic competition

2014 Approvals

- NEW AGENT: Oritavancin (Orbactiv)
  - August 2014
- NEW AGENT: Dalbavancin (Dalvance)
  - May 2014
- NEW AGENT: Tedizolid (Sivextro)
  - June 2014

Vancomycin

- Glycopeptide
- Vancomycin should be dosed according to actual body weight (15-20 mg/kg/dose every 8-12h), not to exceed 2 gram per dose
- Target trough of 15-20 μg/mL in patients with serious infections
- Side Effects: "Red Man Syndrome", nephrotoxicity, ototoxicity
- 10-14 day length of therapy unless endocarditis or osteomyelitis (6 weeks)
- Bacteriostatic agent

Therapeutic monitoring of vancomycin in adult patients: A consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists

Michael Rybak, Ben Lomaestro, John C. Rotschafer, Robert Moellering Jr., William Craig, Marianne Billeter, Joseph R. Dalovisio, and Donald P. Levine

Am J Health-Syst Pharm. 2009; 66:82-98

Linezolid (Zyvox®)

- Oxazolidinone
- Dose 600mg IV or orally q12h with no renal or hepatic adjustment
- Penetrates lung tissue better than vancomycin
- Side effects: thrombocytopenia (higher incidence seen in patients with end-stage renal disease), myelosuppression
- Should not give to patients on SSRIs (multiple reports of serotonin syndrome)
- Bacteriostatic against enterococci and staphylococci
- Bactericidal against a majority of streptococci

CID 2006; 42:66-72
Lexi-Comp

Daptomycin (Cubicin®)

- Lipopeptide
- Dose:
  - 4 mg/kg for skin/skin structure infections
  - 6 mg/kg for bacteremia or endocarditis; renal adjustment needed if CrCl <30 ml/min
- Side Effects: anemia, myopathies
- Monitor CPK levels weekly
- Does not penetrate the lungs and is inactivated by pulmonary surfactants – cannot be used to treat pneumonia
- Bactericidal

Lexi-Comp

Tigecycline (Tygacil®)

- Glycylcycline
- Dose: 100mg IV X1 then 50mg q12h;
  - no renal adjustment needed, but does need to be adjusted for severe hepatic impairment
- Side Effects: nausea/vomiting, diarrhea; similar side effects of the tetracyclines
- Not a good choice for monotherapy in patients with intestinal perforation
- Also has broad-spectrum gram-negative activity, but does not cover *Pseudomonas, Proteus, or Providencia*
- Bacteriostatic
- Black-box warning

CID 2005; 41: S303-314

Quinupristin and Dalfopristin (Synercid®)

- Streptogammin
- Dose: IV: 7.5 mg/kg every 12 hours for at least 7 days
- Complicated skin and skin structure infections caused by methicillin-susceptible *Staphylococcus aureus* or *Streptococcus pyogenes*

TMP/SMX (Bactrim®; Bactrim DS®; Septra DS®; Sulfatrim®)

- Sulfonamide
- Dose:
  - Oral: 1–2 double-strength tablets (sulfamethoxazole 800 mg; trimethoprim 160 mg) every 12–24 hours
  - IV: 8–20 mg TMP/kg/day divided every 6–12 hours
- Many uses…
  - **Skin/soft tissue infection due to community-acquired MRSA (unlabeled use):** Oral: 1–2 double-strength tablets every 12 hours for 5–10 days **Note:** If beta-hemolytic *Streptococcus* spp are also suspected, a beta-lactam antibiotic should be added to the regimen
- Renal impairment: Use with caution in patients with renal impairment; dosage adjustment recommended

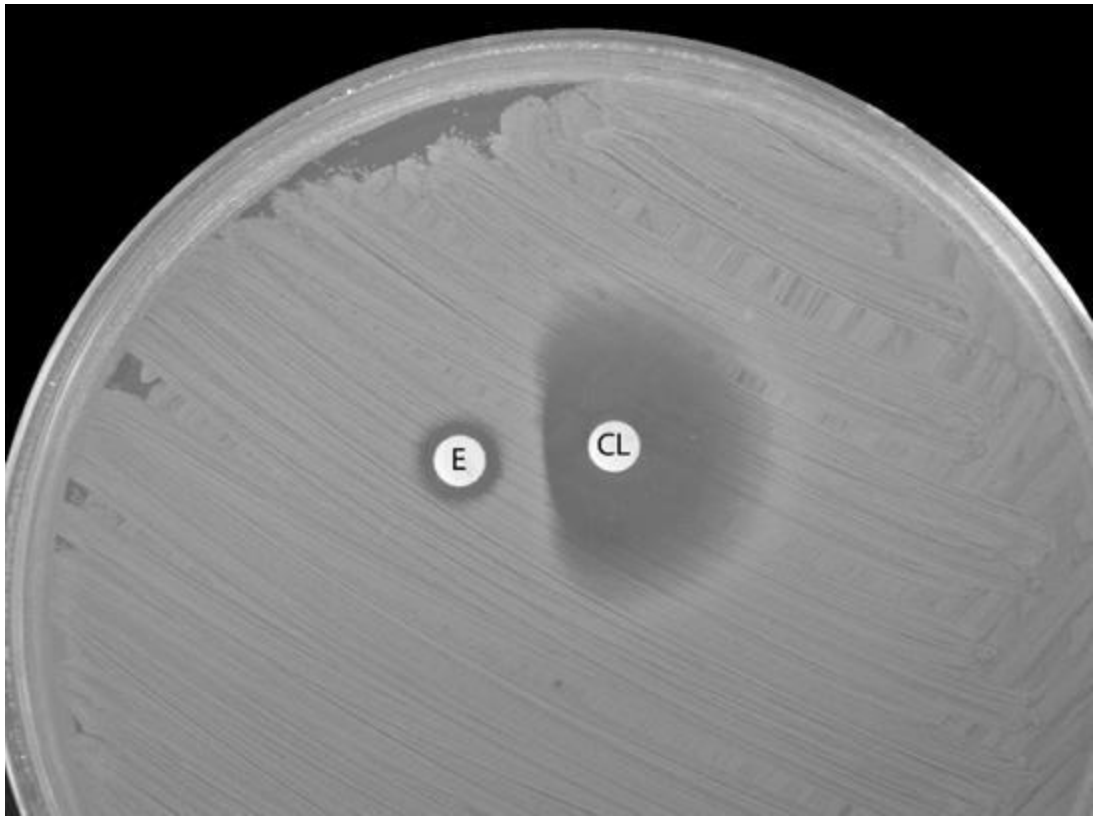
Clindamycin (Cleocin®)

- Lincosamide
- Dose: Oral: 150–450 mg every 6 hours; 600–900 mg IV every 6–8 hours
- Side Effects: abdominal pain, antibiotic-associated colitis, *Clostridium difficile* associated diarrhea
- Caused by *Streptococcus pyogenes*, *S. aureus {+/- MRSA}*, and anaerobes
- Bacteriostatic

Inducible Clindamycin Resistance

- Macrolides can induce Clindamycin resistance
- D-test can be done to confirm and visualize resistance
- Place an erythromycin and clindamycin disk on an agar plate
- If exposure to erythromycin triggers inducible clindamycin resistance, the normally circular zone of inhibition around the clindamycin disk will appear flattened, creating a “D” shape

Inducible Clindamycin Resistance



Antimicrob Agents Chemother 2005; 49(3): 1222-1224

Inducible Clindamycin Resistance

- If a sensitivity report shows a CA-MRSA is erythromycin resistant and clindamycin sensitive, clindamycin might not work
- Local susceptibility patterns should be taken into account when making treatment decisions
- 20-26% of CA-MRSA has inducible clindamycin resistance

Ceftaroline (Teflaro®)

- 5th generation cephalosporin
- Dose: 600 mg every 12 hours by IV infusion administered over 1 hour in adults ≥ 18 years of age (renal adjustment necessary)
- Treatment of community acquired bacterial pneumonia and acute skin and soft tissue infections
- The most common adverse reactions occurring in >2 % of patients are diarrhea, nausea, and rash
- Bacteriocidal

Telavancin (Vibativ®)

- Lipogycopeptide
- Dose: I.V.: 10 mg/kg every 24 hours for 1-3 weeks (renal adjustment necessary)
- Complicated SSTI/Hospital acquired and Ventilator Associated Pneumonia
- Caution is warranted when prescribing VIBATIV to patients taking drugs known to prolong the QT interval
- Most common adverse reaction (≥10% of patients treated with in the HABP/VABP trials is diarrhea

Telavancin (Vibativ®)

- In the cSSSI trials, the most common adverse reactions (≥10%) include: taste disturbance, nausea, vomiting, and foamy urine
- Additional adverse reactions with a > 10%: Insomnia, psychiatric disturbances, headache, increased serum creatinine
- Increased mortality shown in clinical trials with use in patients with CrCl ≤ 50 ml/min compared to vancomycin

Oritavancin (Orbactiv®)

- Semi-synthetic lipoglycopeptide antibiotic
- Dose: Single dose regimen; 1200-mg IV, infused over 3 hours
- Acute bacterial skin and skin structure infections caused by, or strongly suspected to be caused by, susceptible Gram-positive microorganisms (MSSA, MRSA, and Enterococcus *faecalis* (vancomycin-susceptible isolates only

Oritavancin (Orbactiv®)

- Can artificially prolong activated clotting time (ACT), aPTT (for about 48 hours), PT (about 24 hours), and INR (about 24 hours)
- 1200mg dose is approximately $2800.00
- Anticipated availability of oritavancin on market is currently undetermined

Dalbavancin (Dalvance®)

- Lipoglycopeptide related to teicoplanin
- Covers VISA, VRSA, and linezolid-resistant *S. aureus*
- Dosing: 1000mg IV x 1 dose then 500mg IV x 1 dose 7 days later
  - Requires renal adjustment CrCl < 30 x 750mg x 1 then 375mg x 1
- Studied in skin/skin structure and catheter-related bloodstream infections
- Side Effects: nausea, diarrhea, constipation, oral candidiasis, Red-man syndrome with infusion
- Dalbavancin was shown to be non-inferior to linezolid for the treatment of skin and skin structure infections
- Cost: 500 mg vial = $1490

Tedizolid (Sivextro®)

- Oxazolidinone
- Indications: Acute bacterial skin and skin structure infections caused by Gram-positive microorganisms MRSA and VRE
- Dose: 200mg IV infusion over 1 hour or 200mg by mouth once daily for 6 days
- Side Effects: nausea, headache, diarrhea, vomiting
- Exclude patients with neutropenia.
- Monitor those taking MAO-I's and other serotonergic agents

Tedizolid (Sivextro®) –cont

Product	Cost	Cost of total course of therapy
Tedizolid phosphate 200mg tablet	$235.00	$1410.00
Tedizolid phosphate 200mg IV	$235.00	$1410.00
Linezolid 600mg tablet	$119.37	$2387.40
Linezolid 600mg IV	$130.79	$2615.80

Case 3

The patient in case 2 returns 4 weeks later with another abscess on his opposite thigh. He notes that after I & D of his first abscess, he didn't keep his wound covered and occasionally touched the site to "make sure it was healing."

The site of his old abscess is clean with a well-healed scar. He undergoes I&D and receives 1 week of TMP-SMX.

What is the appropriate management of this patient?

A. Emphasize personal hygiene measures
B. Decolonize with mupirocin and chlorhexidine showers
C. Decolonize with TMP-SMX and rifampin
D. A and B
E. A, B, and C

Evidence Grading System

Strength of recommendation

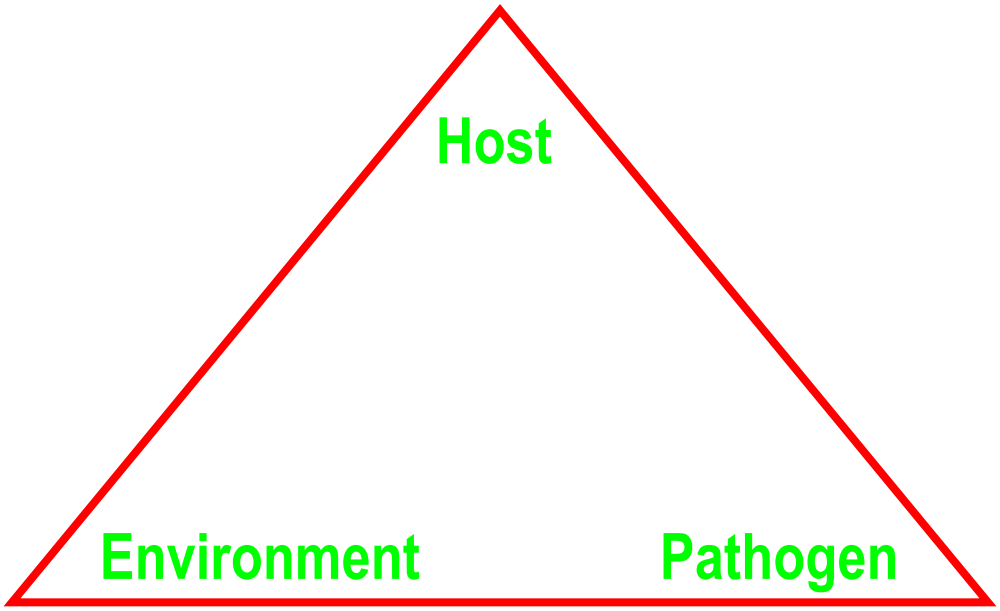
A	Good evidence to support a recommendation for or against use
B	Moderate evidence to support a recommendation for or against use
C	Poor evidence to support a recommendation

Quality of evidence

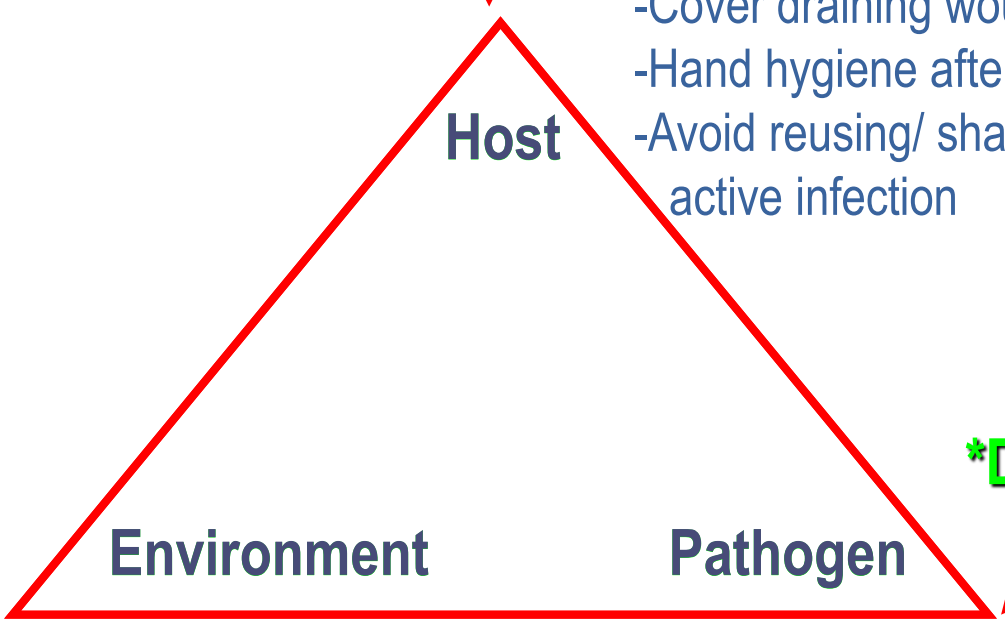
I	Evidence from ≥ 1 properly randomized, controlled trial
II	Evidence from ≥ 1 well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from > 1 center); from multiple time-series; or from dramatic results from uncontrolled experiments
III	Evidence from opinions of respected authorities; based on clinical experience, descriptive studies, or reports of expert committees.

Source: The periodic health examination. Canadian Task Force on the Periodic Health Examination. Health Canada, 1979. Adapted and reproduced with the permission of the Minister of Public Works and Government Services, Canada, 2009

What is the Management of Recurrent Skin and Soft Tissue Infections?



What is the Management of Recurrent Skin and Soft Tissue Infections?



Personal Hygiene/ Wound Care (AIII)

-Cover draining wounds
-Hand hygiene after touching infected skin
-Avoid reusing/ sharing personal items if active infection

***Decolonization (CIII)**

-If above measures fail
-If ongoing household transmission

Environmental Hygiene (CIII)

-Clean high-touch surfaces

Recurrent MRSA SSTI: Decolonization Regimens

- Mupirocin twice daily x 5-10 days **(CIII)**
  - ↓ recurrent MSSA SSTI in small RCT[1]
  - RCT military recruits:↓ in CA-MRSA nasal colonization but <u>not</u> 1st time SSTI[2]
- Mupirocin twice daily x 5-10 days <u>AND</u> topical skin antiseptic (e.g. chlorhexidine) x 5-14 days **(CIII)**
  - RCT military recruits: CHG wipes alone not ↓ SSTI rates[3], transient effect on colonization
  - Consider dilute bleach baths: ¼ cup per ¼ tub (13 gallons) of water for 15 min, 2x/week for 3 mnths

[1]Raz Arch Intern Med 1996; 156:1109-12; [2]Ellis MW AAC 2007; 51: 3591-8 [3]Whitman ICHE 2010; 12: 1207-15

Oral Antibiotics for Decolonization?

- Not routinely recommended for decolonization (AIII). An oral agent in combination with rifampin (if susceptible) may be considered if infections recur despite other measures (CIII).
  - Cochrane review[1]: No benefit of oral abx in MRSA eradication among patients in healthcare settings
  - Systematic review[2]: Rifampin + staph abx vs. staph abx alone
    - Rifampin combo superior in ↓ *S. aureus* colonization
    - No studies evaluated impact on infection rates
  - Watch out for drug interactions, side effects, resistance

[1]Cochrane Review 2003; 4CD003340 [2]Falagas ME AJIC 2007; 35: 106-14


CENTERS FOR DISEASE CONTROL
THE DRUG-RESISTANT STAPH INFECTION KNOWN AS MRSA...
...IS SPREADING LIKE WILDFIRE...
KILLING THOUSANDS UPON THOUSANDS!...
We urge the public not to panic.
MARGULIES
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Questions?

Breast Cancer Update 2014

Helen Mabry, M.D.

Learning Objectives:

Discuss breast cancer treatment overview.

Discuss breast cancer risk factors.

Discuss possibilities for breast cancer prevention.

ACLS/BLS Re-Certification

Brent C. DeVries, D.O.
&
David Degnan, Fire Chief

Learning Objectives:

Apply important concepts including BLS and cardiopulmonary resuscitation.

Apply the ACLS algorithms.

Apply effective resuscitation, team dynamics and immediate post-cardiac arrest care.

NOTES

NOTES